Review of interim funded service: Artificial intervertebral disc replacement - lumbar

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The Secretary
Medical Services Advisory Committee
Department of Health and Ageing
Mail Drop 853
GPO Box 9848
Canberra ACT 2601

Enquiries about the content of the report should be directed to the above address.

The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC's advice does not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared by MSAC with the assistance of Dr Prema Thavaneswaran and Dr Meegan Vandepeer from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) and Ms Bonny Parkinson and Dr Stephen Goodall from the Centre for Health Economics Research and Evaluation (CHERE).

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The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

Assessment of lumbar artificial intervertebral disc replacement

Purpose of application

This assessment updates a previous assessment (Application 1090) of artificial intervertebral disc replacement lumbar that was conducted on behalf on MSAC in 2006, and resulted in MSAC recommending interim funding for single level AIDR in patients with single level intra lumbar disc disease in the absence of osteoporosis and prior fusion at the same level, who have failed consecutive therapy. The interim listing was subject to further MSAC review in three years. The purpose of this assessment was to determine whether there is sufficient evidence, in relation to safety, effectiveness and cost-effectiveness, to have lumbar artificial intervertebral disc replacement (AIDR) listed on the Medicare Benefits Schedule (MBS).

Lumbar AIDR is designed to simulate the mobile load-bearing properties of the natural intervertebral discs. There are two types of artificial intervertebral discs: one type replaces only the nucleus pulposus, and the other replaces the entire intervertebral disc.

Prosthetic discs for total disc arthroplasty generally consist of: (a) two metallic endplates which articulate with each other (metal on metal), or (b) two metallic endplates which sandwich a polymer or plastic core (metal on polymer). The overall design and material composition, however, vary significantly between commercially available prosthetic discs, and new designs appear regularly in this rapidly growing field. Most current prosthetic discs use materials which have been used for many years in other well-established medical devices, eg hip and knee replacements.

All lumbar AIDR procedures are performed under general anaesthetic. Patient positioning and intraoperative real time fluoroscopy, depending on the device used, are critical to the exposure and successful insertion of the arthroplasty device. For lumbar disc arthroplasty a transperitoneal or retroperitoneal approach is required. Because most lumbar fusion procedures are performed posteriorly, many spinal surgeons require the assistance of an 'access surgeon' to minimise rare but serious approach-related complications when undertaking anterior AIDR. Important structures that need to be mobilised include the aorta, iliac vessels, sympathetic plexus, and intraperitoneal structures including the bowel and ureters. An access surgeon such as a general or vascular surgeon is often far more familiar with the approach. Whether an access surgeon is used is dependent on (a) spinal surgeon training and (b) the availability of access surgeons.

A complete discectomy is required prior to removing and shaping variable amounts of vertebral endplate. Small instruments and drills are used under magnification to remove disc material and osteophytes compressing nerve roots or the spinal cord. Finally, implanting the device requires precise sizing, placement and choice of prosthesis to achieve optimal performance. This requires a mixture of freehand surgical skill, fluoroscopy, milling guides and instruments. Implants, rather than being cemented or screwed in, rely on a precise press or friction fit bone implant interface.

The primary indications for AIDR considered in this assessment concern individuals suffering from significant axial back pain and/or radicular (nerve root) pain, secondary to disc degeneration or prolapse, who have failed nonoperative treatment (eg rest, modification of activities, muscle strengthening, weight control, aerobic training, the passage of time, and analgesic medications including anti-inflammatory medications and epidural steroid).

A team from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) and the Centre for Health Economics Research and Evaluation (CHERE) was engaged to conduct a systematic review of the literature and an economic evaluation of lumbar AIDR.

Current arrangements for public reimbursement

Lumbar AIDR is currently listed on the MBS as an interim funded item; details of the MBS listing are provided in the table below (Table 1 in the report).

Current MBS item numbers related to lumbar AIDR procedures

MBS item number	Description	Fee	Benefit
48691	LUMBAR ARTIFICIAL INTERVERTEBRAL TOTAL DISC REPLACEMENT including removal of disc, 1 level, in patients with single-level intralumbar disc disease in the absence of vertebral osteoporosis and prior spinal fusion at the same lumbar level who have failed conservative therapy, with fluoroscopy	$1,695.20	75% = $1,271.40 85% = $1,626.10
48692	LUMBAR ARTIFICIAL INTERVERTEBRAL TOTAL DISC REPLACEMENT including removal of disc, 1 level, in patients with single-level intralumbar disc disease in the absence of vertebral osteoporosis and prior spinal fusion at the same lumbar level who have failed conservative therapy, with fluoroscopy (where an assisting surgeon performs the approach) - principal surgeon	$1,142.60	75% = $856.95 85% = $1,073.50
48693	LUMBAR ARTIFICIAL INTERVERTEBRAL TOTAL DISC REPLACEMENT including removal of disc, 1 level, in patients with single-level intralumbar disc disease in the absence of vertebral osteoporosis and prior spinal fusion at the same lumbar level who have failed conservative therapy (where an assisting surgeon performs the approach) - assisting surgeon	$552.60	75% = $414.45 85% = $483.50

Clinical need

There is considerable uncertainty regarding the prevalence and incidence of axial back pain and/or radicular (nerve root) pain secondary to disc degeneration or prolapse. In 2004-05 'back pain and disc problems' was the most commonly reported long-term condition after long- and short-sightedness, reported in 16 per cent of males and 14.7 per cent of females. Although the prevalence increases with age, back pain is also a common

long-term condition in younger age groups, affecting 15.3 per cent of people aged 25-34 years. 'Back problems and disc disorders'were the most common work-related conditions (36%). However, it is unclear what proportion of these people suffer from discogenic back pain and would therefore be eligible for either artificial disc replacement or spinal fusion.

MBS claims data from July 2005 through to August 2010 has shown that a total of 2,748 procedures were performed in the lumbar region during this time. Of these procedures, a total of 219 were lumbar AIDR procedures, 2,418 were spinal fusion procedures and 111 were a combination of AIDR and spinal fusion techniques. A further 127 AIDR only procedures were also performed however the location of the surgery is unknown due to the MBS item claimed for initiation of anaesthesia[1], although it is likely that these were also performed in the lumbar region.

Comparator

The comparator procedure is lumbar spinal fusion, where a bone graft is used to stop the motion at a painful vertebral segment. There are two main approaches to spinal fusion, *posterolateral fusion* (PLF) and *interbody fusion*, which may be used in conjunction.

Posterolateral fusion involves placing the bone graft between the transverse processes in the back of the spine. The vertebrae are then fixed in place with screws and/or wire through the pedicles of each vertebra attaching to a metal rod on each side of the vertebrae.

Interbody fusion involves placing the bone graft between the vertebrae in the area usually occupied by the intervertebral disc. In preparation for spinal fusion, the disc nucleus and part of the annulus are removed, and endplates cleaned prior to placement of the graft. This allows the fusion to occur between the endplates of contiguous vertebrae. The graft can be placed in between the vertebral bodies in an interbody position using an anterior approach via an incision in the abdomen (anterior lumbar interbody fusion, ALIF), or a posterior approach (posterior lumbar interbody fusion, PLIF). When both an ALIF and a posterior lateral bone grafting and posterior instrumentation are performed it is commonly referred to as 360 degree or circumferential spinal fusion.

In Australia, most surgeons choose a posterior rather than anterior approach for lumbar spinal fusion.

Scientific basis of comparison

A total of 60 studies, including four systematic reviews, five health technology assessments, four randomised controlled trials (RCTs), one nonrandomised comparative study, and 38 case series were eligible for appraisal and inclusion in this assessment.

Forty-three studies were identified for inclusion in the assessment of the safety of lumbar AIDR. This included five comparative studies and 38 case series.

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[1] Cervical procedures are indicated by MBS item number 20600 and lumbar procedures are indicated by MBS item number 20630. Many procedures involved claims for extensive spine/spinal cord procedures (20670) and therefore cannot be identified as occurring in a specific spinal region.

A total of 13 comparative studies were identified and included to inform on the comparative effectiveness of lumbar AIDR, including a total of four RCTs (comprising 12 studies) that compared lumbar AIDR to ALIF, circumferential fusion, or PLF/PLIF, as well as one nonrandomised comparative study that compared lumbar AIDR to ALIF.

Comparative safety

Key results

For the majority of adverse events reported, there were no obvious differences in incidence rates between the lumbar AIDR and lumbar fusion groups, with two studies reporting no statistical differences in the rate of overall complications between the two groups. Wound infection was the most commonly reported adverse event, and demonstrated an incidence rate of 3.2 per cent in the lumbar AIDR population, and 5.1 per cent in the lumbar fusion population. Prosthesis-related adverse events were those relating to movement of the device, including collapse or subsidence (3%), and displacement (0.78%). Fusion-related adverse events included nonunion/pseudarthrosis (6.4%) and bone graft donor-site pain (11.1%). The rate of adjacent segment problems appeared higher following lumbar fusion (8.3%) compared with lumbar AIDR (1.3%).

Major adverse events such as major vessel injury, neurologic damage and nerve root injury were rare in both the lumbar AIDR and fusion groups. There was one reported death following lumbar AIDR which was narcotic-related, while no deaths were reported following lumbar fusion.

Key uncertainties

Overall, safety data was not reported as comprehensively as effectiveness outcomes in the included comparative studies, with only two studies reporting statistical comparisons between lumbar AIDR and lumbar fusion procedures. This may represent study bias when the primary concern of the authors was to present data on effectiveness, rather than safety.

Overall conclusion with respect to comparative safety

Overall, the safety of lumbar AIDR is comparable to that of lumbar fusion. It appears that the lumbar AIDR procedure is relatively safe, and is not associated with serious adverse events.

Comparative effectiveness

Key results

Clinical outcomes were the focus of the majority of comparative studies; however, a number of studies also reported radiographic outcomes following lumbar AIDR and lumbar fusion procedures.

All of the included comparative studies utilised the Oswestry Disability Index (ODI), one of the principal condition specific measures used in the management of spinal disorders, and the gold standard for assessing the extent to which a patient's functional level is limited by low back pain. Three studies reported that patients in the lumbar AIDR group showed statistically greater improvements in ODI scores than lumbar fusion patients at various time points up to 1-year follow-up; however, none of the studies reported significant differences between the groups at 2- or 5-year follow-up. Similarly, two studies reported that at 2-year follow-up overall clinical success was significantly higher

in the lumbar AIDR group compared with the lumbar fusion group, while the rate of reoperation was similar in both groups.

In two studies, patient satisfaction at 2-year follow-up was significantly higher in lumbar AIDR patients compared with lumbar fusion patients, with up to 81 per cent of AIDR patients saying they would have the procedure again, compared with 69 per cent of fusion patients. This may have reflected the fact that lumbar AIDR patients experienced significantly less pain and required less narcotic medication, reported better sexual function, and returned to work at higher rates, when compared with lumbar fusion patients up to 2 years after surgery.

Radiographic outcomes were reported in several studies; however, outcomes were reported differently across studies, and no statistical comparisons between the lumbar AIDR and lumbar fusion groups were reported, making it difficult to draw firm conclusions.

Key uncertainties

The eligibility criteria used to recruit patients was similar across studies, and most studies included patients who had undergone previous spinal surgery, which may impact on patient outcomes following lumbar AIDR or lumbar fusion procedures. Subgroup analyses conducted in one RCT showed that the rate of adverse events (as well as a variety of clinical outcomes including ODI scores, pain scores, rate of reoperation, work status and patient satisfaction with the procedure) was not significantly different in lumbar AIDR and lumbar fusion patients who had undergone previous lumbar decompressive surgery (including microdiscectomy, laminectomy or minimal medial facetectomy), compared with those who had not undergone previous surgery.

Most studies utilised well-known, validated instruments for the assessment of patient outcomes; however, patients and investigators were not blinded to the treatment, which may have led to bias in the reporting of results. A further limitation of the studies included in this assessment was the length of follow-up reported. Certain adverse events and problems associated with the durability of the prosthesis may only become apparent after many years of follow-up. However, the majority of studies in this assessment reported short- to medium-term (2-5 year) follow-up of patients. In addition, a variety of different prostheses and lumbar fusion techniques were used across studies. Importantly, two of the four included RCTs compared lumbar AIDR to circumferential fusion; however, this approach represents only 1 per cent of all spinal fusion procedures performed in Australia.

While the number of patients who remained on narcotics was comparable following lumbar AIDR and lumbar fusion procedures, the clinical expert opinion of the Advisory Panel suggests that this proportion is significantly higher than that observed in clinical practice in Australia.

Overall conclusion with respect to comparative effectiveness

Overall, in the short to medium term the effectiveness of lumbar AIDR, in terms of ODI scores, success of the procedure, pain, patient satisfaction, workstatus, quality of life and sexual function, appears to be comparable to lumbar fusion procedures.

Economic evaluation

The economic evaluation adopted a cost-effectiveness analysis and a cost-utility analysis framework. For AIDR compared to fusion the incremental costs, incremental costs per patient discontinuing narcotic medication at 2 years, incremental costs per additional overall clinical success at 2 years and incremental costs per additional ODI success at 2 years were presented. For AIDR compared to PLF/PLIF the incremental cost per quality-adjusted life year (QALY) gained was presented. This mixed approach was undertaken due to uncertainty about the outcome of most clinical relevance and whether the results were statistically significant.

A Markov model was developed to synthesise data from a variety of sources. Following the decision to treat the patient surgically, patients receive either lumbar AIDR or one of five lumbar fusion approaches. If the initial surgery is considered a success, patients enter the 'successful surgery' health state. If surgery is considered a failure, patients enter the 'failed surgery' health state in which patients may require a re-operation. If re-operation is required patients enter the 'successful surgery post re-operation' health state. Other adverse events and death from complications or other causes are not considered. It is assumed that only one re-operation is conducted, and that AIDR devices and all types of bone grafts are similar in effectiveness.

Estimates of effectiveness, anaesthesia time and time in hospital were obtained from published randomised controlled trials. MBS item numbers were determined by the Advisory Panel and resource use was obtained by analysis of MBS claims data provided by the Department of Health and Ageing. Unit costs were obtained from standard sources. MBS average co-payment data were provided by the Department of Health and Ageing.

Key uncertainties that drive the estimation of costs were the proportion of patients receiving bone morphogenetic proteins (BMP), which was based on a previous MSAC report (1099), the length of hospitalisation, which was based on the published randomised controlled trials, and the AIDR device cost.

The incremental costs associated with each procedure demonstrate that compared to PLIF, combination and circumferential fusion, AIDR is cost saving. Compared to ALIF, AIDR is marginally more expensive. Overall, compared to the average fusion cost, AIDR represents a cost saving of $1,600 per patient.

AIDR was both less costly and more effective than lumbar fusion overall for patients discontinuing narcotic medication and in terms of overall success. In terms of ODI success, AIDR was both less costly but less effective than lumbar fusion overall. The incremental cost per additional patient achieving ODI success was estimated to be $126,191 with lumbar fusion compared to AIDR.

The results varied considerably by fusion approach. AIDR was more costly but achieved a higher rate of patients discontinuing narcotic medication, overall success and ODI success than ALIF. The incremental cost per additional patient discontinuing narcotic medication, achieving overall success, and achieving ODI success with AIDR compared to ALIF was estimated to be $46,439, $20,433 and $34,883, respectively. AIDR was less effective in terms of ODI success compared to PLIF and PLF. PLF was also less costly and thus PLF was considered to dominate AIDR. PLIF was more costly and the incremental cost per additional patient achieving ODI success with PLIF was estimated

to be $35,373. AIDR was both less costly and more effective than circumferential fusion for all measures of efficacy. Therefore AIDR is considered to dominate circumferential fusion.

PLIF and PLF were estimated to be more effective in terms of QALYs gained compared to AIDR. PLF was also less costly and thus PLF was considered to dominate AIDR. The cost per QALY gained was estimated to be $598,794 with PLIF.

Overall the results were most sensitive to using the direct approach to apply utility weights, changes in the relative risk of overall or ODI success and the time in hospital with AIDR. The results were somewhat sensitive to the proportion of fusion patients requiring BMP. When hospitalisation costs with AIDR were assumed to be equal to that with fusion, fusion became less costly compared to AIDR. If a direct approach was used to apply utility weights, the average QALYs gained with lumbar AIDR and PLIF/PLF was 1.25 QALYs and 1.16 QALYs, respectively. Thus QALYs experienced increased by 0.10 QALYs with lumbar AIDR compared to PLIF/PLF. Using this approach AIDR was estimated to be less costly and more effective compared to PLIF. While compared to PLF, AIDR was estimated to be more costly and more effective, and had an additional cost per QALY of $8,443.

Overall conclusion with respect to comparative cost-effectiveness

The results are mixed depending on the outcome considered most clinically relevant. It should be noted that the estimates of effectiveness were based on point estimates. This may not be appropriate if MSAC considers AIDR to be non-inferior in terms of either overall success or the rate of re-operations. If MSAC considers that AIDR is non-inferior compared to the fusion approaches in terms of success but not in terms of the rate of re-operations, then the total costs accounting for the rate of re-operations should be considered. In this case, ALIF is the least costly approach followed by PLF. If MSAC considers that AIDR is non-inferior compared to the fusion approaches in terms of both success and the rate of re-operations, only the initial costs of surgery should be considered. In this case, ALIF is the least costly approach followed by PLF.

There were a number of limitations with the approach to the analysis including: a proportion of AIDR procedures may be combined with other fusion approaches (this was not considered due to a lack of clinical data); there is a lack of a standard definition of overall success; the proportion of patients who discontinue narcotics does not account for lower doses of narcotics following surgery; utility weights were only available for a small number of approaches; and only the costs incurred in the first two years were included in the analysis (there is a potential increased risk of re-operations at adjacent levels following fusion surgery which has not been considered).

Financial/budgetary impacts

In 2009 and 2010 the number of AIDR procedures was 263 and 258[2], respectively. Using the analysis of costs in the economic evaluation, the total cost of AIDR would be $6.23 million in 2013. If these patients instead received lumbar fusion the total cost would be $6.66 million. Hence the cost savings of performing lumbar AIDR as a direct

[2] Based on MBS items 48691 48692, but not MBS item 48693 as this item is for claims by assisting surgeons.

replacement for lumbar fusion would be $0.43 million. The bulk of the cost savings are due to the cost of consumables and other hospital costs. There would be an increase in the costs borne by the patient and a small increase to the MBS.

Other relevant factors

In Australia the lumbar AIDR procedure is only performed in major private and public hospitals. In addition, most public hospitals do not have a prosthetic budget that would enable them to offer this procedure. Therefore, patients who anticipate having their surgery in a public hospital will need to enquire about whether the hospital has a budget that would allow such aprosthesis to be used.Both of these factors raise the issue of equity of access for this procedure.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of lumbar artificial intervertebral disc replacement. MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

MSAC's Terms of Reference and membership are at Appendix A. MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of current evidence for lumbar artificial intervertebral disc replacement.

Background

Anatomy of the spine

The spine is the primary axial supporting structure in the human body, and also conveys and protects the nerve fibres which make up the spinal cord and the nerve roots which leave it. The spine is composed of bony vertebrae stacked one atop the next, separated by fibrocartilagenous discs which function as fluid joints, particularly in the young. The vertebrae are complex structures, each comprising a cylindrical body surmounted by a dorsal arch which encloses the spinal cord and nerve roots. Each arch participates in two pairs of facet joints which both permit and limit movement at the motion segments above and below the vertebra. The nerve roots leave the spine through foramina between adjacent vertebrae on either side.

The spine is subdivided into cervical, thoracic, lumbar and sacral regions. The lumbar region relevant to the current report has both load-bearing function and also that of conveying and protecting the nerve roots which have left the spinal cord as the cauda equina, and which then leave the spine through intervertebral foramina bilaterally at the level of each disc or motion segment.

The intervertebral discs lie between consecutive vertebrae and are composed of an outer fibrous sheath termed the *annulus fibrosis,* and an inner *nucleus pulposis* composed chiefly of cells, water and proteoglycans. In children, the nucleus is a gel, allowing the disc to function as a true fluid joint, but as the body ages the water content of the nucleus falls progressively, leading to deflation of the disc with loss of vertical height, a decrease in elasticity, and a variable degree of annular (360°) bulging. The collagen fibres of the annulus accumulate microtears accentuating diffuse bulging of the disc, and macroscopic tears leading to extrusion of parts of the disc nucleus as prolapse.

Pain from the lumbar spine can come from bulging or prolapsed discs pressing on pain-sensitive structures including nerves, ligaments or dura; from disease of the vertebral bone or the facet joints between vertebrae; or from the degenerating/injured disc annulus.

Lumbar artificial intervertebral disc replacement

AIDR is designed to simulate the mobile load-bearing properties of the natural intervertebral discs.There are two types of artificial intervertebral discs one type replaces only the nucleus pulposus, and the other replaces the entire intervertebral disc (Anderson and Rouleau 2004).

Prosthetic discs for total disc arthroplasty generally consist of: two metallic endplates which articulate with each other (metal on metal); or two metallic endplates which sandwich a polymer or plastic core (metal on polymer). The overall design and material composition, however, vary significantly between commercially available prosthetic discs, and new designs appear regularly in this rapidly growing field. Most current prosthetic discs use materials which have been used for many years in other wellestablished medical devices eg hip and knee replacements.

All lumbar AIDR procedures are performed under general anaesthetic. Patient positioning and intraoperative realtime fluoroscopy, depending on the device used, are critical to the exposure and successful insertion of the arthroplasty device. For lumbar disc arthroplasty a transperitoneal or retroperitoneal approach is required. Because most lumbar fusion procedures are performed posteriorly, many spinal surgeons require the assistance of an 'access surgeon' to minimise rare but serious approachrelated complications when undertaking anterior AIDR. Important structures that need to be mobilised include the aorta, iliac vessels, sympathetic plexus, and intraperitoneal structures including the bowel and ureters. An access surgeon such as a general or vascular surgeon is often far more familiar with the approach (Davies MA 2005, personal communication, 19 June 2005). Whether an access surgeon is used is dependent on spinal surgeon training and availability.

A complete discectomy is required prior to removing and shaping variable amounts of vertebral endplate. Small instruments and drills are used under magnification to remove disc material and osteophytes compressing nerve roots or the spinal cord. Finally implanting the device requires precise sizing, placement and choice of prosthesis to achieve optimal performance. This requires a mixture of freehand surgical skill, fluoroscopy, milling guides and the appropriate instruments. Implants, rather than being cemented or screwed in, rely on a precise press or friction fit bone implant interface (Davies MA 2005, personal communication, 19 June 2005).

Intended purpose

The primary indications for AIDR considered in this review concern individuals suffering from significant axial back pain and/or radicular (nerve root) pain secondary to disc degeneration or prolapse, who have failed non-operative treatment (eg rest, modification of activities, muscle strengthening, weight control, aerobic training, the passage of time, and analgesic medications including anti-inflammatory medications and epidural steroid). Axial back pain represents the most common type of back pain and is characterised by the pain worsening with activity or change in position and relief by rest (Spinehealth.com 2005).

Clinical need / burden of disease

There is considerable uncertainty regarding the prevalence and incidence of:

- axial lumbar back pain with changes secondary to degeneration of the disc or disc prolapse
- radicular pain from compression or irritation of nerve roots
- referred pain from other lumbar spinal structures including facet joints.

Therefore, there is uncertainty about the number of individuals who may be eligible for AIDR. However, some information regarding the prevalence of back problems and disorders of the intervertebral disc may be derived from the Australian Institute of Health and Welfare (AIHW 2008). In 2004-05, 'back pain and disc problems' was the most commonly reported long-term condition after long- and short-sightedness, reported in 16 per cent of males and 14.7 per cent of females (AIHW 2008). Although the prevalence increases with age, back pain is also a common long-term condition in younger age groups, affecting 15.3 per cent of people aged 25-34 years. Back problems

and disc disorders were the most common work-related conditions (36%) (AIHW 2008). However, it is unclear what proportion of these people suffer from discogenic back pain and would therefore be eligible for either artificial disc replacement or spinal fusion.

A 2003 study estimated that the direct cost of lower back pain in 2001 to be A$1.02 billion, with approximately 71 per cent of this amount attributed to treatment by chiropractors, general practitioners, massage therapists, physiotherapists and acupuncturists (Walker et al 2003). The indirect costs associated with lower back pain were estimated to be A$8.15 billion, giving a total cost of A$9.17 billion. Therefore, in Australia lower back pain in general represents a large health problem, with a significant economic burden.

MBS claims data was provided by the Department of Health and Ageing on patients who claimed any of the following MBS items from July 2005 through to August 2010: 48648, 48651, 48654, 48657, 48660, 48663, 48669, 48672, 48675, 48684, 48690, 48691 and 48692.[3] For these patients, any other MBS item claimed by the same patient on the same day was also provided. Due to complexity, a maximum of 20 items for each same patient/same day procedure were extracted and MBS items relating to anaesthesia time were not extracted. Only 10.4 per cent of patients claimed 20 items or more.

Analysis of MBS data indicates that there were:

- 860 claims for MBS items associated with lumbar AIDR procedures[4]
- 58,829 claims for MBS items associated with spinal fusion procedures.[5]

However, many procedures were performed for indications that are not linked to degenerative disc disease (DDD), such as stenosis, scoliosis and spinal fracture. When patients who also claimed for items relating to stenosis, scoliosis and spinal fracture on the same day as their operation are removed[6] there were:

- 852 claims for MBS items associated with lumbar AIDR procedures
- 26,114 claims for MBS items associated with spinal fusion procedures.

It is important to note that many procedures may involve claims for more than one relevant MBS item (ie some patients may claim for MBS items associated with both

[3] Items 48666 and 48693 are missing due to being claimed by an assisting surgeon; however, these items would be claimed concurrently with 48663 and 48692, respectively.

[4] 819 claims for MBS item number 48691 of which one procedure charged for this item number twice, and 41 claims for MBS item number 48692. Note that MBS item number 49693 is the fee charged by an assisting surgeon associated with MBS item number 48692.

[5] MBS item numbers 48642, 48645, 48648, 48651, 48654, 48657, 48660, 48663, 48666, 48669, 48672, 48675, 48684, 48687, 48690, 40321, 40324.

[6] Any procedure involving a claim for MBS item numbers associated with scoliosis (48606, 48612, 48613, 48615, 48618, 48621, 48624, 48627, 48630, 48632, 50600, 50604, 50608, 50612, 50616, 50620, 50624, 50628, 50632, 50636, 50640, 50644), stenosis (40303, 40306) and spinal fracture (47702).

AIDR and spinal fusion procedures, while other patients may claim for MBS items associated with different types of spinal fusion procedures).

When procedures involving claims for MBS items associated with AIDR procedures are removed, there were 12,568 spinal fusion-only procedures (same patient, same day) involving 25,101 claims for spinal fusion MBS items. Some of these spinal fusion procedures can be identified as occurring in the lumbar or cervical region based on the MBS item claimed for initiation of anaesthesia[5]; 4,331 spinal fusion-only procedures also involved claims for initiation of anaesthesia in the cervical region (approximately 866 per year) and spinal fusion 2,418 in the lumbar region (approximately 484 per year).

Similarly, when procedures involving claims for MBS items associated with spinal fusion are removed there were 346 AIDR-only procedures (same patient, same day), of which none involved claims for initiation of anaesthesia in the cervical region and 219 in the lumbar region.

Note that this split between the lumbar and cervical region is only an indication, as many involved claims for extensive spine/spinal cord procedures (20670) and therefore cannot be identified as occurring in a specific spinal region. Furthermore, many of these procedures may relate to revisions of earlier surgeries, and so cannot be taken as an indication of the number of patients.

Existing procedures

The current treatment options for axial lumbar back pain with secondary changes to the degeneration of the disc or due to major disc prolapse are:

- lumbar spinal fusion
- non-surgical treatments including:
    - muscle strengthening
    - rest
    - modification of activities
    - weight control
    - aerobic training
    - normal activities
    - the passage of time
    - analgesic medications including anti-inflammatory medications and epidural injections.

Non-surgical treatments are generally first line treatment options, while lumbar spinal fusion is only a treatment option if non-surgical treatment fails (ie second line treatment).

Comparator

The comparator procedure is lumbar spinal fusion (Figure 1), in which a bone graft is used to stop the motion at a painful vertebral segment. There are two main approaches to spinal fusion, *posterolateral fusion* and *interbody fusion*, which may be used in conjunction.

Posterolateral fusion involves placing the bone graft between the transverse processes in the back of the spine. The vertebrae are then fixed in place with screws and/or wire through the pedicles of each vertebra attaching to a metal rod on each side of the vertebrae.

Interbody fusion involves placing the bone graft between the vertebrae in the area usually occupied by the intervertebral disc. In preparation for spinal fusion, the disc nucleus and part of the annulus are removed, and the endplates cleaned prior to placement of the graft. This allows the fusion to occur between the endplates of contiguous vertebrae. The graft can be placed in between the vertebral bodies in an interbody position using an anterior approach via an incision in the abdomen (anterior lumbar interbody fusion, ALIF), or a posterior approach (posterior lumbar interbody fusion, PLIF). When both an ALIF and a posterior lateral bone grafting and posterior instrumentation are performed it is commonly referred to as 360 degree or circumferential spinal fusion.

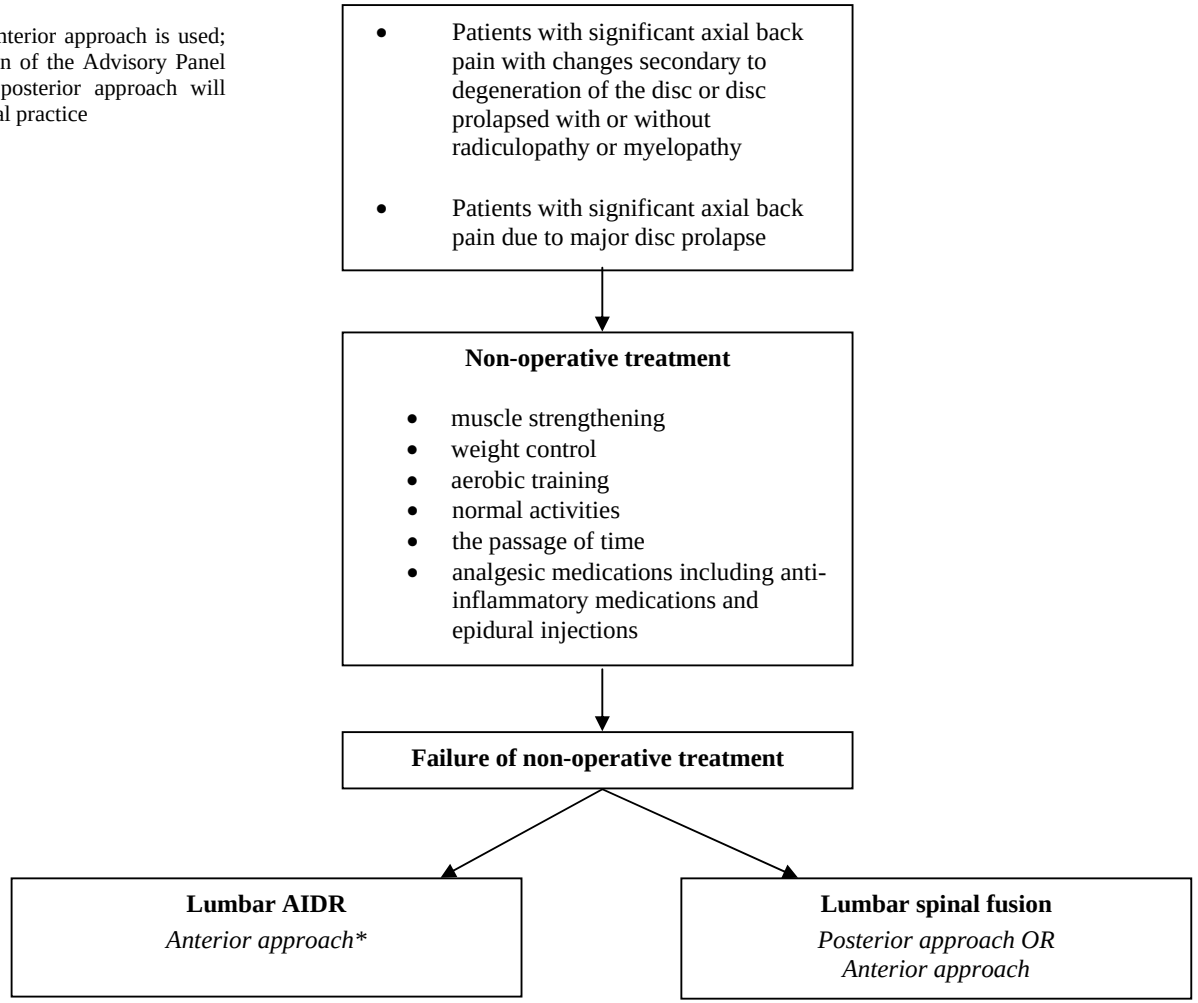
In Australia, most surgeons choose a posterior rather than anterior approach for lumbar spinal fusion, which may occur for a number of reasons (Wilde P 2010, personal communication, 9 September 2010):

- Surgeon familiarity – surgeons perform many more posterior fusion procedures for the treatment of scoliosis or instability.
- It is easier to access multiple levels (more than three) using the posterior approach.
- For some patients, anterior procedures are not technically possible, due to previous abdominal operations which have produced excess peritoneal and retroperitoneal scarring.
- Lack of training – some surgeons may not have learnt how to perform an anterior fusion procedure, or may feel out of their depth with this procedure.
- If there is a need to explore nerve roots (eg occasional leg pain), this can only be done using the posterior approach.
- Surgeons practising in remote locations, who are unable to access vascular surgical support in the case of an inadvertent major vessel injury during an anterior approach to the spine, would opt for a posterior approach.

Anterior versus posterior lumbar fusion operations necessarily involve quite different approaches, techniques and instrumentation, and have different spectra of complications. Therefore, from an economic and clinical perspective, it is important that, where possible, outcomes for posterior and anterior lumbar fusions are reported separately.

Figure 1 Clinical decision-making pathway

*Currently in Australia, only the anterior approach is used; however, the clinical expert opinion of the Advisory Panel suggests that it is likely that a posterior approach will eventually be introduced into clinical practice



Marketing status of the technology

The clinical experts on the Advisory Panel have identified the following lumbar artificial disc prostheses as the most commonly used in Australia:

- Maverick (Medtronic Australasia Pty Ltd)
- In Motion (previously marketed in Australia under the name 'Charité') (Johnson & Johnson Medical Pty Ltd T/A Depuy Australia)
- Flexicore (Stryker Australia Pty Ltd)
- ProDisc (Synthes Australia Pty Ltd).

Current reimbursement arrangement

The lumbar AIDR procedure is currently reimbursed on an interim basis. Relevant MBS item numbers used for the current reimbursement of lumbar AIDR procedures are listed in Table 1. A comprehensive list of all MBS item numbers related to lumbar AIDR and lumbar spinal fusion procedures are listed in Table 26 in the economic considerations section of the assessment.

Table 1 Current MBS item numbers related to lumbar AIDR procedures

MBS item number	Description	Fee	Benefit
48691	LUMBAR ARTIFICIAL INTERVERTEBRAL TOTAL DISC REPLACEMENT including removal of disc, 1 level, in patients with single-level intralumbar disc disease in the absence of vertebral osteoporosis and prior spinal fusion at the same lumbar level who have failed conservative therapy, with fluoroscopy	$1,695.20	75% = $1,271.40 85% = $1,626.10
48692	LUMBAR ARTIFICIAL INTERVERTEBRAL TOTAL DISC REPLACEMENT including removal of disc, 1 level, in patients with single-level intralumbar disc disease in the absence of vertebral osteoporosis and prior spinal fusion at the same lumbar level who have failed conservative therapy, with fluoroscopy (where an assisting surgeon performs the approach) - principal surgeon	$1,142.60	75% = $856.95 85% = $1,073.50
48693	LUMBAR ARTIFICIAL INTERVERTEBRAL TOTAL DISC REPLACEMENT including removal of disc, 1 level, in patients with single-level intralumbar disc disease in the absence of vertebral osteoporosis and prior spinal fusion at the same lumbar level who have failed conservative therapy, (where an assisting surgeon performs the approach) - assisting surgeon	$552.60	75% = $414.45 85% = $483.50

NOTES: MBS = Medicare Benefits Schedule.

Approach to assessment

Objective

To determine whether there is sufficient evidence, in relation to safety, effectiveness and cost-effectiveness, to have lumbar AIDR listed on the Medicare Benefits Schedule.

Review of literature

Literature sources and search strategies

The medical literature was searched to identify relevant studies and reviews from 1 January 2005 until April 2010. Appendix C describes the electronic databases that were used for this search and other sources of evidence that were investigated.

The search terms used to identify literature in electronic bibliographic databases on the safety, effectiveness and cost-effectiveness of lumbar AIDR are also presented in Appendix C.

Inclusion/exclusion criteria

Detailed inclusion and exclusion criteria applied to the identified citations for assessing the safety and effectiveness of lumbar AIDR are detailed in Appendix C.

PICO (population, intervention, comparator, and outcome) criteria were developed with the assistance of the Advisory Panel to assist in specifying the search strategy (Table 2).

Table 2 PICO criteria

Population	Intervention	Comparator	Outcomes
Patients with significant axial back pain with changes secondary to degeneration of the disc or disc prolapse with or without radiculopathy or myelopathy who have failed non-operative treatment. *Contraindications*: • Facet joint arthropathy • Age over 60 years • Obesity • Spinal infection • Spinal neoplasm • Spinal trauma • Instability eg spondylolisthesis • deformity eg scoliosis • Severe osteoporosis • Spinal canal stenosis • Pars defects • Previous surgery performed posteriorly • Previous significant abdominal surgery and/or pathology • Vascular disease in the aorta or its major branches	Lumbar AIDR (Posterior approach OR Anterior approach)	Lumbar spinal fusion (Posterior approach OR Anterior approach)	*Efficacy* • Reduction in pain (eg use of pain medication, rating scales) • Adjacent segment degeneration • Quality of life (including SF-36) • Length of hospital stay • Unplanned readmission within 30 days • Ability to perform activities of daily living (work and/or recreation) • Return to work • Improvement in positional tolerance (motion, strength and endurance) • Disability (disability rating scales, back specific scales eg ODI, Waddell, Roland-Morris) • Emotional wellbeing (depression scales) • Device failure (revision, re-operation or removal)
Patients with significant axial back pain due to major disc prolapse who have failed non operative treatment. *Contraindications*: *as above*			*Safety* • Complication (eg pain, spinal infection, vascular damage, neurological damage or nerve root injury) • Migration or dislocation of disc • Device failure (revision, re-operation or removal) • Adjacent segment degeneration • Polyethylene wear
Clinical questions			
Is lumbar AIDR as safe as, or safer than lumbar spinal fusion?			
Is lumbar AIDR as effective as, or more effective than lumbar spinal fusion?			
Is lumbar AIDR as cost effective as, or more cost effective than lumbar spinal fusion?			

Data extraction and analysis

Data were extracted by one researcher and checked by a second using standardised data extraction tables developed a priori. Data were only reported if stated in the text, tables, graphs or figures of the article, or if they could be accurately extrapolated from the data presented. If no data were reported for a particular outcome then no value was tabulated. Descriptive statistics were extracted or calculated for all safety and effectiveness outcomes in the individual studies, including numerator and denominator information.

Validity assessment of individual studies

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2000).

These dimensions (Table 3) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature identified as informing a particular intervention. The last two require expert clinical input as part of their determination.

Table 3 Evidence dimensions

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design.*
Quality	The methods used by investigators to minimise bias within a study design.
Statistical precision	The *P*-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect.
Size of effect	The distance of the study estimate from the 'null' value and the inclusion of only clinically important effects in the confidence interval.
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

NOTES: *See Table 4

Strength of the evidence

The three subdomains (level, quality and statistical precision) are collectively a measure of the strength of the evidence.

Level

The 'level of evidence' reflects the effectiveness of a study design to answer a particular research question. Effectiveness is based on the probability that the design of the study has reduced or eliminated the impact of bias on the results.

The National Health and Medical Research Council (NHMRC) evidence hierarchy provides a ranking of various study designs ('levels of evidence') by the type of research question being addressed (Table 4).

Table 4 Designations of levels of interventional evidence (NHMRC 2009)

Level	Intervention[a]
I[b]	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudorandomised controlled trial (ie alternate allocation or some other method)
III-2	A comparative study with concurrent controls: Non-randomised, experimental trial[c] Cohort study Case-control study Interrupted time series with a control group
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm study[d] Interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test/post-test outcomes

[a]A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence.
[b]Definitions of these study designs are provided on pages 7-8 How to use the evidence: assessment and application of scientific evidence (NHMRC 2000b).
[c]This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (ie utilise A vs B and B vs C, to determine A vs C).
[d]Comparing single arm studies ie case series from two studies.
Note 1: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.
Note 2: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question eg level II intervention evidence; level IV diagnostic evidence.

Quality

The appraisal of intervention studies pertaining to treatment safety and effectiveness was undertaken using a checklist developed by the NHMRC (NHMRC 2000). This checklist was used for trials and cohort studies. Uncontrolled before-and-after case series are a poorer level of evidence with which to assess effectiveness. The quality of this type of study design was assessed according to a checklist developed by the United Kingdom National Health Service (NHS) Centre for Reviews and Dissemination (Khan et al 2001).

Statistical precision

Statistical precision was determined using statistical principles. Small confidence intervals and *P*-values give an indication as to the probability that the reported effect is real and not attributable to chance (NHMRC 2000).

Size of effect

For intervention studies, it was important to assess whether statistically significant differences between the comparators were also clinically important. Where possible, the size of the effect was determined, as well as whether the 95 per cent confidence interval included only clinically important effects.

Relevance of evidence in individual studies

The outcomes being measured in this report should be appropriate and clinically relevant. Clinical input from the Advisory Panel was provided to ensure that inadequately validated (predictive) surrogate measures of a clinically relevant outcome were avoided wherever possible (NHMRC 2000).

Assessment of the body of evidence

Appraisal of the body of evidence was conducted as suggested by the NHMRC in their guidance on clinical practice guideline development (NHMRC 2008). Five components are considered essential by the NHMRC when judging the body of evidence:

- the evidence base — this includes the number of studies sorted by their methodological quality and relevance to patients
- the consistency of the study results — whether the better quality studies had results of a similar magnitude and in the same direction (ie homogenous or heterogenous findings)
- the potential clinical impact — appraisal of the precision, size and clinical importance or relevance of the primary outcomes used to determine the safety and effectiveness of the test
- the generalisability of the evidence to the target population
- the applicability of the evidence — integration of this evidence for conclusions about the net clinical benefit of the intervention in the context of Australian clinical practice.

A matrix for assessing the body of evidence for each research question, according to the components above, was used for this assessment (see Table 5) (NHMRC 2008).

Table 5 Body of evidence assessment matrix

Component	A Excellent	B Good	C Satisfactory	D Poor
Evidence base	Several level I or II studies with low risk of bias	One or two level II studies with low risk of bias, or a systematic review or multiple level III studies with low risk of bias	Level III studies with low risk of bias, or level I or II studies with moderate risk of bias	Level IV studies, or level I to III studies with high risk of bias
Consistency	All studies consistent	Most studies consistent and inconsistency may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Population/s studied in body of evidence are the same as the target population	Population/s studied in the body of evidence are similar to the target population	Population/s studied in body of evidence different from target population for guideline, but it is clinically sensible to apply this evidence to target population	Population/s studied in body of evidence different from target population and hard to judge whether it is sensible to generalise to target population
Applicability	Directly applicable to Australian health care context	Applicable to Australian health care context with few caveats	Probably applicable to Australian health care context with some caveats	Not applicable to Australian health care context

Source: NHMRC (2008)

Expert advice

An Advisory panel with expertise in orthopaedics, pain and rehabilitation medicine, and consumer issues was established to evaluate the evidence and provide advice to MSAC from a clinical perspective. In selecting members for advisory panels, MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the Advisory panel is provided at Appendix B.

Results of assessment

Descriptive characteristics of included studies

From the search strategy, 1088 potentially relevant articles were identified, of which 330 were retrieved for more detailed evaluation. Retrieved studies included systematic reviews and primary studies. In total, 275 retrieved articles were excluded (Appendix G).

A total of 60 studies, including four systematic reviews, five health technology assessments, four randomised controlled trials (RCTs) (comprising 12 studies), one nonrandomised comparative study, and 38 case series were eligible for appraisal and inclusion in this assessment (Appendix E).

Studies for assessment of safety

Forty-three studies were identified for inclusion in the assessment of the safety of lumbar AIDR. This included five comparative studies and 38 case series. Comparative studies compared lumbar AIDR to anterior lumbar interbody fusion (ALIF), circumferential fusion, posterolateral lumbar fusion (PLF) or posterior lumbar interbody fusion (PLIF). Sample sizes ranged from 10 to 427 patients, with safety data reported for a total of 3,224 patients overall.

Studies for assessment of effectiveness

A total of 13 comparative studies were identified and included to inform on the comparative effectiveness of lumbar AIDR.

The systematic literature search revealed:

- a total of four RCTs (comprising 12 studies) that directly compared lumbar AIDR to ALIF (Blumenthal et al 2005; Geisler et al 2008a; Geisler et al 2008b; Geisler et al 2009; Guyer et al 2009; McAfee et al 2005; McAfee et al 2006), circumferential fusion (Auerbach et al 2009; Sasso et al 2008; Zigler et al 2007) or PLF/PLIF (Berg et al 2009a; Berg et al 2009b)
- one nonrandomised comparative study that directly compared lumbar AIDR to ALIF (Schroven and Dorofey 2006).

A subsequent section will examine these studies in greater detail and appraise their methodological quality.

Duplication of results

It is possible that significant duplication of results has occurred across this dataset. There were various cases where the same patient population (or part of the patient population) was used in multiple reports. In some cases, different outcomes were reported in those different reports. In cases where the same outcome was reported in more than one report, the most recent data was used for analysis.

Systematic reviews and health technology assessments

A list of electronic databases and websites of international health technology assessment (HTA) agencies searched can be found in Appendix C. A total of five health technology assessments were identified (Blue Cross Blue Shield Association (BCBS) 2007; California Technology Assessment Forum (CTAF) 2008; Medical Advisory Secretariat Ontario (MASO) 2006; Vlayen et al 2006; Washington Health Technology Assessment (WHTA) 2008).

An additional four systematic reviews were also identified through the literature search (Chou et al 2009; Freeman and Davenport 2006; Harrop et al 2008; Yajun et al 2010).

Study description

Three of the HTAs investigated the safety and effectiveness of both cervical and lumbar AIDR (MASO 2006; Vlayen et al 2006; WHTA 2008), and two investigated lumbar AIDR only (BCBS 2007; CTAF 2008). Three of the HTAs included an economic evaluation of AIDR in addition to investigating safety and effectiveness (MASO 2006; Vlayen et al 2006; WHTA 2008). The HTA by CTAF (2008) was an update of a previous review published in October 2005. All HTAs searched multiple databases. Two HTAs contacted suppliers and manufacturers of artificial discs for references (CTAF 2007; Vlayen et al 2006). The HTA by Vlayen et al (2006) only used systematic reviews and RCTs, whilst the HTAs by CTAF (2008), WHTA (2008), BCBS (2007), and MASO (2006) included lower levels of evidence, such as nonrandomised comparative trials and case series, if they reported outcomes of interest. WHTA (2008), MASO (2006), and Vlayen et al (2006) provided specific inclusion criteria, and WHTA (2008) used two independent researchers to assess studies for inclusion and quality. CTAF (2008) and BCBS (2007) did not describe the study selection process in detail. Both the WHTA (2008) and the MASO (2006) HTAs conducted meta-analyses to summarise the data whilst the other HTAs discussed studies separately.

Three of the systematic reviews assessed the safety and effectiveness of lumbar AIDR compared with other treatment options (Chou et al 2009; Freeman and Davenport 2006; Yajun et al 2010). One systematic review specifically assessed the incidence of adjacent segment degeneration or disease after lumbar AIDR or arthrodesis (Harrop et al 2008). All reviews searched two or more databases, with some also hand-searching reference lists of relevant journals, or communicating with international experts. The reviews by Yajun et al (2010) and Chou et al (2009) included only high level evidence, while Harrop et al (2008) and Freeman and Davenport (2006) included lower level evidence such as relevant cohort studies. Yajun et al (2010) and Chou et al (2009) provided specific inclusion criteria, and used two independent researchers to assess studies for inclusion and quality. The other two reviews did not describe their study selection process in detail. Yajun et al (2010) and Harrop et al (2008) pooled data from different studies, while the two remaining reviews only reported studies separately.

Effectiveness

A recent HTA by WHTA (2008) included seven RCTs, three level III cohort studies, two economic studies and four FDA reports. The report concluded that there was moderate evidence that the effectiveness of lumbar AIDR, as measured by overall clinical success, reduced disability and pain, neurological success, and patient satisfaction, was comparable with ALIF or circumferential fusion up to two years following surgery. This

evidence was based on two moderate quality RCTs conducted as FDA Investigational Device Exemption (IDE) non-inferiority trials. Overall clinical success was achieved in 56 per cent of patients receiving lumbar AIDR and 48 per cent of patients receiving lumbar fusion. The authors note that a non-inferiority trial requires the reference treatment to have an established efficacy or be in widespread use; however, in this case the efficacy of the comparator treatment, lumbar fusion, for the treatment of degenerative disc disease (DDD) remains uncertain, especially when it is compared with operative care. Evidence that only compares lumbar AIDR with lumbar fusion limits the ability to fully assess efficacy.

Another recent HTA by CTAF (2008) was an update of a previous review on the safety and efficacy of artificial spinal disc replacement for the treatment of low back pain caused by DDD. The search identified six case series and one RCT for the Charité artificial disc and seven case series and one RCT for the ProDisc artificial disc. From their report, CTAF concluded that both the Charité and ProDisc artificial discs, when used in highly selected populations with intractable pain from DDD, improve net health outcomes at two years. However, from the available evidence the review concluded that neither disc type offered any advantages over established therapies. In addition, it was unclear whether the possible benefits of lumbar AIDR outweighed the surgical risks and possibility of long-term device failure.

The HTA by the BCBS (2007) included six case series and one clinical trial on the Charité disc and six case series and one small nonrandomised comparative trial on ProDisc. In summary, the evidence supporting the effectiveness of both the Charité and ProDisc was deemed to be limited and their use for the treatment of DDD did not meet the Technology Evaluation Center (TEC) criteria.

The HTA by MASO (2006) included two RCTs and six case series that assessed the effectiveness and adverse event profile of lumbar AIDR for the treatment of DDD. The quality of this evidence was deemed moderate for effectiveness, and lumbar AIDR was not found to be inferior to spinal fusion. Based on a Bayesian meta-analysis, the probability of lumbar AIDR being superior to spinal fusion was 79 per cent.

Vlayen et al (2006) included one RCT on lumbar AIDR. The RCT that was identified showed equivalence between the SB Charité III disc and ALIF, and was deemed to be of questionable quality. The investigators concluded that lumbar AIDR should be considered an experimental procedure until the results of high quality trials become available.

The most recent systematic review by Yajun et al (2010) included five RCTs, involving use of the Charité artificial disc, Prodisc-L artificial disc, FlexiCore artificial disc, and Maverick artificial disc. A meta-analysis showed that compared with lumbar fusion, lumbar AIDR results in slightly better functioning and back or leg pain status, and significantly greater patient satisfaction. When one study which used a problematic fusion technique was omitted from the analysis, these differences disappeared. The authors concluded that lumbar AIDR does not show significant superiority for the treatment of lumbar DDD compared with fusion, and that more high-quality RCTs with long term outcomes are needed.

The review by Chou et al (2009) had similar findings to Yajun et al (2010). This review included 24 systematic review articles (covering 22 different systematic reviews) and 84

RCT articles (covering 74 different trials). Of the trials, 14 compared surgery to non-surgical therapy and two compared AIDR to fusion surgery. One AIDR trial examined the Prodisc II and another examined the Charité artificial disc. Both were manufacturer sponsored. The authors suggested that based on the two trials there was evidence that AIDR is as effective as fusion for the treatment of nonradicular low back pain with single level DDD. The conclusion was that there was insufficient evidence to assess long term benefits, and high-quality, non-industry sponsored trials would strengthen the evidence base.

Freeman and Davenport (2006) reached similar conclusions to the other systematic reviews. Forty articles were included, including two systematic reviews and two RCTs involving the use of the Charité artificial disc and the Prodisc II total disc replacement. The Charité artificial disc was found to be equivalent to fusion for single-level DDD. The authors concluded that the long term benefits of AIDR in preventing adjacent level disc degeneration and the role for two- or multi-level disc replacement remain unproven, and that further well-designed prospective RCTs are required.

The review by Harrop et al (2008) focused specifically on the incidence of adjacent segment degeneration or disease and included 27 articles, of which seven involved AIDR. No RCTs were included. The systematic analysis found that 9 per cent of AIDR patients were noted to have adjacent segment degeneration based on radiographic assessment and 1 per cent of patients were shown to have clinically symptomatic adjacent segment disease. In comparison, following lumbar fusion, 34 per cent of patients had adjacent segment degeneration and 14 per cent had clinical adjacent segment disease. Pooled data suggested that AIDR offers a lower risk of adjacent segment degeneration or disease than fusion, although the authors noted that this finding is limited by the heterogeneous nature of the available literature and the lack of quality evidence.

Safety

With respect to safety, the HTA by WHTA (2008) concluded that there was moderate evidence that lumbar AIDR was as safe as lumbar anterior or circumferential fusion. There was insufficient data to determine the long term safety of lumbar AIDR. CTAF (2008) reported that with respect to case series data on the Charité disc, one study with 100 patients and at least 10 years follow-up found that there were no device failures or unexpected neurologic syndromes. In a second case series with 17 year follow up, 83 per cent of the patients had either surgical or spontaneous fusion at the level of the artificial disc. With regard to the ProDisc, one case series reporting results over 8.7 years reported no device failures and only one case of spontaneous fusion. No reoperations were required. Owing to the lack of sufficient evidence, the use of AIDR for the treatment of DDD did not meet the TEC criteria. BCBS (2007) reported on two comparative trials, one on Charité and one on ProDisc. In the Charité trial AIDR had higher rates of severe and life threatening events and device-related events, but lower rates of device failure. Results were not statistically significant. In the ProDisc trial, adverse events were experienced by 87.5 per cent of fusion patients and 84 per cent of AIDR patients. Twenty percent of fusion patients and 17.9 per cent of AIDR patients experienced a device-related adverse event, respectively. The use of AIDR for the treatment of DDD did not meet the TEC criteria. The MASO (2006) HTA reported that the rate of major complications associated with lumbar AIDR ranged from 0 to 13 per cent per device implanted. The rates for device failure and neurological complications two years after surgery did not differ between AIDR and fusion patients. The rate of adjacent segment

degeneration in one case series was 2 per cent over an 11 year follow-up period. The quality of this evidence was deemed moderate for short term (2 year follow-up) complications, but very low for the purposes of evaluating adjacent segment degeneration. The one RCT appraised by Vlayen et al (2006) found equivalent complication rates between AIDR and spinal fusion. This report concluded that information on long term results and adverse events (exceeding 2 years) were lacking.

The earliest included systematic review by Freeman and Davenport (2006) noted that at the time of the review, complications associated with the AIDR procedure may not become apparent for several years. The more recent systematic review by Yajun et al (2010) used five studies to determine that complication and reoperation rates were similar between AIDR and fusion groups at 2 and 5 years. The review by Chou et al (2009) reported similar findings. From two trials, Chou et al (2009) identified that one death was reported among 205 patients randomised to Charité total disc replacement, and no deaths were reported in 161 patients randomised to Prodisc II artificial disc replacement. There were no major complications in the Prodisc II trial, and in the Charité trial there were no differences between AIDR and fusion in terms of overall and major complications. The authors noted that long term data following AIDR are limited. The review by Harrop et al (2008) which focused specifically on the incidence of adjacent segment degeneration, concluded that based on pooled low level evidence, AIDR offers a lower risk of adjacent segment degeneration or disease than fusion.

Cost-effectiveness

The HTA by WHTA (2008) identified and critically appraised two studies comparing the costs of AIDR with those of fusion. Neither study was a full economic evaluation. These studies suggested that the costs associated with lumbar AIDR may be at least similar or perhaps less than those for fusion. Vlayen et al (2006) concluded that economic/cost information on AIDR was lacking. Budget impact related to the surgery, hospital stay and the treatment of possible complications was expected to be considerable even without direct reimbursement of the implant. The HTA by MASO (2006) found lumbar AIDR to be more costly than fusion. The total cost of a lumbar AIDR procedure was estimated to be $CAN 15,371 (including costs related to the device, physicians and procedure), whereas the total cost of a lumbar fusion surgery procedure was $CAN 11,311 (including physician and procedural costs).

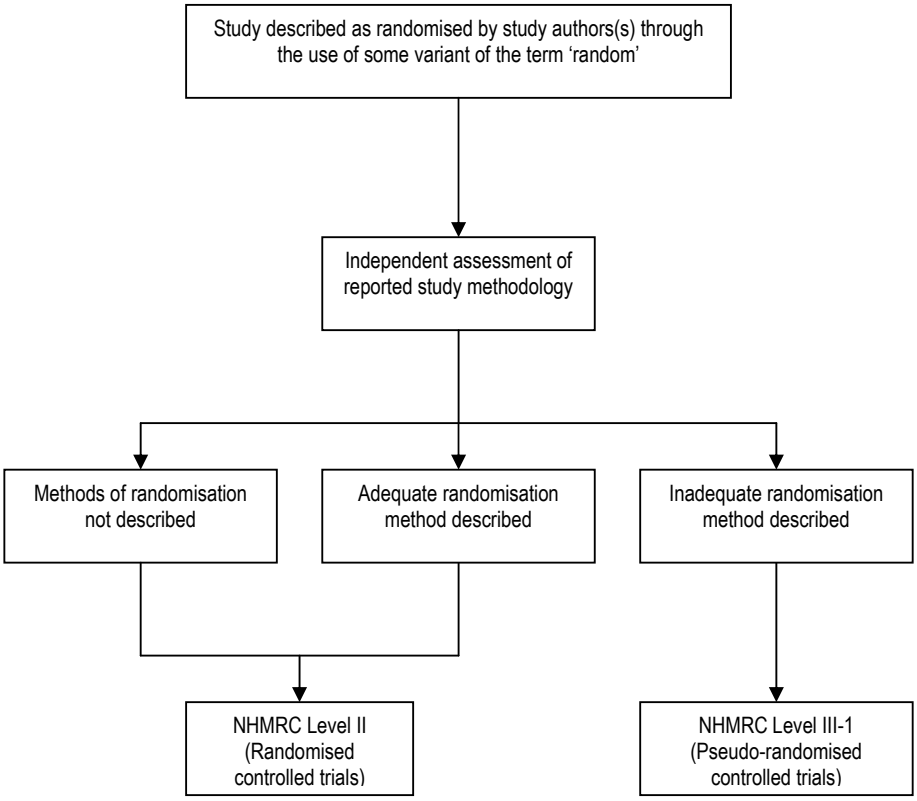
Critical appraisal of randomised controlled studies

Summaries of the quality of the four RCTs included in this review are reported in Table 16 and Table 17 in Appendix D and briefly described below.

Studies were classified utilising the National Health and Medical Research Council (NHMRC) Hierarchy of Evidence (NHMRC 2000) and allocated the classification of level II randomised controlled trial or level III-1 pseudo-randomised controlled trial based on the process outlined in Figure 2. Study quality was assessed according to the methods outlined in Section 6 of the Cochrane Reviewers' Handbook (Higgins & Green 2008) and the CONSORT Statement (Altman et al 2001).

A number of key appraisal parameters are applicable to both RCTs and pseudo-RCTs. Hence, for parameters where differentiation between the study designs is not relevant, these studies have been grouped together to better allow for the description of the higher-level evidence as a whole.

Figure 2 Method of assessing studies for assignment of NHMRC levels of evidence II & III-1



Study design details

Sample size

Across the four RCTs, sample sizes for individual studies ranged from 688 patients (589 in the lumbar AIDR group and 99 in the ALIF group) to 76 patients (50 the lumbar AIDR group and 26 in the circumferential fusion group).

Participants

All four included RCTs clearly described their eligibility criteria for the recruitment of patients. These four studies which described both the inclusion and exclusion criteria, considered a variety of factors when recruiting patients, including age, body mass index (BMI), previous spinal surgery, diagnosis of degenerative disc disease, back and/or leg (radicular) pain, comorbidities, and willingness to provide written informed consent and comply with the follow-up schedule.

Study groups were generally well-matched at baseline with respect to factors such as age, gender, height, BMI, race, smoking status, implant level, activity level and workstatus. Three studies reported on previous surgical treatments, and study groups were generally well-matched for this outcome at baseline.

Randomisation, concealment and implementation

Of the four RCTS, three employed adequate methods of randomisation, including sealed numbered envelopes and fixed randomised blocking, while one study did not report the randomisation method. Further prevention of selection bias through assignment concealment was not reported in one study, while the remaining three studies reported that assignment concealment was not used.

Blinding

One of the four studies did not report on blinding status, while the remaining three studies reported that patients and surgical staff were not blinded to the treatment assignment. None of the studies reported whether blinding of outcome assessors was employed.

Interventions and outcomes

Interventions were generally clearly detailed and most studies defined primary outcomes. The majority of studies utilised commonly used, validated outcome instruments for assessment of patient outcomes.

Results reporting and analyses

Numbers analysed

One of the four studies did not report undertaking a power calculation. The three remaining studies reported undertaking power calculations on appropriate outcomes and recruiting the sample size necessary to detect statistically meaningful differences between treatment groups.

None of the included RCTs reported whether an intention-to-treat or per-protocol analysis was undertaken.

Statistical methods

The analysis techniques employed were not consistently reported; two of the four RCTs explicitly listed the statistical tests employed. Only one RCT prospectively identified an alpha level for statistical significance.

Outcomes and estimation

The included studies were thorough in reporting the results of each primary outcome defined. The mean was the most frequently employed indicator of central tendency, with almost all studies including some measure of estimation; standard deviations and ranges were reported where appropriate.

Safety outcomes were not reported as comprehensively as effectiveness outcomes. While all four RCTs reported adverse events, most studies listed individual events and incidence rates for these events, but did not report how or if these events were resolved.

Follow-up and losses to follow-up

All of the included RCTs employed a medium-term follow-up period. Three of the four included studies followed-up patients for two years after surgery, while the remaining RCT employed a maximum follow-up period of five years.

One of the four RCTs explicitly stated that no patients were lost to follow-up, while one study did not report whether there were any losses to follow-up. Of the two remaining studies, one reported a follow-up rate of 57 per cent of all eligible, randomised patients at 5 years, while the other reported a follow-up rate of 98.2 per cent at 2 years.

Critical appraisal of nonrandomised comparative studies

An appraisal of the quality of the one level III-2 study included in this review is reported in Appendix D, and briefly summarised below.

Study design details

Participants

The study had a sample size of 24 patients (14 in the lumbar AIDR group and 10 in the ALIF group). The study groups were generally well-matched at baseline with respect to factors such as age, gender, implant level and preoperative ODI score.

Blinding

The study did not report whether blinding of patients, surgical staff or outcome assessors was undertaken.

Interventions and outcomes

Both the lumbar AIDR and ALIF procedures were clearly detailed. There was a clear focus on clinical outcomes, with the study reporting both safety and effectiveness outcomes.

Results reporting and analysis

Statistical methods

Statistical analysis was not performed due to the small number of patients in each study group.

Follow-up and losses to follow-up

The length of the follow-up period was one year, and no losses to follow-up were reported.

Is it safe?

Summary of safety data from level II and III studies

Included studies

Of the 13 comparative studies included (NHMRC level II and III evidence), five studies provided some information on adverse events. The remaining eight studies presented no adverse events numerical data or statements; however, one study examined the effect of previous surgery on the rate of adverse events following lumbar AIDR or fusion. Safety outcomes of interest were clinical adverse events and technical adverse events related to lumbar AIDR and fusion procedures. The adverse events reported by each study are shown in Table 6. From the safety data provided in these studies, it was possible to calculate incidence rates for the various adverse events reported. All but one study involved single level procedures. Thus, incidence rates were calculated in terms of the number of patients, rather than the number of discs, in each study group.

Table 6 Adverse events following lumbar AIDR and fusion procedures

Study	Lumbar AIDR			Lumbar fusion		
	Disc type	No. of patients	Adverse event (number of events) (resolution of adverse event, where reported)	Fusion type	No. of patients	Adverse event (number of events) (resolution of adverse event, where reported)
Level II studies						
Blumenthal 2005	CHARITÉ™	205	Death (narcotic-related) (1) Approach-related (20) Venous injury (9) Retrograde ejaculation (3)[a] Ileus (2) Perioperative vein thrombosis (2) Clinically significant blood loss >1500cc (1) Incisional hernia (1) Epidural hematoma (1) Dural tear (1) Deep vein thrombosis (0) Arterial thrombosis (0) Infection (26) Superficial wound with incision site pain (13) Other nonwound related (5) UTI (5) Wound swelling (2) Pulmonary (1) Peritonitis (0) Graft site (0) Fusion treatment related (0) Nonunion/pseudarthrosis (0) Bone graft donor site pain (0) Prosthesis-related (8) Collapse or subsidence of implant into adjacent vertebrae (7) Implant displacement (1) Additional surgery index level (11) Revision (5) Reoperation (4) Removal (2) Other (2) Annulus ossification (1) Calcification resulting in bridging trabecular bone (1)	ALIF	99	Death (0) Approach-related (10) Venous injury (2) Retrograde ejaculation (3)[b] Ileus (1) Perioperative vein thrombosis (0) Clinically significant blood loss >1500cc (2) Incisional hernia (2) Epidural hematoma (0) Dural tear (0) Deep vein thrombosis (0) Arterial thrombosis (0) Infection (8) Superficial wound with incision site pain (2) Other nonwound related (1) UTI (1) Wound swelling (0) Pulmonary (0) Peritonitis (1) Graft site (3) Fusion treatment related (27) Nonunion/pseudarthrosis (9) Bone graft donor site pain (18) Prosthesis related (1) Collapse or subsidence of implant into adjacent vertebrae (1) Implant displacement (0) Additional surgery index level (9) Revision (0) Reoperation (8) Removal (1) Other (0) Annulus ossification (0) Calcification resulting in bridging trabecular bone (0)
Zigler 2007	ProDisc®-L	161	Death (0) Major vessel injury (0) Neurologic damage (0) Nerve root injury (0)	Circumferential spinal fusion	75	Death (0) Major vessel injury (0) Neurologic damage (0) Nerve root injury (0)

			Retrograde ejaculation (2) Infection (0) Deep vein thrombosis (2) (successfully treated medically)			Clinically significant blood loss (2) Infection (2) Deep vein thrombosis (1) (successfully treated medically)
Berg 2009a	CHARITÉ™, ProDisc®-L or Maverick™	80	Infection (0) Haematoma (2) Facet joint problem (6) Pseudarthrosis (0) Wound hernia (1) Nerve entrapment (1) Donor site pain (0) Adjacent (1) Dural tear (1) Meralgia paresthetica (1) Subsidence/re-operation (1)	PLF or PLIF	72	Infection (4) Haematoma (1) Facet joint problem (0) Pseudarthrosis (2) Wound hernia (0) Nerve entrapment (0) Donor site pain (1) Adjacent (6) Dural tear (1) Meralgia paresthetica (0) Subsidence/re-operation (0)
Sasso 2008	FlexiCore™	50	Wound infection (1) (required irrigation and debridement) Low back pain requiring removal of hardware (0) Low back pain requiring subsequent fusion procedure (1) Radicular leg pain (2) (resolved following microlumbar diskectomy and hemilaminotomy) Retroperitoneal hematoma (1) (required surgical evacuation) Vertebral end plate fracture (1) (required removal of a bony fragment through a laminotomy) Hardware migration (1) (resolved after revision to larger FlexiCore prosthesis) Vascular injury (1) (vessel repaired during the index procedure with 5-0 prolene suture) Stridor/hypoxia (1) (did not require surgical intervention) Tachyarrhythmia (1) (did not require surgical intervention) Pulmonary embolism (0) Extraperitoneal seroma (0)	Circumferential spinal fusion	26	Wound infection (3) (1 patient required repeat irrigation and debridement) Low back pain requiring removal of hardware (5) (CT scan confirmed a solid fusion, and on removal of the posterior hardware the pain gradually resolved) Low back pain requiring subsequent fusion procedure (0) Radicular leg pain (0) Retroperitoneal hematoma (0) Vertebral end plate fracture (0) Hardware migration (0) Vascular injury (0) Stridor/hypoxia (0) Tachyarrhythmia (0) Pulmonary embolism (1) (did not require surgical intervention) Extraperitoneal seroma (1) (did not require surgical intervention)
Level III-2 studies						
Schroven and Dorofey 2006	ProDisc®-L	14	Facet arthritis noted after 6 months (1) Transient sciatica (2) Subsidence (1)	ALIF	10	Intraoperative haemorrhage due to specific technical difficulties (1)

NOTES: ALIF = anterior lumbar interbody fusion; PLF = posterolateral fusion; PLIF = posterior lumbar interbody fusion; UTI = urinary tract infection; [a]Of 92 males in the lumbar AIDR group; [b]Of 55 males in the lumbar fusion group.

Adverse events

In terms of adverse events, few included studies reported statistical comparisons between lumbar AIDR and fusion procedures. Blumenthal et al (2005) reported that there was no significant difference in the rate of overall complications, approach-related complications, or device failures necessitating re-operation, revision, or removal between the lumbar AIDR and ALIF groups. Similarly, Berg et al (2009a) reported that that there was no significant difference in the rate of overall complications between the lumbar AIDR and PLF/PLIF groups.

Table 7 displays the incidence rates of the various reported adverse events. There were no clear differences between the lumbar AIDR and fusion groups for the majority of adverse events reported. Wound infection was the most commonly reported adverse event, and demonstrated an incidence rate of 3.2 per cent in the lumbar AIDR population, and 5.1 per cent in the lumbar fusion population. Prosthesis-related adverse events were those relating to movement of the device, including collapse or subsidence (3%), and displacement (0.78%). Fusion-related adverse events included nonunion/pseudarthrosis (6.4%) and bone graft donor-site pain (11.1%). The rate of reoperation appeared higher following lumbar fusion (6.4%) compared with lumbar AIDR (2%). Similarly, the rate of adjacent segment problems appeared higher following lumbar fusion (8.3%) compared with lumbar AIDR (1.3%).

Major morbidities such as major vessel injury, neurologic damage and nerve root injury were rare in both the lumbar AIDR and fusion groups. There was one reported death following lumbar AIDR which was narcotic-related, while no deaths were reported following lumbar fusion.

A study by Geisler et al (2008a) reported that the rate of adverse events was not significantly different in lumbar AIDR patients who had undergone previous lumbar decompressive surgery (including microdiscectomy, laminectomy or minimal medial facetectomy) compared with those who had not undergone previous surgery. Similarly, the rate of adverse events was not significantly different in ALIF patients who had undergone previous lumbar decompressive surgery, compared with those who had not undergone previous surgery. However, when lumbar AIDR and ALIF patients were combined, the rate of pain at the incision site was higher in those patients who had undergone previous surgery (7.4%) compared with those who had not undergone previous surgery (4.4%) (p=0.049).

Table 7 Summary of adverse events in level II and III studies providing safety evidence

Adverse event	Lumbar AIDR		Lumbar fusion	
	Incidence* n/N (%)	No. of studies reporting outcome	Incidence* n/N (%)	No. of studies reporting outcome
Death	1/366 (0.27%)	2	0/174 (0%)	2
Vascular injury	10/416 (2.4%)	3	2/200 (1%)	3
Perioperative thrombosis	2/205 (0.98%)	1	0/99 (0%)	1
Deep vein thrombosis	2/366 (0.55%)	2	1/174 (0.57%)	2
Arterial thrombosis	0/205 (0%)	1	0/99 (0%)	1
Pulmonary embolism	0/50 (0%)	1	1/26 (3.8%)	1
Tachyarrhythmia	1/50 (2%)	1	0/26 (0%)	1
Haematoma	4/335 (1.2%)	3	1/197 (0.51%)	3
Blood loss	1/205 (0.49%)	1	4/174 (2.3%)	2
Haemorrhage	NR	NR	1/10 (10%)	1
Retrograde ejaculation	5/366 (1.4%)	2	3/99 (3%)	1
Ileus	2/205 (0.98%)	1	1/99 (1%)	1
Hernia	2/285 (0.70%)	2	2/171 (1.2%)	2
Dural tear	2/285 (0.70%)	2	1/171 (0.58%)	2
Wound infection	16/496 (3.2%)	4	14/272 (5.1%)	4
Other non-wound related infection	5/205 (2.4%)	1	1/99 (1%)	1
Urinary tract infection	5/205 (2.4%)	1	1/99 (1%)	1
Pulmonary infection	1/205 (0.49%)	1	0/99 (0%)	1
Peritonitis	0/205 (0%)	1	1/99 (1%)	1
Collapse or subsidence of implant	9/299 (3.0%)	3	NA	NA
Implant displacement	2/255 (0.78%)	2	NA	NA
Revision surgery	5/205 (2.4%)	3	0/99 (0%)	1
Reoperation	5/255 (2.0%)	2	8/125 (6.4%)	2
Removal of prosthesis	2/205 (0.98%)	1	6/125 (4.8%)	2
Nonunion/pseudarthrosis	NA	NA	11/171 (6.4%)	2
Bone graft donor-site pain	NA	NA	19/171 (11.1%)	2
Adjacent segment problems	1/80 (1.3%)	1	6/72 (8.3%)	1
Annulus ossification	1/205 (0.49%)	1	0/99 (0%)	1
Calcification resulting in bridging trabecular bone	1/205 (0.49%)	1	0/99 (0%)	1
Facet joint problems	7/94 (7.4%)	2	0/72 (0%)	1
Vertebral end plate fracture	1/50 (2%)	1	0/26 (0%)	1
Neurologic damage	0/161 (0%)	1	0/75 (0%)	1
Nerve root injury	0/161 (0%)	1	0/75 (0%)	1
Nerve entrapment	1/80 (1.3%)	1	0/72 (0%)	1
Meralgia paresthetica	1/80 (1.3%)	1	0/72 (0%)	1
Transient sciatica	2/14 (14.3%)	1	NR	NR
Low back pain	1/50 (2%)	1	5/26 (19.2%)	1
Radicular leg pain	2/50 (4%)	1	0/26 (0%)	1
Stridor/hypoxia	1/50 (2%)	1	0/26 (0%)	1
Extraperitoneal seroma	0/50 (0%)	1	1/26 (3.8%)	1

NOTE: *Incidence is reported in terms of number of patients; NA = not applicable; NR = not reported.

Summary of safety data from level IV studies

Included studies

Thirty eight level IV studies reported adverse events resulting from approximately 2,817 lumbar AIDR procedures performed on 2,432 patients. A summary of included studies is displayed in Table 47 (Appendix F). With respect to the prosthesis type, twenty one studies used ProDisc (1,107 discs in total), six studies used Maverick (166 discs in total), 11 studies used Charité (1,025 discs in total) and one study used Physio-L (16 discs in total). In one study that reported results for 497 disc replacements, the type of prosthesis used was not stated. Of the 38 studies, 19 studies included patients who had at least one lumbar procedure prior to AIDR, including discectomies, nucleotomies, laminotomies, chemonucleolysis and thermocoagulation, and arthrodeses. Twenty three studies included patients who had lumbar AIDR at more than one level, including six studies in which patients underwent AIDR at three levels.

The mean age across the studies ranged from 18 to 71 years, and there were more females than males. One of the 38 studies did not specify its follow-up period; however, where reported, follow-up was longer than that reported for the comparative studies and ranged from the early postoperative period to 17.3 years. A total of 16 studies reported no losses to follow-up.

It should be noted that ten of the 38 studies reported one of the following scenarios: they had financial relationships which may indirectly relate to the manuscript; one or more of the authors was a consultant for the company producing the disc used in the study; one or more of the authors received corporate/industry funds in support of their work; or one or more of the authors received benefits or grants for personal or professional use from a commercial party related directly or indirectly to the subject of the manuscript.

Adverse events

The 38 included studies reported intraoperative and/or postoperative adverse events, and these are detailed in Table 48 (Appendix F). There were a total of 676 adverse events reported in the studies, which occurred across 2,817 patients; however, many of the events reported were not serious in nature. Commonly reported adverse events included vascular injury, infections and poor wound healing, and increased or continued radicular pain. With regard to the prosthesis, the most commonly reported adverse events were those relating to movement of the device (subsidence, migration, loosening, displacement or dislocation), with subsidence being the most frequently reported event. Major morbidities such as major vessel injury, neurologic damage and nerve root injury were rare, and there were no reports of any deaths as a result of lumbar AIDR procedures.

Is it effective?

Clinical outcomes

Perioperative outcomes

Five studies (four randomised controlled trials and one nonrandomised comparative study) were identified that compared perioperative outcomes for patients that underwent lumbar AIDR with patients that underwent ALIF (Blumenthal et al 2005; Schroven and Dorofey 2006), circumferential fusion (Sasso et al 2008; Zigler et al 2007) or PLF/PLIF (Berg et al 2009a) (Table 8).

Three studies reported that operative time was significantly shorter for lumbar AIDR patients compared with patients undergoing lumbar fusion, while one study reported no difference between the groups. Similarly, two studies reported that estimated blood loss was significantly lower during lumbar AIDR compared with circumferential fusion. In four studies, length of stay in hospital was shown to be significantly shorter following lumbar AIDR compared with lumbar fusion.

Table 8 Perioperative outcomes following lumbar AIDR and fusion procedures

Study	Lumbar AIDR					Lumbar fusion				
	Disc type	No. of patients	Operative time (mins)	EBL (ml)	LOS (days)	Fusion type	No. of patients	Operative time (mins)	EBL (ml)	LOS (days)
Level II studies										
Blumenthal 2005	CHARITÉ™	205	110.8 (47.7)	205 (211.7)	3.7 (1.18)[a]	ALIF	99	114 (67.9)	208.9 (283.9)	4.2 (1.99)
Zigler 2007	ProDisc®-L	161	121 (59.2)[a]	204 (231.3)[a]	3.5 (1.29)[a]	Circumferential spinal fusion	75	229 (75.9)	465 (440)	4.4 (1.54)
Berg 2009a	CHARITÉ™, ProDisc®-L or Maverick™	80	138 (48)[a]	560 (400)	4.4 (1.6)[a]	PLF or PLIF	72	162 (36)	444 (228)	5.9 (1.2)
Sasso 2008	FlexiCore™	50	82[a]	97[a]	2[a]	Circumferential spinal fusion	26	179	179	3
Level III-2 studies										
Schroven and Dorofey 2006	ProDisc®-L	14	Mean [Range] 93 [80-100]	100	Mean [Range] 3.85 [3-10]	ALIF	10	Mean [Range] 135 [100-180]	330	Mean [Range] 6.3 [5-9]

NOTES: All data is presented as Mean (SD) unless otherwise stated; ALIF = anterior lumbar interbody fusion; EBL = estimated blood loss; LOS = length of stay; PLF = posterolateral fusion; PLIF = posterior lumbar interbody fusion; [a]$p<0.05$ compared with lumbar fusion.

Oswestry disability index (ODI)

Five studies (four randomised controlled trials and one nonrandomised comparative study) were identified that compared ODI scores for patients that underwent lumbar AIDR with patients that underwent ALIF (Blumenthal et al 2005; Schroven and Dorofey 2006), circumferential fusion (Sasso et al 2008; Zigler et al 2007) or PLF/PLIF (Berg et al 2009a) (Table 9).

Three studies reported that patients in the lumbar AIDR group showed statistically greater improvements in ODI scores than lumbar fusion patients at various time points up to 1-year follow-up; however, none of the studies reported significant differences between the groups at 2- or 5-year follow-up.

ODI scores at 2- and 5-year follow-up were not significantly different in lumbar AIDR patients or ALIF patients who had undergone previous lumbar decompressive surgery, compared with those who had not undergone previous surgery (Geisler et al 2008a; Geisler et al 2009). In addition, the mean absolute improvement in ODI scores at 2-year follow-up was significantly lower in patients who underwent revision surgery (7.3 points) compared with patients who did not undergo revision surgery (26.4 points) ($p<0.0001$). Similarly, the relative improvement in ODI scores at 2-year follow-up was significantly lower in patients who underwent revision surgery (12.7%), compared with patients who did not undergo revision surgery (53%) ($p<0.0001$) (Geisler et al 2008b).

Table 9 Oswestry Disability Index (ODI) scores following lumbar AIDR and fusion procedures

Study	Lumbar AIDR			Lumbar fusion		
	Disc type	N	ODI score	Fusion type	N	ODI score
Level II studies						
Blumenthal 2005	CHARITÉ™		Mean (% improvement)	ALIF		Mean (% improvement)
		205	*Baseline* 50.6		99	*Baseline* 52.1
		197	*6 weeks* 37.7 (23.9)[a]		91	*6 weeks* 43.7 (12.7)
		189	*3 months* 29.9 (40.2)[a]		93	*3 months* 37.4 (25.7)
		189	*6 months* 27.5 (46.2)[a]		88	*6 months* 35.8 (30.8)
		186	*1 year* 26 (48.8)[a]		80	*1 year* 31.8 (37.9)
		185	*2 years* 26.3 (48.5)		82	*2 years* 30.5 (42.4)
		90	*5 years* 25 (50.5)		43	*5 years* 24 (53.9)
Zigler 2007	ProDisc®-L		Mean	Circumferential spinal fusion		Mean
		161	*Baseline* 63.4		75	*Baseline* 62.7
			6 weeks 42[a]			*6 weeks* 49
			3 months 36[a]			*3 months* 46
			6 months 35[a]			*6 months* 42
			1 year 34			*1 year* 40
			18 months 33			*18 months* 39
			2 years 34.5			*2 years* 39.8
Berg 2009a	CHARITÉ™, ProDisc®-L or Maverick™		Mean ODI % (SD)	PLF or PLIF		Mean ODI % (SD)
		80	*Baseline* 41.8 (11.8)		72	*Baseline* 41.2 (14.6)
			1 year 19.5 (18.7)[a]			*1 year* 24.9 (16.1)
			2 years 20.0 (19.6)			*2 years* 23.0 (17.0)
Sasso 2008	FlexiCore™		Mean	Circumferential spinal fusion		Mean
		44	*Baseline* 62		23	*Baseline* 58
		42	*6 weeks* 36		20	*6 weeks* 50
		39	*3 months* 30		19	*3 months* 32
		37	*6 months* 25		17	*6 months* 25
		35	*1 year* 18		17	*1 year* 26
		11	*2 years* 6		7	*2 years* 12
Level III-2 studies						
Schroven and Dorofey 2006	ProDisc®-L		Mean [range]	ALIF		Mean [range]
		14	*Baseline* 38.42 [25-49]		10	*Baseline* 38 [30-46]
			6 months 15.21 [10-25]			*6 months* 25 [15-30]
			1 year 12.5 [10-25]			*1 year* 21.4 [15-30]

NOTES: ALIF = anterior lumbar interbody fusion; ODI = Oswestry Disability Index; PLF = posterolateral fusion; PLIF = posterior lumbar interbody fusion;
[a]$p<0.05$ compared with lumbar fusion.

Success of procedure

Three randomised controlled trials were identified that compared the success of lumbar AIDR with that of ALIF (Blumenthal et al 2005), circumferential fusion (Zigler et al 2007) or PLF/PLIF (Berg et al 2009a).

Blumenthal et al (2005) reported that overall clinical success (defined as ≥15 pts in ODI vs baseline, no device failure requiring additional surgery, absence of major complications, and maintenance or improvement of neurological status) was achieved in 57.1 per cent of patients in the lumbar AIDR group and 46.5 per cent of the ALIF group (p=0.0001) at 2-year follow-up. At 5-year follow-up, overall clinical success was achieved in 57.8 per cent of patients in the lumbar AIDR group and 51.2 per cent of the ALIF group (Guyer et al 2009). ODI success, defined a ≥25 per cent improvement in ODI score, was achieved in 63.9 per cent of lumbar AIDR patients and 50.5 per cent of ALIF patients at 2-year follow-up (p=0.0038).

Zigler et al (2007) reported that overall clinical success, defined as achieving success in all of 10 primary endpoints (ODI, SF-36, device success, radiographic success (6 endpoints) and neurologic success), was achieved in 63.5 per cent of lumbar AIDR patients and 45.1 per cent of circumferential fusion patients at 2 years follow-up (p=0.0053). When an alternative FDA-approved definition of overall success was used, 53.4 per cent of lumbar AIDR patients and 40.8 per cent of circumferential fusion patients achieved success (p=0.0438). ODI success, defined as a ≥15 per cent improvement in ODI score, was achieved in 79.6 per cent of lumbar AIDR patients and 68.9 per cent of circumferential fusion patients at 1-year follow-up (p=NS), and 77.2 per cent of lumbar AIDR patients and 64.8 per cent of circumferential fusion patients at 2-year follow-up (p=0.039). ODI success, defined as a ≥25 per cent improvement in ODI score, was achieved in 69.1 per cent of lumbar AIDR patients and 54.9 per cent of circumferential fusion patients at 2-year follow-up (p=0.0396).ODI success, defined as a ≥15 point improvement in ODI score, was achieved in 57.7 per cent of lumbar AIDR patients and 53.2 per cent of circumferential fusion patients at - year follow-up (p=NS), and 67.8 per cent of lumbar AIDR patients and 54.9 per cent of circumferential fusion patients at 2- year follow-up (p=0.0449).

Berg et al (2009a) reported that ODI success was achieved in 44 per cent of lumbar AIDR patients and 49 per cent of PLF/PLIF patients at 1-year follow-up (p=NS), and 31 per cent of lumbar AIDR patients and 39 per cent of PLF/PLIF patients at 2-year follow-up (p=NS).

While a significant difference in overall success was reported between lumbar AIDR and ALIF (Blumenthal et al 2005) and circumferential fusion (Zigler et al 2007) at 2-year follow-up, it is uncertain whether the p-value was correctly calculated, and the difference may not actually be statistically significant.

The clinical expert opinion of the Advisory Panel suggested that the overall success of the procedure and ODI success were key clinical outcomes. As such, these outcomes were used to inform the cost-effectiveness analysis, and the relative risks for these outcomes are presented on page 58.

Device failure and need for reoperation

Three randomised controlled trials were identified that reported device failure and need for reoperation following lumbar AIDR compared with ALIF (McAfee et al 2006), circumferential fusion (Zigler et al 2007) or PLF/PLIF (Berg et al 2009a).

McAfee et al (2006) reported that 9 per cent (62/688) of patients required reoperation. The rate of revision at the index level was 8 per cent (52/589) in the lumbar AIDR group and 10 per cent (10/99) in the ALIF group (p=0.7041). In the lumbar AIDR group, 24 of the reoperations involved removal of the device (7 replacements with the same device, 7 revisions to anterior fusion, 8 revisions to circumferential fusion and 2 failed removals/posterior instrumented fusion) and 28 did not involve removal of the device (1 posterior supplemental fixation, 13 posterior instrumented fusions, 6 posterior decompressions plus instrumented fusion, and 8 posterior decompressions). In the ALIF group, one of the reoperations involved removal of the device (1 revision to circumferential fusion) and nine did not involve removal of the device (4 posterior instrumented fusions and 5 posterior decompressions plus instrumented fusions). Geisler et al (2008a) reported that the rate of reoperation was not significantly different in lumbar AIDR patients who had undergone previous lumbar decompressive surgery compared with those who had not undergone previous surgery. Similarly, the rate of reoperation was not significantly different in ALIF patients who had undergone previous lumbar decompressive surgery, compared with those who had not undergone previous surgery.

Berg et al (2009a) reported that within 2 years of surgery, reoperations were performed in 10 per cent (8/80) of the lumbar AIDR group and 10 per cent (7/72) of the PLF/PLIF group (excluding patients complaining of supposed screw/instrument irritation). In the lumbar AIDR group, 5 per cent (4/80) of patients underwent fusion at the index level, 2.5 per cent (2/80) underwent evacuation of haematoma, 1.2 per cent (1/80) underwent decompression and 1.2 per cent (1/80) underwent hernia repair. In the PLF/PLIF group, 7 per cent (5/72) of patients underwent operation at an adjacent level, 1.4 per cent (1/72) underwent decompression together with extraction of pedicular screws, and 1.4 per cent (1/72) underwent repair of a dural tear.

Zigler et al (2007) reported that device success, defined as the absence of any reoperation required for the modification or removal of implants and no need for supplemental fixation, was achieved in 96.3 per cent (155/161) of lumbar AIDR patients and 97.3 per cent (73/75)of circumferential fusion patients, at 2-year follow-up (p=NS). There were six patients in the lumbar AIDR group considered device failures (4 migration failures, 1 technical error and 1 case where a patient required supplemental fixation due to unresolved pain). There were two fusion patients who were considered device failures when both patients had unresolved pain requiring reoperation. Two additional patients in the fusion group had their posterior instrumentation routinely removed. Overall, the reoperation rate was 3.7 per cent for the lumbar AIDR group and 5.4 per cent for the fusion group.

The rate of reoperation (including replacement, removal with no replacement, supplementation and revision) was identified as a key clinical outcome. As such, this outcome was used to inform the cost-effectiveness analysis, and the relative risks for this outcome are presented on pages 61 and 62.

Pain

Four randomised controlled trials were identified that compared Visual Analog Score (VAS) pain scores for patients that underwent lumbar AIDR with patients that underwent ALIF (Blumenthal et al 2005), circumferential fusion (Sasso et al 2008; Zigler et al 2007) or PLF/PLIF (Berg et al 2009a) (Table 10).

Three studies reported that patients in the lumbar AIDR group showed statistically greater improvements in VAS pain scores than lumbar fusion patients at various time points up to 2-year follow-up; however, the one study that reported this time point showed no significant differences between the groups at 5-year follow-up.

VAS pain scores at 2- and 5-year follow-up were not significantly different in lumbar AIDR patients or ALIF patients who had undergone previous lumbar decompressive surgery compared with those who had not undergone previous surgery (Geisler et al 2008a; Geisler et al 2009). However, the mean absolute improvement in VAS pain scores at 2-year follow-up was significantly lower in patients who underwent revision surgery (20.8 mm), compared with patients who did not undergo revision surgery (42.9 mm) (p=0.0022). Similarly, the relative improvement in VAS pain scores at 2-year follow-up was significantly lower in patients who underwent revision surgery (23.4%), compared with patients who did not undergo revision surgery (59.1%) (p<0.0001) (Geisler et al 2008b).

Berg et al (2009a) reported 28 per cent (20/72) of patients in the PLF/PLIF group had their pedicular screws removed due to persistent or recurrent pain.

Table 10 Visual Analog Scale (VAS) pain scores following lumbar AIDR and fusion procedures

Study	Lumbar AIDR			Lumbar fusion		
	Disc type	N	VAS pain score	Fusion type	N	VAS pain score
Level II studies						
Blumenthal 2005	CHARITÉ™		Mean (improvement)	ALIF		Mean (improvement)
		205	*Baseline* 72		99	*Baseline* 71.8
		196	*6 weeks* 36.4 (35.9)[a]		92	*6 weeks* 44.1 (27.7)
		188	*3 months* 35.7 (35.7)[a]		93	*3 months* 44.5 (27.4)
		188	*6 months* 33.1 (39)[a]		87	*6 months* 43.9 (28.2)
		185	*1 year* 32.9 (39.1)[a]		79	*1 year* 40.4 (30.9)
		186	*2 years* 31.2 (40.6)		82	*2 years* 37.5 (34.1)
		90	*5 years* 29 (43)		43	*5 years* 27 (44.8)
Zigler 2007	ProDisc®-L		Mean	Circumferential spinal fusion		Mean
		161	*Baseline* 75		75	*Baseline* 74
			6 weeks 41			*6 weeks* 44
			3 months 38[a]			*3 months* 48
			6 months 40			*6 months* 42
			1 year 39			*1 year* 42
			18 months 39			*18 months* 43
			2 years 37			*2 years* 43
Berg 2009a	CHARITÉ™, ProDisc®-L or Maverick™		Mean (SD)	PLF or PLIF		Mean (SD)
		80	*Baseline* 62.3 (20.8)		72	*Baseline* 58.5 (21.7)
			1 year 25.5 (26.5)[a]			*1 year* 33.4 (26.8)
			2 years 25.4 (29.8)[a]			*2 years* 29.2 (24.6)
Sasso 2008	FlexiCore™		Mean	Circumferential spinal fusion		Mean
		44	*Baseline* 86		23	*Baseline* 82
		42	*6 weeks* 36		20	*6 weeks* 43
		39	*3 months* 39		19	*3 months* 33
		37	*6 months* 33		17	*6 months* 26
		35	*1 year* 24		18	*1 year* 32
		11	*2 years* 16		8	*2 years* 20

NOTES: ALIF = anterior lumbar interbody fusion; VAS = Visual Analog Scale; PLF = posterolateral fusion; PLIF = posterior lumbar interbody fusion; [a]$p<0.05$ compared with lumbar fusion.

Narcotic medication use

Two randomised controlled trials were identified that reported narcotic medication use following lumbar AIDR compared with ALIF (Blumenthal et al 2005) or circumferential fusion (Zigler et al 2007).

Blumenthal et al (2005) reported that during follow-up, 72.2 per cent (148/205) of lumbar AIDR patients used narcotic medication to control pain, compared with 85.9 per cent (85/99) of ALIF patients (p=0.0083). Of the patients that demonstrated clinical success at 2-year follow-up, 64 per cent (73/114) of lumbar AIDR patients remained on narcotics, compared with 80.4 per cent (37/46) of circumferential fusion patients (p=0.0428).

Zigler et al (2007) reported that at baseline, 84 per cent of patients in the lumbar AIDR group and 76 per cent of patients in the circumferential fusion group used narcotic medication for pain relief. Of the patients that demonstrated clinical success at 2-year follow-up, only 39 per cent of lumbar AIDR patients and 31 per cent of circumferential fusion patients remained on narcotics; however, in patients that did not achieve clinical success, narcotic usage remained relatively unchanged from baseline values (79% lumbar AIDR, 76% fusion).

The clinical expert opinion of the Advisory Panel suggested that the proportion of patients using narcotic medication to control pain was a key clinical outcome. As such, this outcome was used to inform the cost-effectiveness analysis, and the relative risks for this outcome are presented on page 59.

Patient satisfaction

Three randomised controlled trials were identified that reported patient satisfaction following lumbar AIDR compared with ALIF (Blumenthal et al 2005), circumferential fusion (Zigler et al 2007) or PLF/PLIF (Berg et al 2009a).

Blumenthal et al (2005) reported that at - year follow-up, 71.3 per cent of lumbar AIDR patients were satisfied with their treatment, compared with 59 per cent of ALIF patients (p=0.0559). At 2-year follow-up, 73.7 per cent of lumbar AIDR patients were satisfied with their treatment, compared with 53.1 per cent of ALIF patients (p=0.0011). When patients were asked whether they would have the same surgical treatment again, more lumbar AIDR patients answered 'yes' (73.4%) compared with ALIF patients (57.7%) at 1-year follow-up (p=0.0550). Similarly, at 2-year follow-up, significantly more lumbar AIDR patients answered 'yes' (69.9%) compared with ALIF patients (50%) (p=0.0062). Additionally, patient satisfaction at 2- and 5-year follow-up was not significantly different in lumbar AIDR patients or ALIF patients who had undergone previous lumbar decompressive surgery compared with those who had not undergone previous surgery (Geisler et al 2008a; Geisler et al 2009).

Zigler et al (2007) reported that VAS patient satisfaction scores were not significantly different in lumbar AIDR patients compared with circumferential fusion patients at 6-week, and 3-, 6-, 12-, and 1- month follow-up; however, at 24-month follow-up, patient satisfaction scores were significantly higher in lumbar AIDR patients (mean 76.7 mm, SD 29.2 mm) compared with circumferential fusion patients (mean 67.3 mm, SD 31.5 mm) (p=0.015). When patients were asked whether they would have the same surgical treatment again, significantly more lumbar AIDR patients answered 'yes' (81.6%) compared with circumferential fusion patients (63.8%) at 1-year follow-up (p=0.0004). Similarly, at 2-year follow-up, more lumbar AIDR patients answered 'yes' (81%) compared with circumferential fusion patients (69%); however, this was not statistically significant (p=0.1304).

Berg et al (2009a) reported that at 1-year follow-up, 77 per cent of lumbar AIDR patients were satisfied with their treatment, compared with 64 per cent of PLF/PLIF patients (p=0.072); at 2-year follow-up, 71 per cent of lumbar AIDR patients were satisfied with their treatment compared with 67 per cent of PLF/PLIF patients (p=0.586).

Work status

Three randomised controlled trials were identified that reported patient work status following lumbar AIDR compared with ALIF (Blumenthal et al 2005), circumferential fusion (Zigler et al 2007) or PLF/PLIF (Berg et al 2009a).

Blumenthal et al (2005) reported that at baseline, the combined employment rate (full-time plus part-time) was 53.2 per cent in lumbar AIDR patients and 57.6 per cent in ALIF patients. At 1-year follow-up, the combined employment rate was 58.4 per cent in lumbar AIDR patients and 62.5 per cent in ALIF patients (p=0.5302). At 2-year follow-up, 62.4 per cent of lumbar AIDR patients were employed, compared with 65 per cent of ALIF patients (p=0.6329), which represented an increase in employment of 9.2 per cent in the lumbar AIDR group and 7.4 per cent in the ALIF group. At 5-year follow-up, 65.6 per cent of lumbar AIDR patients were in full-time employment, compared with 46.5 per cent of ALIF patients (p=0.0403) (Guyer et al 2009). Similarly, 8 per cent of lumbar AIDR patients were on long-term disability, compared with 20.9 per cent patients in the ALIF group (p=0.0441) (Guyer et al 2009). Additionally, return to work rates at 2- and 5-year follow-up were not significantly different in lumbar AIDR patients or ALIF patients who had undergone previous lumbar decompressive surgery, compared with those who had not undergone previous surgery (Geisler et al 2008a; Geisler et al 2009).

Zigler et al (2007) reported that at baseline, the employment rate (full-time plus part-time) was 83.5 per cent in lumbar AIDR patients and 78.1 per cent in circumferential fusion patients. At 2-year follow-up, 92.4 per cent of lumbar AIDR patients were employed, compared with 85.1 per cent of fusion patients (p=0.0485).

Berg et al (2009a) reported that at baseline, 69 per cent of patients in both the lumbar AIDR and PLF/PLIF groups were on sick leave. However, after less than 3 months, 30 per cent (24/80) of the lumbar AIDR group had returned to work, compared with 18 per cent (13/72) of the PLF/PLIF group (p=0.102). At 1-year follow-up, 71 per cent of the lumbar AIDR group and 68 per cent of the PLF/PLIF group were back at work (full or part-time) (p=0.776), while at 2-year follow-up, 76 per cent of the lumbar AIDR group and 72 per cent of the PLF/PLIF group were back at work (p=0.750).

Quality of life

Three randomised controlled trials were identified that reported quality of life outcomes following lumbar AIDR compared with ALIF (Guyer et al 2009), circumferential fusion (Zigler et al 2007) or PLF/PLIF (Berg et al 2009a).

Guyer et al (2009) reported that at 2-year follow-up the mean improvement in SF-36 Physical Component Scores (PCS) from baseline was 14.2 points in the lumbar AIDR group, compared with 11.2 points in the ALIF group (p=NS). At 5-year follow-up, the mean improvement in SF-36 PCS from baseline was 12.6 points in the lumbar AIDR group, compared with 12.3 points in the ALIF group (p=NS).

Zigler et al (2007) reported that SF-36 success, defined as any improvement from baseline in the composite score of the mental and physical components, was significantly higher in lumbar AIDR patients compared with circumferential fusion patients at 6-week (72.1% vs 56.9%) (p=0.0183) and 3-month (86.6% vs 70%) (p=0.0036) follow-up; however, no significant differences between the groups were observed at 6-, 12-, 18- and 24-month follow-up.

Berg et al (2009a) reported that with respect to SF-36, lumbar AIDR patients had shown greater improvement in the domains of Role-Physical, Bodily Pain and Social Functioning at 1-year follow-up compared with PLF/PLIF patients; however, this difference was not seen at 2-year follow-up. Similarly, quality of life measured using the EuroQol Group 5-Dimension Self-Report Questionnaire (EQ5D) was significantly higher in lumbar AIDR patients (mean 0.71, SD 0.28) compared with PLF/PLIF patients (mean 0.63, SD 0.27) (p=0.046) at 1-year follow-up; however, this difference was not seen at 2-year follow-up.

Sexual function

One randomised controlled trial was identified that reported on sexual function following lumbar AIDR compared with PLF/PLIF (Berg et al 2009b).

Berg et al (2009b) reported that at baseline, 84 per cent (127/152) of patients reported disturbances in their sex life, with 34 per cent (51/152) reporting that their sex life was normal but caused some extra low back pain, 20 per cent (30/152) reporting that their sex life was normal but very painful, and 30 per cent (46/152) reporting that their sex life was severely restricted or prevented by low back pain. Overall sex life, measured using ODI item 8, was not significantly different in the lumbar AIDR and PLF/PLIF groups at baseline (p=0.40) or postoperatively (p=0.30); however, at 2-year follow-up, sex life according to ODI 8 had improved in both groups (p<0.001). This improvement correlated with both a decrease in back pain VAS (r=0.55, p<0.001) and an improvement in global assessment of back pain (r=0.55, p<0.001).

When sexual function was evaluated using a gender-specific questionnaire, at 2-year follow-up, 17 per cent (5/29) of men in the lumbar AIDR group reported an erection improvement and 7 per cent (2/29) reported an erection disturbance, compared with preoperative status. In the PLF/PLIF group, 4 per cent (1/27) of men reported an erection improvement and 19 per cent (5/27) reported an erection disturbance. In the lumbar AIDR group, 7 per cent (2/29) of men reported an orgasm improvement and 3 per cent (1/29) reported orgasm deterioration, compared with preoperative status. In the PLF/PLIF group, 4 per cent (1/27) of men reported an orgasm improvement and 26 per cent (7/27) reported orgasm deterioration. Retrograde ejaculation was reported in 10 per cent (3/29) of men in the lumbar AIDR group, compared with 4 per cent (1/27) of men in the PLF/PLIF group, at 2-year follow-up.

In women, at 2-year follow-up, 11 per cent (5/44) reported an orgasm improvement and 13 per cent (6/44) reported orgasm deterioration, compared with preoperative status. In the PLF/PLIF group, 8 per cent (3/38) of women reported an orgasm improvement and 18 per cent (7/38) reported orgasm deterioration. Inability to have children after surgery was reported in 87 per cent (39/44) of women in the lumbar AIDR group, compared with 90 per cent (36/39) of women in the PLF/PLIF group.

Radiographic outcomes

Range of motion

Two randomised controlled trials were identified that reported range of motion following lumbar AIDR compared with ALIF (Guyer et al 2009) or circumferential fusion (Auerbach et al 2009); however, neither study reported statistical comparisons between the two groups. A third study reported range of motion following lumbar AIDR; however, no corresponding data for lumbar fusion was provided (Sasso et al 2008).

Table 11 Range of motion (ROM) following lumbar AIDR and fusion procedures

Study	Lumbar AIDR			Lumbar fusion		
	Disc type	N	ROM	Fusion type	N	ROM
Level II studies						
Guyer 2009	CHARITÉ™	90	Mean index-level ROM Surgery at L4-L5 *Baseline* 8.7° *2 years* 7° *5 years* 6° Surgery at L5-S1 *Baseline* 7.6° *2 years* 5.7° *5 years* 6°	ALIF	43	Mean index-level ROM Surgery at L4-L5 *Baseline* 9.2° *2 years* 1.5° *5 years* 1° Surgery at L5-S1 *Baseline* 8.2° *2 years* 1.7° *5 years* 1.2°
Auerbach 2009	ProDisc®-L	155	Total lumbar ROM Surgery at L4-L5 *Baseline* 32° *2 years* 38.3° Surgery at L5-S1 *Baseline* 36.6° *2 years* 36.8°	Circumferential spinal fusion	45	Total lumbar ROM Surgery at L4-L5 *Baseline* 31.7° *2 years* 27.9° Surgery at L5-S1 *Baseline* 36.9° *2 years* 30.9°
Sasso 2008	FlexiCore™	44 42 44 42	Mean Angular rotation *Baseline* 2.8° *6 weeks* 3.8° Lateral bending *Baseline* 4.7° *6 weeks* 4.2°	Circumferential spinal fusion	NR	NR

NOTES: ALIF = anterior lumbar interbody fusion; NR = not reported; ROM = range of motion.

Other radiographic outcomes

Two randomised controlled trials (comprising three studies) were identified that reported on other radiographic outcomes following lumbar AIDR, ALIF (McAfee et al 2005; Guyer 2009) or circumferential fusion (Zigler et al 2007).

Zigler et al (2007) reported that of the patients that reached 2-year follow-up without reoperation, in the lumbar AIDR group three cases of device migration and one case of device subsidence (0.7%) were observed radiographically; however, none of these were clinically significant. No cases of radiolucency, loss of disc height, or spontaneous fusion were observed. In the circumferential fusion group, two cases of failure to achieve fusion (3%), five cases of loss of disc height (7.2%), and one case each of migration and radiolucency were reported.

McAfee et al (2005) reported that at 2-year follow-up, lumbar AIDR was significantly more effective than ALIF for restoring the height of the collapsed disc space at both L4–L5 (6.82 mm vs 4.52 mm) and L5–S1 (8.2 mm vs 5.98 mm) ($p<0.05$ for both). In addition, significantly less subsidence was identified following lumbar AIDR compared with ALIF at both L4–L5 (0.54 mm vs 1.3 mm) ($p=0.0206$) and L5–S1 (0.43 mm vs 0.97 mm) ($p=0.0208$) from 6 weeks to 24 months after surgery. At 5-year follow-up, changes in disc height were not significantly different in the lumbar AIDR and ALIF groups (decrease of 0.7 mm for both) ($p=0.9827$) (Guyer 2009).

What are the economic considerations?

Economic evaluation of new health care technologies is important when determining whether the new initiative offers additional benefits and at what cost. Economic evaluations are able to determine whether the new initiative is dominated by (or dominates) the existing technology, such that the costs are higher (lower) and the effectiveness is less (greater). Economic evaluation is particularly important when the new initiative offers health benefits at additional costs. Within a constrained health care budget, determining the additional cost that would be paid for a given health gain is important when ascertaining whether such incremental costs represent value for money.

The usual process for an economic evaluation is to determine: firstly, the incremental effectiveness, which is the additional benefits associated with the new technology relative to current practice; secondly, the incremental cost, which is the difference in costs between the new initiative and current practice; and finally, the incremental cost-effectiveness ratio (ICER), which can be calculated using the following ratio:

$$ICER = \frac{Cost_{New} - Cost_{Comparator}}{Effectiveness_{New} - Effectiveness_{Comparator}}$$

The ICER can then be compared to a threshold, or range of thresholds, to determine whether the health system should invest in the new technology.

If the technology is just as effective as the existing technology, then a cost-minimisation approach is warranted.

Objective

The objective of this section is to conduct an economic evaluation of AIDR. As suggested by the Advisory Panel, lumbar fusion is the most appropriate comparator for the cost-effectiveness analysis.

Search strategies

As mentioned in the clinical review, three of the HTAs included an economic evaluation of AIDR (MASO 2006; Vlayen et al 2006; WHTA 2008). Vlayen et al (2006) concluded that economic and cost information on AIDR was lacking, while WHTA (2008) identified two studies comparing the costs of AIDR with those of fusion (Guyer 2007 and Levin 2007).[7] A further study comparing the costs of AIDR with those of fusion (Patel 2008) was also identified by the clinical review.[8]

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[7] Guyer, R.D., Tromanhauser, S.G., Regan, J.J. 2007. 'An economic model of one-level lumbar arthroplasty versus fusion', Spine J, 7 (5), 558-562.

Levin, D.A., Bendo, J.A. et al, 2007. 'Comparative charge analysis of one- and two-level lumbar total disc arthroplasty versus circumferential lumbar fusion', Spine (Phila Pa 1976), 32 (25), 2905-2909.

[8] Patel, V.V., Estes, S. et al, 2008. 'Lumbar spinal fusion versus anterior lumbar disc replacement: the financial implications', J Spinal Disord Tech, 21 (7), 473-476.

Finally a cost-effectiveness analysis of AIDR compared with lumbar fusion (PLIF and PLF) was published in November 2010.[9]

Background –evidence of cost-effectiveness

Maso et al (2006) presented a cost analysis of lumbar AIDR compared to fusion procedures. Surgeon costs were based on the 2005 Ontario Schedule of Benefits Physician Claims (the average of a PLIF, an ALIF, and an ALIF with an approach by a separate surgeon). Hospital cost data was based on the Ontario Case Costing Initiative for 148 cases of lumbar fusion surgeries and five AIDRs. It was not reported whether re-operations were considered. The Ontario Province Government perspective was taken by the study and direct treatment costs only were considered. Costs were reported in Canadian dollars (year unknown). Overall it was found that AIDR (CAD$15,371 or A$19,370) was more costly than fusion (CAD$11,311 or A$14,254)[10].

Guyer et al (2007) presented a cost-minimisation analysis of lumbar AIDR (using a CHARITE disc) compared to three fusion procedures: ALIF using an iliac crest bone graft, ALIF using an INFUSE bone graft and LT-cages, and PLIF using an iliac crest bone graft. Resource use data and average charges for AIDR procedures were based on patient-level data from 71 hospitals in the United States, while for fusion procedures these were based on 1,145 claims from the Miliman Database from 2002 to 2003. The study estimated the rate of re-operations based on the published literature and multiplied the rate by the average cost of unsuccessful procedures and re-operations. Costs were reported in 2006 US dollars. Overall it was found that AIDR was less costly from both a hospital and payer (insurer) perspective. The total costs from a hospital perspective were US$16,601 (A$25,274) for lumbar AIDR, US$18,596 (A$28,311) for ALIF using an iliac crest bone graft, US$22,668 (A$34,511) for ALIF using an INFUSE bone graft and LT-cages, and US$22,662 (A$34,502) for PLIF using an iliac bone graft. The total costs from a payer perspective were US$17,614 (A$26,816) for lumbar AIDR, US$32,960 (A$50,180) for ALIF using an iliac crest bone graft, US$32,196 ($A49,017) for ALIF using an INFUSE bone graft and LT-cages, and US$35,052 (A$53,365) for PLIF using an iliac bone graft. Note that as the type of re-operation following each procedure required was not considered this may impact on the results.[11]

Levin et al (2007) presented a cost-minimisation analysis of one- and two-level lumbar AIDR compared to circumferential fusion. Resource use data and average charges were based on 53 randomised patients (36 received AIDR using ProDisc and 17 underwent circumferential fusion). As no re-operations due to surgical or implant complications were recorded, the cost of re-operations was not considered. The perspective of the study was not reported; however, indirect costs were not included. Costs were reported in 2006 US dollars. Overall it was found that one-level AIDR (US$35,592 or A$54,187) was less costly than circumferential fusion (US$46,280 or A$70,459), while two-level

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[9] Fritzell, P. et al. Cost effectiveness of disc prosthesis versus lumbar fusion in patients with chronic low back pain: randomized controlled trial with 2-year follow-up.

[10] Converted using Purchasing Power Parity AUD1.26 per CAD. Source: http://stats.oecd.org/ Table 4. PPPs and exchange rates.

[11] Converted using Purchasing Power Parity AUD1.52 per USD. Source: http://stats.oecd.org/ Table 4. PPPs and exchange rates.

AIDR (US$55,524 or A$84,533) was of similar cost compared to circumferential fusion (US$56,823 or A$86,510).[12]

Patel et al (2008) presented a cost analysis of one-level lumbar AIDR compared to the transforaminal approach (TLIF), ALIF and circumferential fusion. Resource use data and average charges were based on 40 patients (ten per group). The need for re-operations was based on published clinical trial data. The perspective of the study was not reported, however indirect costs were included. Costs were reported in US dollars (year unknown). When BMP was not considered, it was found that AIDR (US$27,972 or A$42,586) was less costly than TLIF (US$29,260 or A$44,547) and circumferential fusion (US$39,233 or A$59,730) but more costly than ALIF (US$26,767 or A$40,751). When BMP was considered, it was found that AIDR (US$27,972 or A$42,586) was less costly than all fusion procedures (TLIF US$34,660 or A$52,768, circumferential US$44,633 or A$67,952, and ALIF $32,167 or A$48,973).[13]

None of the above studies considered clinical effectiveness or the impact on quality of life explicitly.

Fritzell (2010) was the only study that considered quality of life and presented a cost-effectiveness analysis of lumbar AIDR compared to fusion (PLIF/PLF). The study reported the results from both the health care and societal perspective. The time horizon of the study was 2 years. Clinical effectiveness and quality of life (measured using EQ-5D) was based on Berg (2009a). Resource use data was based on cost diaries completed by patients involved in the RCT. Cost diaries were completed after 1, 3, 6, 12, 18 and 24 months. The cost of re-operations was included. Data on sick leave and employment was also captured. Costs were reported in 2006 Swedish Kroner (SEK). The study estimated that the mean health care cost per patient was SEK 147,750 (A$24,753) for AIDR and SEK 170,746 (A$28,605) for fusion.[14] The difference was statistically significant. The key driver of the difference was the cost of reoperations (mostly removal of implants) in the fusion group. The study also estimated that the mean QALY gain was 0.41 for AIDR and 0.40 for fusion. The difference was not statistically significant. Overall the study estimated that AIDR was both less costly and slightly more effective than fusion. However, the authors cautioned that there was a high level of uncertainty with these results, especially in terms of quality of life. The authors also found that excluding re-operation costs significantly reduced the cost difference between the study groups.

Rationale for the cost-effectiveness analysis

As suggested by the Advisory Panel, lumbar fusion is the most appropriate comparator for the cost-effectiveness analysis.

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[12] Converted using Purchasing Power Parity AUD1.52 per USD. Source: http://stats.oecd.org/ Table 4. PPPs and exchange rates.

[13] Converted using Purchasing Power Parity AUD1.52 per USD. Source: http://stats.oecd.org/ Table 4. PPPs and exchange rates.

[14] Converted using Purchasing Power Parity AUD0.17 per SEK. Source: http://stats.oecd.org/ Table 4. PPPs and exchange rates.

The Advisory Panel suggested that the proportion of patients using narcotic medication to control pain is a key clinical outcome. Two other key clinical outcomes reported in the literature include the proportion of patients who achieve overall success and the proportion of patients who achieve ODI success (≥25% improvement in ODI at 2 years).

As previously discussed in the clinical review, a significant difference in overall success was reported between lumbar AIDR and ALIF (Blumenthal 2005) and circumferential fusion (Zigler 2007) at 2 years post-surgery (see p. 35); however, it is uncertain whether the *p*-value was correctly calculated and the difference may not actually be statistically significant (see Table 14). Furthermore the definition of overall success was inconsistently defined across the RCTs, which hinders synthesis and interpretation of the results.

A significant difference in ODI success was not found between lumbar AIDR and lumbar fusion at 2 years across three RCTs (Berg 2009a, Zigler 2007 and Blumenthal 2005), although the results were borderline in favour of AIDR compared to circumferential fusion (see p. 35 and Table 15).

A significant difference in the proportion of patients using narcotic medication to control pain was found between lumbar AIDR and lumbar fusion at 1 year (Blumenthal 2005) but not 2 years (Zigler 2007) (see p. 39 and Table 16). Unfortunately the statistically significant result may be driven by a pre-existing difference at baseline, but this data was not reported. One RCT also reported a statistically significant difference preoperatively versus postoperatively for those who achieved overall success, but not for those who did not achieve overall success (Zigler 2007) (see Table 17).

No significant difference in the complication rates overall was reported; however, subsequent analysis found significant differences in the rate of re-operations, in particular, a decreased rate of removal of hardware with AIDR compared to PLF and circumferential fusion, and an increased rate of supplemental fixation compared to circumferential fusion (see Table 18 to Table 22).

Improvements in quality of life measured with SF-36 was found for AIDR when compared to PLF/PLIF (Berg 2009a), ALIF (Blumenthal 2005, reported by Guyer 2009), and circumferential fusion (Zigler 2007). However, these differences were not significant at 2 years post-surgery. No difference in quality of life measured using EQ-5D was found between AIDR and PLF or PLIF preoperatively or at 2 years postoperatively, but a statistically significant improvement in quality of life was found with AIDR 1 year postoperatively (Berg 2009a). However the difference at 1 year may be driven by the small difference in quality of life at baseline. The data was not presented for patients achieving ODI success or failure, or undergoing re-operations separately, which highly limits the applicability to the model and the other fusion procedures. Consequently only QALYs experienced by patients treated with AIDR compared to PLF and PLIF (ignoring whether the patient achieved operative success or failure) were estimated.

Thus the economic evaluation estimated:

- the incremental cost of AIDR compared to each of the fusion approaches and fusion overall
- the incremental costs per additional overall success at 2 years with AILF and circumferential fusion compared to AIDR

- the incremental costs per additional ODI success at 2 years with ALIF, PLIF, PLF and circumferential fusion compared to AIDR

- the incremental costs per patient discontinuing narcotics at 2 years with AILF and circumferential fusion compared to AIDR

- the incremental costs per QALY gained for PLF and PLIF compared to AIDR.

As the Advisory Panel suggested that lumbar fusion (ie all fusion approaches used in Australia) is the most appropriate comparator, the incremental cost-effectiveness ratios were also estimated for all fusion approaches based on a weighted average of the cost-effectiveness of each approach. The relative risks were set as one (no difference) where efficacy data was missing and the proportion of patients receiving each fusion approach was based on MBS claims data (see p. 4).

Estimates of cost-effectiveness were based on point estimates of efficacy. This may not be appropriate if MSAC considers AIDR to be non-inferior in terms of the clinical outcome measures or the rates of re-operations.

If MSAC considers that AIDR is non-inferior compared to the fusion approaches in terms of success but not in terms of the rate of re-operations, then the total costs accounting for the rate of re-operations should only be considered (Table 33).

If MSAC considers that AIDR is non-inferior compared to the fusion approaches in terms of both success and the rate of re-operations, only the initial costs of surgery (Table 30) should be considered.

Assumptions

- Patients are treated with either lumbar AIDR or lumbar fusion only after non-surgical interventions have failed.

- For both lumbar AIDR and lumbar fusion there are a number of surgical approaches, which subsequently impacts on the costs and benefits of the interventions. For lumbar AIDR an anterior approach is mainly used in Australia, while for lumbar fusion either a posterior (for PLF or PLIF) or anterior approach (for ALIF) is used. Supplemental fixation using posterolateral fusion may also be considered with posterior interbody fusion (PLF+PLIF, referred to as combined fusion) and anterior interbody fusion (PLF+ALIF, referred to as circumferential fusion) is also considered. The transforaminal (TLIF) approach for both lumbar fusion and lumbar AIDR, and the posterior approach to lumbar AIDR, were not considered as these approaches are rarely used in Australia at present (see Table 12).

Table 12 Surgical approaches in Australia

Surgical approach	Lumbar AIDR	Lumbar fusion		
		Posterolateral fusion	Interbody fusion	Supplemental fixation (Interbody + posterolateral)
Posterior	Not currently used in Australia	✓	✓	✓
Anterior transforaminal	✓ Not considered by economic evaluation	×	✓	✓

- Successful surgery was defined as: patients who achieve overall success (as defined in the clinical trial), patients who achieve ODI success (>25% improvement in ODI at two years follow-up), or patients who discontinue narcotic medication. Re-operations were also considered when estimating costs (ie replacement15, removal with no replacement, supplementation16, revision 17 or other re-operation18). Other definitions of success, such as absence of major complications, neurological status, radiological success and SF-36, were not considered because there is likely to be a high level of correlation between ODI success and device success and these other definitions of success. There is a small potential for some patients to achieve ODI success even though they experience replacement or revision; however, this is likely to be rare. Geisler et al (2008b) found that the relative improvement in ODI scores at 2-year follow-up was significantly lower in patients who underwent revision surgery (12.7%) compared to patients who did not undergo revision surgery (53%).
- Only one re-operation is conducted.
- All AIDR devices were assumed to be similar in effectiveness.
- All types of bone grafts were assumed to be similar in effectiveness.

Structure of the economic evaluation

A Markov model was developed to synthesise data from a variety of sources. The general structure of the model is shown in Figure 3. Following the decision to treat the patient surgically, patients receive either lumbar AIDR or lumbar fusion. If the patients receive lumbar AIDR then this is always taken from an anterior approach. If the patients receive lumbar fusion the most appropriate of the following approaches (as defined by the surgeon) is used: an interbody graft only from an anterior approach (ALIF); an interbody graft only from a posterior approach (PLIF); a posterolateral graft only from a posterior approach (PLF); anterior interbody fusion with supplemental fixation (CIRC); or posterior interbody fusion with supplemental fixation (COMB).

[15] Removal with replacement to either AIDR or fusion

[16] Implantation of additional instrumentation without removal of original device (ie posterolateral fusion).

[17] Any surgical procedure done to modify the original implant without removal of the entire implant.

[18] Any subsequent surgical procedure to the site not involving the implant, such as a decompression.

All patients receive an initial procedure with the appropriate approach. If the initial surgery is considered a success, patients enter the 'successful surgery' health state.

If surgery is considered a failure, patients enter the 'failed surgery' health state in which patients may require: replacement (with a new AIDR or fusion), hardware removal without replacement, supplemental fixation, revision of the device, or another type of re-operation at the index level. Removal without replacement is not an option for AIDR and interbody fusions. Supplemental fixation is not an option for PLF, circumferential (CIRC) or combination (COMB) fusions. Due to a lack of available data, for approaches other than AIDR, hardware replacement was assumed to involve the same approach as the initial approach. The Advisory Panel advised that in practice it would be rare that following device failure an AIDR device would be replaced with a new AIDR device; consequently, it was assumed that no AIDR devices are replaced with a new AIDR device and that the split across fusion approaches was similar to the split for initial surgery (excluding PLF).

After re-operation patients enter the 'successful surgery post re-operation' health state.

Other adverse events were not explicitly considered, such as infections, vascular injury, and excessive blood loss. The costs of many adverse events are likely to be captured by longer operating times and length of stay in hospital. Furthermore there was little evidence of differences in adjacent segment degeneration between lumbar AIDR and lumbar fusion. Consequently re-operations on adjacent levels were not considered in the model (Freeman and Davenport 2006, and Harrop et al 2008).

Death from complications or other causes was not considered.

Perspective

A health care cost perspective was used in the cost analysis, which includes all health care costs regardless of who incurs the cost, such as patients. Productivity impacts (such as early return to work) were not included.

Time horizon

The time horizon of the analysis was 2 years.

Economic evaluation outcomes

The primary measure of health outcomes was the proportion of patients achieving overall success, ODI success or discontinuing narcotics. A secondary measure of health outcome was QALYs gained (which was calculated for AIDR relative to PLIF or PLF only, due to data availability).

Methods to generate the results

The Markov cohort model had a cycle length of 1 month. For each cycle, all costs and outcomes in each health state were evaluated, and multiplied by the likelihood of an individual progressing into that health state. By summing these costs and outcomes, the expected costs and outcomes associated with using the two technologies were estimated. No half-cycle correction was applied since the cycle length was relatively short and a half cycle correction would halve the cost of the procedure (due to the significant upfront costs). The model was constructed in TreeAge Pro 2011.

Discounting

Due to the short time horizon, no discounting was applied.

Figure 3 Structure of the economic evaluation

Estimates of fusion approaches

The proportion of patients undergoing each treatment approach was based on MBS claims data (July 2005 to August 2010) (see Appendix H). These data refer to 2,748 procedures in the lumbar region.[19] Of patients undergoing lumbar fusion – interbody only, posterolateral only, combination (PLIF+PLF) and circumferential (ALIF+PLF) approaches were performed in 48 per cent, 24 per cent, 27 per cent and 1 per cent of patients, respectively. The split between posterior (PLIF) and anterior approaches (ALIF) when undertaking an interbody graft only (excluding circumferential and combination fusion) was approximately 23 per cent and 77 per cent, respectively. The overall split between posterior and anterior approaches when undertaking any interbody graft (including those involving supplemental fixation ie combination or circumferential fusion) was 49 per cent and 51 per cent, which concurred with the Advisory Panel estimates of 50 per cent and 50 per cent.

Table 13 Surgical approaches in Australia based on MBS data

Surgical approach for the lumbar spine[1]	Number of procedures (same patient, same day)	%
AIDR only[2]	219	8%
Spinal fusion only	2,418	88%
Posterolateral fusion (PLF) [3]	545	(20%)
Posterior interbody fusion (PLIF)[4]	229	(8%)
Anterior interbody fusion(ALIF) [5]	864	(31%)
Combination (PLF + PLIF)[6]	624	(23%)
Circumferential (PLF + ALIF)[7]	29	(1%)
Posterior approach but unknown fusion technique[8]	62	(2%)
Other combination of spinal fusion techniques	65	(2%)
Combination of AIDR and spinal fusion techniques	111	4%
Total	2,748	100%

[1] Lumbar procedures are indicated by MBS item number 20630
[2] Procedures involving MBS items 48691, 48692 or 48693
[3] Procedures involving MBS items 48648 or 48651
[4] Procedures involving MBS items 48654 or 48657
[5] Procedures involving MBS items 48660, 48663, 48666, 48669, 48672 or 48675
[6] Procedures involving MBS items (48648 or 48651) AND (48654 or 48657)
[7] Procedures involving MBS items (48648 or 48651) AND (48660, 48663, 48666, 48669, 48672 or 48675)
[8] Procedures involving MBS items 40321, 40324, 48642, or 48645

Estimates of overall success, ODI success and re-operations

Overall success

Overall success was measured by two RCTs, but each study defined overall success differently. Blumenthal et al (2005) defined overall success as achieving success in four endpoints: ≥15 pts in ODI versus baseline; no device failure requiring additional surgery; absence of major complications; and maintenance or improvement of neurological status. While Zigler et al (2007) defined overall success as achieving success in ten endpoints: ODI, SF-36, device success, radiographic success (six endpoints) and neurologic success. An alternative, FDA-approved definition of overall success was also reported. This latter definition was used as the input in the economic evaluation.

[19] Identified based on the MBS item claimed for initiation of anaesthesia. Lumbar procedures are indicated by MBS item number 20630.

Across the two RCTs reporting overall success (using the FDA-approved definition only) the probability of overall success with AIDR is 55.5 per cent (95% CI: 50.4%, 60.6%) (summarised using the inverse variance method). Given the differences in the definition of overall survival, taking an average across the two RCTs may be inappropriate and sensitivity analysis was conducted on this parameter. The relative risk of overall success was higher for AIDR (see Table 14). None of the relative risks were statistically significant.

With no further information regarding overall success of PLF, PLIF and combination fusion (PLF+PLIF) compared to AIDR, the relative risk of overall success was assumed to be 1.

Table 14 Overall success at 2 years

			AIDR			Fusion			Relative risk# (95% CI)
RCT	n	Fusion type	N	N	%	n	N	%	
Blumenthal 2005	304	ALIF	117	205	57.1%	46	99	46.5%	0.81 [0.64, 1.04]
Zigler 2007									
Sponsor defn	236	Circumferential	102	161	63.5%	34	75	45.1%	0.72 [0.54, 0.94]
FDA defn^	236	Circumferential	86	161	53.4%	31	75	40.8%	0.77 [0.57, 1.05]
Average for AIDR*					55.5%				

#fusion versus AIDR; * inverse variance method; ^used in evaluation

ODI success

ODI success was defined as a ≥ 25 per cent improvement in ODI at 2 years in three RCTs (Berg 2009a, Blumenthal 2005 and Zigler 2007). Across these three RCTs the probability of ODI success with AIDR was 53.1 per cent (95%CI: 48.7%, 57.6%) (summarised using the inverse variance method). The relative risk of ODI success was higher for ALIF and circumferential fusion, but lower for PLF and PLIF (see Table 15). None of the relative risks were statistically significant.

With no further information regarding ODI success of combination fusion (PLF+PLIF) compared to AIDR, the relative risk of ODI success for combination fusion was assumed to be 1.

Table 15 ODI Success at 2 years

			AIDR			Fusion			Relative risk# (95% CI)
RCT	n	Fusion type	N	N	%	n	N	%	
Berg 2009a	152	PLF (44) or PLIF (28)	25	80	31%	28	72	39%	1.24 [0.81, 1.92]
Blumenthal 2005	304	ALIF	99	205	48.50%	42	99	42.40%	0.88 [0.67, 1.15]
Zigler 2007	236	Circumferential	111	161	69.10%	41	75	54.90%	0.79 [0.63, 1.00]
Average for AIDR*					53.1%				

#fusion versus AIDR; * inverse variance method

Narcotics

Two RCTs reported the proportion of patients who used narcotic medication to control pain at 2 years following treatment with AIDR or fusion.

Blumenthal (2005) reported a statistically significant difference between AIDR and fusion postoperatively (at 1 year) in all patients and those who achieved overall success

(at 1 year), in favour of AIDR. It is worth noting that these differences may be driven by pre-existing differences at baseline; however, preoperative narcotic medication use was not reported.

Zigler (2007) reported no difference in narcotic medication use between AIDR and fusion preoperatively, postoperatively (at 2 years) and regardless of whether the patients achieved overall success (see Table 16). However, a statistically significant decrease in narcotic medication use postoperatively was reported for all patients who achieved overall success, but not for those who did not achieve overall success (see Table 17).

Table 16 Proportion of patients who used narcotic medication to control pain at 2 years

	AIDR			Fusion			Relative risk# (95% CI)
RCT	n	N	%	n	N	%	
Blumenthal 2005 (ALIF)							
Preoperative	NR	205	NR	NR	205	NR	-
Postoperative (achieved OS)	73	114	64%	37	46	80.4%	1.26 [1.03, 1.53]
Postoperative (did not achieve OS)	75	91	82%	48	53	91%	1.10 [0.97, 1.25]
Postoperative (all)	148	205	72.2%	85	99	85.9%	1.19 [1.06, 1.34]
Zigler 2007 (Circumferential)							
Preoperative	135	161	84%	57	75	76%	0.91 [0.78, 1.05]
Postoperative (achieved OS)	40	102	39%	11	34	31%	0.82 [0.48, 1.42]
Postoperative (did not achieve OS)	46	59	79%	31	41	76%	0.97 [0.78, 1.21]
Postoperative (all)	86	161	53%	42	75	56%	1.05 [0.82, 1.34]

OS = overall success; #fusion versus AIDR; * inverse variance method

Table 17 Proportion of patients who used narcotic medication to control pain at 2 years (combined data)

Time period	N	N	%	Relative risk# (95% CI)
Preoperative	192	236	81%	
Postoperative (achieved OS)	50	136	37%	0.45 [0.36, 0.57]
Postoperative (did not achieve OS)	77	100	77%	0.95 [0.84, 1.07]

#postoperative versus preoperative
Source: Zigler (2007)

In the economic evaluation it was assumed that preoperatively a patient has a 81 per cent risk of requiring narcotic medication for control of pain based on Zigler (2007). If a patient achieves overall success then they have a 37 per cent (95%CI: 81%*0.36=29%, 81%*0.57=46%) risk of requiring narcotic medication for control of pain. This was applied to treatment with AIDR and the fusion approaches where estimates of overall success at 2 years were available.

Re-operations

Failure at the index level can occur for a variety of reasons and the rate of re-operation varies depending on the device used and approach taken. For AIDRs, reasons for re-operation include subsistence, migration, displacement, pain or vertebral end plate fracture. For fusions, reasons for re-operation include non-union/arthrodis, pain or vertebral end plate fracture. Technical failures may also result in re-operations. Patients may also require or request removal of a posterolateral device (used in PLF and circumferential fusion) due to irritation or pain.

Overall 1.8 per cent of AIDR devices were replaced with either a new AIDR device or a fusion device, after conservatively including all four fusions at the index level recorded by Berg (2009a) (see Table 18). The Advisory Panel advised that in practice it would be rare that following device failure an AIDR device would be replaced with a new AIDR

device; consequently it was assumed that no AIDR devices are replaced with a new AIDR device and that the split across fusion approaches were similar to the split for initial surgery (excluding PLF).

The relative risk of a fusion device being replaced compared to an AIDR device was lower for all fusion approaches; however, none of the relative risks were statistically significant. With no further information regarding replacement of combination fusion compared to AIDR, the relative risk of replacement for combination fusion was assumed to be 1. Due to a lack of available data, hardware replacement of a fusion device was assumed to involve the same approach as the initial approach.

No AIDR or ALIF devices were removed without replacement, and presumably no PLIF devices were removed due to the need for something to be placed between the vertebrae. However, hardware was removed from patients who received PLF (47.7%) or circumferential fusion (3.6%) (see Table 19). With no further information regarding removal without replacement of combination fusion compared to AIDR, the probability of removal was assumed to be 0 (ie the relative risk of removal without replacement for combination fusion was assumed to be 1).

Both AIDR and interbody fusion (PLIF and ALIF) devices can be supplemented with further fixation with PLF, whereas circumferential, combination and PLF cannot be supplemented with further fixation with PLF. Overall 3.2 per cent of AIDR devices received supplemental fixation, after conservatively including all four fusions at the index level recorded by Berg (2009a). The relative risk of supplemental fixation compared to an AIDR device was higher for ALIF but lower for PLIF and circumferential fusion (see Table 20). None of the relative risks were statistically significant.

Revisions of a device not involving replacement, supplementation or removal were rare, with only 0.8 per cent of AIDR procedures and no fusion procedures involving revision (see Table 21). Finally, a variety of other re-operations at the index level not involving the device itself may be required. Overall 3.6 per cent of AIDR devices required further re-operations. The relative risk of any of the fusion approaches requiring further re-operation compared to an AIDR devices was lower (see Table 22). None of the relative risks were statistically significant. With no further information regarding revision and other re-operations of combination fusion compared to AIDR, the relative risks were assumed to be 1.

Re-operations on the adjacent level or multiple levels are also possible although these are less common. Berg (2009a) was the only study that reported re-operations on an adjacent or multiple levels (5 out of 152). The actual rate of adjacent and multiple level re-operations is unknown since there is a shortage of longer-term observational studies (see p. 36).

In the economic evaluation it was assumed that all patients experiencing re-operation did not achieve overall or ODI success. Thus the probability of re-operations at 2 years among all patients was divided by the proportion of patients who did not achieve overall or ODI success in order to estimate the probability of re-operations at 2 years among patients who did not achieve overall or ODI success. These estimates were then converted into 1-month probabilities for application in the model.

Table 18 Replacement

RCT	n	Fusion type	AIDR			Fusion			Relative risk# (95% CI)
			n	N	%	n	N	%	
Berg 2009a	152	PLF (44) or PLIF (28)	4 fusions at index level, unclear whether replacement or supplementation**	80	5.0%	0^	72	0%	0.12 [0.01, 2.25]
Blumenthal 2005*	304	ALIF	1 to AIDR, 1 to anterior interbody, 1 to circumferential	205	1.5%	1 to circum-ferential	99	1.0%	0.69 [0.07, 6.55]
Sasso 2008	76	Circum-ferential	1 to AIDR	50	2.0%	0	26	0.0%	0.67 [0.07, 6.32]***
Zigler 2007	236	Circum-ferential	1 fusion, probably circumferential	161	0.6%	0	75	0.0%	
Average for AIDR****					1.8%				

#fusion versus AIDR; * reported in McAffe (2006); **included to be conservative; ^ 5 AIDR at adjacent level; *** risk ratio, mantel haenszel method, fixed effects, heterogeneity: Chi² = 0.00, df = 1 (p = 0.96); I² = 0%; test for overall effect: Z = 0.35 (p = 0.73); **** weighted average

Table 19 Removal with no replacement

RCT	n	Fusion type	AIDR			Fusion			Rate of removal for fusion
			n	N	%	n	N	%	
Berg 2009a	152	PLF (44) or PLIF (28)	0	80	0.0%	21	72 (44 PLF)**	47.7%*	47.7%**
Blumenthal 2005*	304	ALIF	0	205	0.0%	0	99	0.0%	NA
Sasso 2008	76	Circum-ferential	0	50	0.0%	5	26	19.2%	3.6%***
Zigler 2007	236	Circum-ferential	0	161	0.0%	2	75	2.7%	
Average for AIDR					0.0%				

*reported in McAffe (2006); **assuming all were PLF cases; ***inverse variance method

Table 20 Supplementation

RCT	n	Fusion type	AIDR			Fusion			Relative Risk# (95% CI)
			n	N	%	n	N	%	
Berg 2009a	152	PLF (44) or PLIF (28)	4 fusions at index level, unclear whether replacement or supplementation**	80	5.0%	0	72 (28 PLIF)	0.0%***	0.31 [0.02, 5.59]##
Blumenthal 2005*	304	ALIF	10 supplemental fixation/ instrumental fusion without device removal	205	4.9%	9 supplemental fixation/ instrumental fusion without device removal	99	9.1%	1.86 [0.78, 4.44]
Sasso 2008	76	Circum-ferential	1 instrumented posterior fusion	50	2.0%	0	26	0.0%	0.67 [0.07, 6.32]^^
Zigler 2007	236	Circum-ferential	1 supplemental fixation	161	0.6%	0	75	0.0%	
Average for AIDR^					3.2%				

#fusion versus AIDR; ## of PLIF cases; *reported in McAffe (2006); **included to be conservative; ^ weighted average; ^^ risk ratio, mantel haenszel method, fixed effects, heterogeneity: Chi² = 0.00, df = 1 (p = 0.96); I² = 0% Test for overall effect: Z = 0.35 (p = 0.73)

Table 21 Revision

RCT	n	Fusion type	AIDR			Fusion			Relative Risk# (95% CI)
			n	N	%	n	N	%	
Berg 2009a	152	PLF (44) or PLIF (28)	0	80	0.0%	0	72	0.0%	NA
Blumenthal 2005*	304	ALIF	0	205	0.0%	0	99	0.0%	NA
Sasso 2008	76	Circum-ferential	0	50	0.0%	0	26	0.0%	NA
Zigler 2007	236	Circum-ferential	1 technical error 3 migration	161	2.5%	0	75	0.0%	0.24 [0.01, 4.34]
Average for AIDR***					0.8%				

#fusion versus AIDR; *reported in McAffe (2006); ***weighted average

Table 22 Other reoperation

RCT	n	Fusion type	AIDR			Fusion			Relative risk# (95% CI)
			n	N	%	n	N	%	
Berg 2009a	152	PLF (44) or PLIF (28)	1 decompression 2 haematoma 1 hernia repair	80	5.0%	1 dural tear	72	1.4%	0.28 [0.03, 2.43]
Blumenthal 2005*	304	ALIF	9 vessel injury	205	4.4%	2 vessel injury	99	2.0%	0.46 [0.10, 2.09]
Sasso 2008	76	Circum-ferential	2 radicular leg pain 1 hematoma 1 vertebral end plate fracture 1 vascular injury	50	10.0%	0	26	0.0%	0.98 [0.26, 3.77]**
Zigler 2007	236	Circum-ferential	0	161	0.0%	2 unknown reason and treatment	75	2.7%	
Average for AIDR***					3.6%				

#fusion versus AIDR; *reported in McAffe (2006); ** risk ratio, mantel haenszel method, fixed effects, heterogeneity: Chi² = 3.82, df = 1 (p = 0.05); I² = 74%, test for overall effect: Z = 0.02 (p = 0.98); ***Weighted average

Utility weights

Quality of life measured using multi-attribute utility instruments, such as EQ-5D, was only collected by Berg (2009a) (see Table 23).[20]

An improvement in quality of life was not found for AIDR when compared to PLF and PLIF pre-operatively or at 2 years postoperatively, but was statistically different in favour of AIDR at 1 year postoperatively (Berg 2009a). However, the difference at 1 year may be driven by the small difference in quality of life at baseline. To account for this difference the average utility weight across the two treatment arms was used as the baseline utility weight (0.39) and then the monthly growth rate for each treatment arm was applied to estimate the utility weight over time. Sensitivity analysis was conducted on this approach by directly applying the utility weights for each treatment in cycle 1, 12 and 24 and interpolating the utility weights in the intervening cycles.

[20] It is unknown whether the data was age-weighted.

Table 23 Quality of life

Time period	AIDR	PLF/PLIF	*p*-value
Preoperative	0.42 ± 0.31	0.36 ± 0.33	0.167
1 year postoperative	0.71 ± 0.28	0.63 ± 0.27	0.046
Growth per month	0.0242	0.0225	
2 years postoperative	0.67 ± 0.33	0.69 ± 0.25	Not significant
Growth per month	-0.0033	0.0050	

Source: Berg et al (2009a).

Estimates of costs

The estimated costs of lumbar AIDR and lumbar fusion were taken from a number of sources. These included the Medicare Benefits Schedule (MBS May 2010), Australian Refined Diagnostic Related Group (AR-DRG) (Version 5.1 round 12 – Private), and the Prosthesis List (August 2010). Resource use and MBS item numbers were determined by the Advisory Panel and analysis of MBS claims data provided by the Department of Health and Ageing. MBS average co-payment data was also provided by the Department of Health and Ageing.

Implant costs

Table 24 describes the device costs for each procedure. For all types of fusion surgery excluding ALIF, it was assumed that patients receive a pedicle screw system (four multi-axial screws per level, four set screws per level, two rods). It was also assumed that ALIF patients also receive one anterior cage and 50 per cent receive one plate, both PLIF patients and combination (PLF+PLIF) patients receive two posterior interbody cages, and circumferential (PLF+ALIF) patients receive one anterior interbody cage and 30 per cent receive one plate. Some PLF and circumferential (PLF+ALIF) patients may also receive a crosslink; however, this was not included and consequently the results favour fusion over AIDR. Femoral ring allografts were also not considered as allografts are rare in Australia (Advisory Panel). The cost of devices were based on the average minimum benefit across all available brands listed in the August 2010 Prostheses List.[21] Sensitivity analysis was conducted on the unit cost of the AIDR device.

[21] Department of Health and Ageing, August 2010 Prostheses List. Available: http://www.health.gov.au/internet/main/publishing.nsf/content/health-privatehealth-prostheseslist.htm

Table 24 Device costs

Device	Unit cost	Units required	Total cost	Source*
AIDR				
Maverick	$9,550.00			MC585
Flexicor	$9,550.00			SK459
Prodisc	$9,550.00			SY327 to SY329
In Motion	$9,550.00			DY356 and DY359
Average	$9,550.00	1	$9,550.00	
Fusion – ALIF				
Anterior interbody cage	$3,600.00	1	$3,600.00	SV010
Plate	$2,317.65	0.5	$1,158.82	Average of AJ032, JJ518, LH363, MC610, MC612, MC661, MC819, SK488, SX024, SY139, ZI518, ZI519, DP828, DP829, NV033, NV035, NV038
Total			$4,758.82	
Fusion – PLIF and Combination (PLF+PLIF)				
Multi-axial screw	$1,316.73	4	$5,266.91	Average of neurosurgical, group 1b
Set screw	$168.40	4	$673.59	Average of neurosurgical, group 2b
Rod	$450.49	2	$900.99	Average of neurosurgical, group 7a
Posterior interbody cage	$3,000.00	2	$6,000.00	SV012 and SU223
Total			$12,841.49	
Fusion – PLF				
Multi-axial screw	$1,316.73	4	$5,266.91	Average of neurosurgical, group 1b
Set screw	$168.40	4	$673.59	Average of neurosurgical, group 2b
Rod	$450.49	2	$900.99	Average of neurosurgical, group 7a
Total			$6,841.49	
Fusion – Circumferential (PLF + ALIF)				
Multi-axial screw	$1,316.73	4	$5,266.91	Average of neurosurgical, group 1b
Set screw	$168.40	4	$673.59	Average of neurosurgical, group 2b
Rod	$450.49	2	$900.99	Average of neurosurgical, group 7a
Anterior interbody cage	$3,600.00	1	$3,600.00	SV010
Plate	$2,317.65	0.3	$695.29	Average of AJ032, JJ518, LH363, MC610, MC612, MC661, MC819, SK488, SX024, SY139, ZI518, ZI519, DP828, DP829, NV033, NV035, NV038
Total			$11,136.78	

* Source: August 2010 Prostheses List.

Osteo-conductive bone substitute use is frequent in Australia. It was estimated that approximately 30 per cent of patients who undergo fusion surgery receive bone morphogenetic proteins (BMP) plus a bone graft substitute (20 cm^3 per vertebral level) (MSAC, 1099, Non fusion) (see Table 25).

Table 25 Osteo-conductive bone substitute costs

Device	Unit cost	Units required	Total cost	Source
BMP (12mg or 1 vial)	$6,400.00	1	$6,400.00	MC684 and ST865
Kainos granules, 20 cm3	$1,390.00	1	$1,390.00	LH355
Total			$7,790.00	

Source: August 2010 Prostheses List

MBS items

The MBS item fees represent the government contribution to each procedure and were obtained from the MBS (see Table 26). It was assumed that all lumbar AIDR and fusion procedures are performed in the inpatient setting, while the initial and follow-up surgeon consultations and imaging are performed in the outpatient setting. The benefit amount and not the actual Medicare schedule fee were used in the model, as the patient usually receives a reimbursement of 75 per cent and 85 per cent of the schedule fee for inpatient services and outpatient services, respectively. Using the full fee would double count some of the copayment contribution.

Average copayments

Average copayments were sourced from the Department of Health and Ageing. The copayment component was calculated as the MBS fee charged minus the MBS benefit paid plus any additional specialist fees. The copayments were calculated as averages of all procedures claimed under the item number. Consequently there may be a degree of heterogeneity; therefore, the accuracy of the copayment is dependent on the other procedures that are also claimed under the same item number.

Table 26 MBS item numbers, fees and copayments

MBS item	MBS item number	MBS schedule fee	MBS benefit	Average copay-ment
Outpatient (MBS benefit = 85% of MBS schedule)*				
NEUROSURGERY SPECIALIST, REFERRED CONSULTATION, SURGERY OR HOSPITAL – Initial attendance in a single course of treatment.	6007	$122.50	$104.15	$90.71
LEVEL 1: Each MINOR attendance SUBSEQUENT to the first in a single course of treatment. – An attendance of not more than 15 minutes duration.	6009	$40.60	$34.55	$44.74
LEVEL 2: Each attendance SUBSEQUENT to the first in a single course of treatment being an attendance involving a detailed and comprehensive examination, arranging or evaluating any necessary investigations in relation to one or more complex problems. – An attendance of more than 15 minutes duration but not more than 30 minutes duration.	6011	$80.85	$68.75	$42.58
COMPUTED TOMOGRAPHY – scan of spine, cervical region, without intravenous contrast medium, payable once only, whether 1 or more attendances are required to complete the service	56220	$240.00	$204.00	$19.20
MAGNETIC RESONANCE IMAGING – cervical radiculopathy	63173	$358.40	$304.65	$45.52
RADIOGRAPHIC EXAMINATION OF SPINE, LUMBOSACRAL	58106	$77.00	$65.45	$6.27
Inpatient (MBS benefit = 75% of MBS schedule)				
LUMBAR ARTIFICIAL INTERVERTEBRAL TOTAL DISC REPLACEMENT including removal of disc, 1 level, in patients with single-level intralumbar disc disease in the absence of vertebral osteoporosis and prior spinal fusion at the same lumbar level who have failed conservative therapy, with fluoroscopy	48691	$1,695.20	$1,271.40	$3,228.63
SPINE, bone graft to, (postero-lateral fusion) – 1 or 2 levels	48648	$1,023.25	$767.45	$788.44
SPINAL FUSION (posterior interbody), with partial or total laminectomy, 1 level	48654	$1,023.25	$767.45	$522.75
SPINAL FUSION (anterior interbody) to cervical, thoracic or lumbar regions – 1 level, not being a service associated with artificial intervertebral total disc replacement	48660	$1,023.25	$767.45	$1,130.76
SPINE, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 48642 to 48675 applies – 1 or 2 levels, not being a service associated with artificial intervertebral total disc replacement	48684	$889.80	$667.35	$378.33
INTERVERTEBRAL DISC OR DISCS, microsurgical partial or total discectomy of	40301	$905.40	$679.05	$837.90
INTERVERTEBRAL DISC OR DISCS, partial or total laminectomy for removal of	40300	$902.55	$676.95	$995.26
SPINAL RHIZOLYSIS involving exposure of spinal nerve roots – for lateral recess, exit foraminal stenosis, adhesive radiculopathy or extensive epidural fibrosis, at 1 or more levels – with or without partial or total laminectomy	40330	$902.55	$676.95	$444.07
BONE GRAFT, harvesting of, via separate incision, in conjunction with another service – autogenous – small quantity	47726	$133.50	$100.15	$129.95
BONE GRAFT, harvesting of, via separate incision, in conjunction with another service – autogenous – large quantity	47729	$222.55	$166.95	$191.18
FLUOROSCOPY using a mobile image intensifier, in conjunction with a surgical procedure lasting less than 1 hour	60506	$63.75	$47.85	$47.79
FLUOROSCOPY using a mobile image intensifier, in conjunction with a surgical procedure lasting 1 hour or more	60509	$98.90	$74.20	$66.77
ANAESTHETIST, PRE-ANAESTHESIA CONSULTATION (Professional attendance by a medical practitioner in the practice of ANAESTHESIA), a BRIEF consultation involving a targeted history and limited examination (including the cardio-respiratory system), AND of not more than 15 minutes duration, not being a service associated with a service to which items 2801 – 3000 apply	17610	$40.60	$30.45	$43.73
ANAESTHETIST, PRE-ANAESTHESIA CONSULTATION a consultation on a patient undergoing advanced surgery or who has complex medical problems, involving a selective history and an	17615	$80.85	$60.65	$79.39

MBS item	MBS item number	MBS schedule fee	MBS benefit	Average copay-ment
extensive examination of multiple systems and the formulation of a written patient management plan documented in the patient notes, AND of more than 15 minutes but not more than 30 minutes duration				
INITIATION OF MANAGEMENT OF ANAESTHESIA for procedures in lumbar region	20630	$149.6	$112.2	$432.12
ANAESTHESIA, 1:01 HOURS TO 1:05 HOURS (5 basic units)	23051	$93.50	$70.15	$105.85
ANAESTHESIA, 2:01 HOURS TO 2:10 HOURS (9 basic units)	23091	$168.30	$126.25	$203.92
ANAESTHESIA, 2:41 HOURS TO 2:50 HOURS (13 basic units)	23113	$243.10	$182.35	$292.35
ANAESTHESIA, 3:01 HOURS TO 3:10 HOURS (15 basic units)	23115	$280.50	$210.40	$330.46
Assistance at any operation identified by the word 'Assist.' for which the fee does not exceed $527.65 or at a series or combination of operations identified by the word 'Assist.' where the fee for the series or combination of operations identified by the word 'Assist.' does not exceed $527.65	51300	$81.60	$61.20	$64.34
Assistance at any operation identified by the word 'Assist.' For which the fee exceeds $527.65 or at a series of operations identified by the word 'Assist.' For which the aggregate fee exceeds $527.65	51303	One fifth of the established fee for the operation or combination of operations		
PLATE, ROD OR NAIL AND ASSOCIATED WIRES, PINS OR SCREWS, 1 or more of, all of which were inserted for internal fixation purposes, removal of, not being a service associated with a service to which item 47924 or 47927 applies – per bone	47930	$249.15	$186.90	$191.16
VERTEBRAL BODY, total or subtotal excision of, including bone grafting or other form of fixation	48639	$1,290.10	$967.60	$783.80

* These MBS items are undertaken in the outpatient setting and therefore will contribute to the extended safety net
Source: MBS May 2010

Pre-surgery work-up

Table 27 provides the MBS items used for pre-surgery work-up applied equally to both lumbar AIDR and each of the lumbar fusion approaches, for both 'initial surgery' and 're-operation' health states. It was assumed that subsequent consultations may be brief or more complex (MBS items 6009 or 6011) and all patients receive a MRI scan and 50 per cent receive a CT scan prior to surgery.

Table 27 MBS costs associated with pre-surgery work-up per patient per procedure

Service	Unit cost	Units	Total cost
Initial consultation (MBS 6007)	$104.15	1	$104.15
MBS 6007 Copayment	$90.71	1	$90.71
Subsequent consultation (MBS 6009)	$34.55	0.5	$17.28
MBS 6009 Copayment	$44.74	0.5	$22.37
Subsequent consultation (MBS 6011)	$68.75	0.5	$34.38
MBS 6011 Copayment	$42.58	0.5	$21.29
CT scan (MBS 56220)	$204.00	0.5	$102.00
MBS 56220 Copayment	$19.20	0.5	$9.60
MRI scan (MBS 67173)	$304.65	1	$304.65
MBS 67173 Copayment	$45.52	1	$45.52
Total MBS fees			$562.45
Total patient out-of-pocket			$189.49
Total			$751.94

Source: MBS May 2010, Advisory Panel

Procedure costs

Table 50 and Table 51 (Appendix H) provide the MBS items used for AIDR and each of the fusion approaches in the submission for the 'surgery' and 're-operation' health states. The multiple operation rule[22] was applied when estimating MBS costs.

Exploration of MBS data revealed that:

- No lumbar AIDR procedures involved claims for segmental internal fixation of spine (MBS item 48684). In comparison, around 92 per cent, 89 per cent, 73 per cent, 98 per cent and 93 per cent of ALIF, PLIF, PLF, combination (PLF+PLIF) and circumferential fusions (PLF+ALIF) in the lumbar region involved claims for segmental internal fixation of spine.

- Despite the main MBS item for AIDR (48691) including removal of intervertebral disc, a significant proportion of AIDR procedures were associated with claims for spinal rhizolysis (MBS item 40330) and intervertebral disc removal (MBS items 40300 or 40301). Overall approximately 23 per cent, 31 per cent, 80 per cent, 35 per cent, 90 per cent and 31 per cent of AIDR, ALIF, PLIF, PLF, combination (PLF+PLIF) and circumferential fusions (PLF+ALIF) in the lumbar region involved claims for spinal rhizolysis (MBS item 40330). While 24 per cent, 25 per cent, 37 per cent, 20 per cent, 27 per cent and 14 per cent of AIDR, ALIF, PLIF, PLF, combination (PLF+PLIF) and circumferential fusions (PLF+ALIF) in the lumbar region involved claims for intervertebral disc removal (MBS items 40300 or 40301). Given the similarity in costs, the cost for MBS item 40330 was used as a proxy for this part of the procedure.

- Approximately 91 per cent, 86 per cent, 76 per cent, 81 per cent, 86 per cent and 93 per cent of AIDR, ALIF, PLIF, PLF, combination (PLF+PLIF) and circumferential fusions (PLF+ALIF) in the lumbar region involved claims for assistance (MBS item 51303).

- Almost all pre-anaesthesia consultations were brief (MBS item 17610), rather than complex (MBS item 17615). However, the analysis of this data was complicated by the removal of MBS item 17603. It was assumed that all consultations are brief, which favours fusions.

- Despite the main MBS item for AIDR (48691) including fluoroscopy, around 50 per cent and 34 per cent of lumbar AIDR procedures involved claims for fluoroscopy lasting less than (MBS item 60506) and more than 1 hour (MBS item 60509), respectively. In comparison:

    - Approximately 44 per cent and 39 per cent of ALIF in the lumbar region required fluoroscopy lasting less than and more than one hour, respectively.

[22] The MBS schedule fee for two or more operations performed on a patient on the one occasion was calculated by the following rule: 100% for the item with the greatest Schedule fee, plus 50% for the item with the next greatest Schedule fee, plus 25% for each other item.

- Approximately 43 per cent and 34 per cent of PLIF in the lumbar region required fluoroscopy lasting less than and more than one hour, respectively.

- Approximately 39 per cent and 25 per cent of PLF in the lumbar region required fluoroscopy lasting less than and more than one hour, respectively.

- Approximately 30 per cent and 48 per cent of combination (PLF+PLIF) fusions in the lumbar region required fluoroscopy lasting less than and more than one hour, respectively.

- Approximately 34 per cent and 59 per cent of circumferential (PLF+ALIF) fusions in the lumbar region required fluoroscopy lasting less than and more than one hour, respectively.

It was assumed that no lumbar AIDR procedures required harvesting of bone grafts, which was supported by the MBS data.

While all patients receiving fusion require a bone graft, not all bone grafts are required to be harvested from the iliac crest. Other sources include the laminar bone from decompression, bone morphogenetic proteins and femoral ring allografts, although the latter source of bone grafts is rarely used in Australia. Exploration of MBS data revealed that the proportion of fusions in the lumbar region that involved claims for harvesting of small (MBS item 47726) and large (MBS item 47729) quantities of bone grafts (mainly from the iliac crest) was:

- 3 per cent (small quantity) and 17 per cent (large quantity) of ALIF
- 1 per cent (small quantity) and 11 per cent (large quantity) of PLIF
- 1 per cent (small quantity) and 35 per cent (large quantity) of PLF
- 1 per cent (small quantity) and 30 per cent (large quantity) of combination (PLF+PLIF) fusions
- 0 per cent (small quantity) and 52 per cent (large quantity) of circumferential (PLF+ALIF) fusions.

As previously noted, it was estimated that a further 30 per cent of patients who undergo fusion surgery also receive bone morphogenetic proteins (BMP) (MSAC, 1099, Non fusion). Bone grafts for remaining patients were assumed to be harvested locally, and no additional costs for these patients were assumed.

Post-surgery follow-up

Table 28 provides the MBS items used for post-surgery follow-up applied during the 'failed surgery', 'successful surgery after re-operation' and 'successful surgery' health states. It was assumed that patients require follow-up consultations at 6 weeks, 12 weeks and 12 months post-surgery, and all patients require x-rays at 6 weeks and 12 months post-surgery to either ensure satisfactory healing of the bone graft or check whether the device has subsided or shifted.

As physiotherapy after surgery will be common to both treatments, this was not included in the economic evaluation.

Table 28 MBS costs associated with post-surgery follow-up per patient per procedure

Service	MBS item	Units	Total cost
6 weeks			
Follow-up consultation (MBS 6007)	$104.15	1	$104.15
MBS 6007 copayment	$90.71	1	$90.71
X-ray (MBS 28106)	$65.45	1	$65.45
MBS 28106 copayment	$6.27	1	$6.27
Sub-total MBS fees			$169.60
Sub-total patient out-of-pocket			$96.98
Sub-total			$266.58
12 weeks			
Follow-up consultation (MBS 6007)	$104.15	1	$104.15
MBS 6007 copayment	$90.71	1	$90.71
Sub-total MBS fees			$104.15
Sub-total patient out-of-pocket			$90.71
Sub-total			$194.86
12 months			
Follow-up consultation (MBS 6007)	$104.15	1	$104.15
MBS 6007 copayment	$90.71	1	$90.71
X-ray (MBS 28106)	$65.45	1	$65.45
MBS 28106 copayment	$6.27	1	$6.27
Sub-total MBS fees			$169.60
Sub-total patient out-of-pocket			$96.98
Sub-total MBS fees			$266.58
Total MBS fees			$443.35
Total patient out-of-pocket			$284.67
Total cost of post-surgery follow-up			$728.02

Source: MBS May 2010, Advisory Panel

Hospital stay

Hospitalisation costs per day were derived from the AR-DRG information for DRG I09A and I09B for spinal fusion with or without complications, respectively (version 5.1 round 12). Direct and indirect costs of prostheses, ward medical and imaging were excluded. A weighted average was calculated based on the number of private patient separations in public and private hospitals. It was estimated that between 15 per cent (I09B) and 23 per cent (I09A) of hospital separations in public hospitals are private patients (Australian hospital statistics 2008-09). See Table 29.

Table 29 Hospitalisation costs per day

Type of resource item	No. of separ-ations	No. of separ-ations (private patients)	ALOS	Unit cost	Unit cost minus prostheses, ward medical, imaging	Cost per day
Public hospital admissions						
With complications (I09A)	833	195	14.18	$36,262	$22,017	$1,552.68
Without complications (I09B)	1,561	235	6.17	$19,665	$11,134	$1,804.54
					Private hospitals admissions	
With complications (I09A)	1,215	1,209	12.45	$31,105	$14,070	$1,130.12
Without complications (I09B)	5,643	5,625	6.25	$20,870	$7,860	$1,257.60
Weighted average cost of hospitalisation per separation						$1,261.94

Source: AR-DRG version 5.1 round 12, and 2008-08 Australian Hospital Statistics

For each treatment, the hospitalisation cost per day was multiplied by the average length of stay. The review indicated that the average length of stay was 3.79 days for lumbar AIDR and 5.12 days for lumbar fusion.,

Table 50 and Table 51 present the average hospitalisation costs for each treatment.

Initial surgery costs

Table 30 presents the initial surgery costs; see Appendix 2 for more detail of costings.

Table 30 Initial surgery costs

	AIDR	ALIF	PLIF	PLF	COMB	CIRC
Total consumables	$9,550.00	$7,095.82	$15,178.49	$9,178.49	$15,178.49	$13,473.78
Total MBS fees	$2,008.88	$1,684.33	$1,814.88	$1,626.69	$2,160.48	$2,046.38
Total patient out-of-pocket	$4,471.59	$2,882.90	$2,563.40	$2,447.13	$3,388.90	$3,650.74
Total other hospital costs	$4,780.80	$6,464.42	$6,464.42	$6,464.42	$6,464.42	$6,464.42
Total cost	$20,811.27	$18,127.47	$26,021.18	$19,716.72	$27,192.28	$25,635.33

MBS: Medicare Benefits Schedule May 2010; COMB: combination fusion (PLF+PLIF); CIRC: circumferential fusion (PLF+ALIF).

Re-operation costs

To estimate the costs of re-operations the following assumptions were made:

- If replacement with an entirely new device is required, the full cost of the relevant AIDR or fusion is incurred plus either MBS items 48639 or 47930, depending on whether the initial procedure was PLF or another procedure, respectively, and minus spinal rhizolysis and removal of invertebral disc (see Table 31 and Appendix 2 for more detail). An operating time of 3 hours was assumed.

- If hardware is revised without removal or replacement, it was assumed that the costs would be the same as a replacement re-operation minus consumables (see Table 31 and Appendix H for more detail). An operating time of 3 hours was assumed.

- If supplemental fixation is required, the full cost of PLF is incurred (see Table 52).

- If hardware is removed, the costs were estimated to be $2,535.79 (see Table 61). It was assumed that patients remain in hospital for 1 day and the operating time is 1 hour.

- When re-operation is required at the index level not involving the device itself, the types of re-operations required are disparate and not easily costed (Advisory Panel). Consequently costs were set as $0.

- The MBS costs associated with pre-surgery work-up is incurred before any procedure.

- No additional post-surgery follow-up costs are incurred.

Table 31 Re-operation costs, hardware replacement

	AIDR	ALIF	PLIF	PLF	COMB	CIRC
Total consumables	$9,550.00	$7,095.82	$15,178.49	$9,178.49	$15,178.49	$13,473.78
Total MBS fees	$2,476.85	$2,174.53	$2,131.48	$1,634.23	$2,470.66	$2,504.46
Total patient out-of-pocket	$5,040.92	$3,318.33	$2,661.80	$2,321.92	$3,733.58	$4,386.81
Total other hospital costs	$4,780.80	$6,464.42	$6,464.42	$6,464.42	$6,464.42	$6,464.42
Total cost	$21,848.57	$19,053.11	$26,436.18	$19,599.06	$27,847.14	$26,829.47
Total minus consumables	$12,298.57	$11,957.28	$11,257.69	$10,420.57	$12,668.66	$13,355.69

MBS: Medicare Benefits Schedule May 2010; COMB: combination fusion (PLF+PLIF); CIRC: circumferential fusion (PLF+ALIF); ^currently no data available regarding co-payments for inpatient services.

Results

Average effectiveness gains

The total estimated percentage of patients discontinuing narcotics with lumbar AIDR and lumbar fusion was 24.4 per cent and 22.6 per cent, respectively (see Table 32). The incremental gain in patients discontinuing narcotics with lumbar AIDR as opposed to lumbar AIDR was 1.8 per cent. None of the specific fusion approaches were considered more effective than AIDR.

The total estimated percentage of patients achieving overall success with lumbar AIDR and lumbar fusion was 55.5 per cent and 51.5 per cent, respectively (see Table 32). The incremental gain in patients achieving overall success with lumbar AIDR as opposed to lumbar fusion was 4.0 per cent. None of the specific fusion approaches were considered more effective than AIDR.

The total estimated percentage of patients achieving ODI success with lumbar AIDR and lumbar fusion was 53.1 per cent and 55.1 per cent, respectively (see Table 32). The incremental gain in patients achieving ODI success with lumbar fusion as opposed to lumbar AIDR was 2.0 per cent. This opposite direction of effect, compared to overall success, was driven by the higher rate of ODI success with PLIF and PLF compared to AIDR and the frequency of use of these approaches.

The QALYs experienced with lumbar AIDR and PLIF/PLF was 1.32 QALYs and 1.33 QALYs, respectively (see Table 32). The incremental QALY loss of using lumbar AIDR as opposed to PLIF/PLF was 0.01 QALYs.

Table 32 Average effectiveness gains per procedure

	AIDR	ALIF	PLIF	PLF	COMB	CIRC	Fusion total*
Proportion of patients discontinuing narcotics	24.4%	19.8%	NA	NA	NA	18.8%	22.6%
Increment over AIDR		-4.6%	NA	NA	NA	-5.6%	-1.8%
Patients achieving overall success	55.5%	45.0%	NA	NA	NA	42.7%	51.5%
Increment over AIDR		-10.5%	NA	NA	NA	-12.8%	-4.0%
Patients achieving ODI success	53.1%	46.7%	65.8%	65.8%	NA	41.9%	55.1%
Increment over AIDR		-6.4%	12.7%	12.7%	NA	-11.2%	2.0%
QALYs growth approach	1.32	NA	1.33	1.33	NA	NA	NA
Increment over AIDR			0.01	0.01			

COMB: combination fusion (PLF+PLIF); CIRC: circumferential fusion (PLF+ALIF); *effectiveness of PLIF, PLF and COMB is assumed to be equal to AIDR in the absence of specific data.

Average costs of each procedure

The total estimated 2-year cost of lumbar AIDR and lumbar fusion was $23,117 and $24,716, respectively (see Table 33). The incremental savings of using lumbar AIDR as opposed to lumbar fusion was $1,600 (rounded to the nearest dollar). These costs include the risk and type of re-operations. When considering specific fusion approaches, ALIF and PLIF were estimated to be cheaper approaches compared to AIDR.

The main cost drivers of fusion compared to AIDR were consumable costs, mainly due to the use of BMP, and hospital costs. Total MBS fees were higher for AIDR compared to ALIF, PLIF and PLF. Patient out-of-pocket costs were higher for AIDR compared to all fusion approaches; however, it was unclear what proportion of these out-of-pocket costs are covered by private health insurance.

Table 33 Average costs per procedure

	AIDR	ALIF	PLIF	PLF	COMB	CIRC	Fusion total
Total consumables	$9,896	$7,655	$15,268	$9,185	$16,017	$13,618	$11,180
Total MBS fees	$3,108	$2,832	$2,853	$2,885	$3,440	$3,121	$3,014
Total patient out-of-pocket	$5,080	$3,556	$3,078	$3,288	$4,211	$4,227	$3,623
Total other hospital costs	$5,033	$6,918	$6,558	$6,950	$6,979	$6,598	$6,899
Total cost per procedure	$23,117	$20,961	$27,757	$22,308	$30,646	$27,564	$24,716
Increment over AIDR		-$2,155	$4,640 (AIDR cost saving)	-$807	$7,530 (AIDR cost saving)	$4,448 (AIDR cost saving)	$1,600 (AIDR cost saving)

COMB: combination fusion (PLF+PLIF); CIRC: circumferential fusion (PLF+ALIF); MBS: Medicare Benefits Schedule. Figures are rounded tp the nearest dollar.

Incremental cost-effectiveness

Patients discontinuing narcotic medication

In terms of patients discontinuing narcotic medication, the results reflect that of overall success. AIDR was both less costly and more effective than lumbar fusion overall, although the results varied by fusion approach. AIDR was more costly but achieved a higher rate of patients discontinuing narcotic medication than ALIF. The incremental cost per additional patient discontinuing narcotic medication with AIDR compared to ALIF was estimated to be $46,439. On the other hand, AIDR was both less costly and more effective than circumferential fusion. Therefore AIDR is considered to dominate

circumferential fusion. No data was available regarding the proportion of patients discontinuing narcotic medication with PLIF, PLF and combination fusion compared to AIDR.

Table 34 Incremental cost per patient discontinuing narcotic medication (Fusion - AIDR)

	ALIF	PLIF	PLF	COMB	CIRC	Fusion total
Cost per patient discontinuing narcotics	$46,439 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective

COMB: combination fusion (PLF+PLIF); CIRC: circumferential fusion (PLF+ALIF).
Legend:
AIDR less effective, no decision threshold necessary
AIDR less effective, decision threshold necessary
AIDR more effective, no decision threshold necessary
AIDR more effective, decision threshold necessary

Overall success

In terms of overall success lumbar AIDR was both less costly and more effective than lumbar fusion overall. Again the results varied by fusion approach. AIDR was more costly but achieved a higher rate of overall success than ALIF. The incremental cost per additional patient achieving overall success with AIDR compared to ALIF was estimated to be $20,433. On the other hand, AIDR was both less costly and more effective than circumferential fusion. Therefore AIDR is considered to dominate circumferential fusion. No data was available regarding the proportion of patients achieving overall success with PLIF, PLF and combination fusion compared to AIDR.

Table 35 Incremental cost per patient achieving overall success (Fusion - AIDR)

	ALIF	PLIF	PLF	COMB	CIRC	Fusion Total
Cost per patient achieving overall success	$20,433 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective

COMB: combination fusion (PLF+PLIF); CIRC: circumferential fusion (PLF+ALIF).
Legend:
AIDR less effective, no decision threshold necessary
AIDR less effective, decision threshold necessary
AIDR more effective, no decision threshold necessary
AIDR more effective, decision threshold necessary

ODI success

In terms of ODI success, lumbar AIDR was both less costly but less effective than lumbar fusion overall. The incremental cost per additional patient achieving ODI success was estimated to be $73,662 with fusion compared to AIDR.

Again the results varied by fusion approach. AIDR was less effective in terms of ODI success compared to PLIF and PLF. PLF was also less costly and thus PLF was considered to dominate AIDR. PLIF was more costly and the incremental cost per additional patient achieving ODI success with PLIF was estimated to be $35,373.

On the other hand AIDR was more costly but achieved a higher rate of ODI success compared to ALIF. The incremental cost per additional patient achieving ODI success with AIDR compared to ALIF was estimated to be $34,883.

AIDR was both less costly and more effective than circumferential fusion and thus AIDR was considered to dominate circumferential fusion. No data was available regarding the proportion of patients achieving ODI success with combination fusion compared to AIDR.

Table 36 Incremental cost per patient achieving ODI success (Fusion - AIDR)

	ALIF	PLIF	PLF	COMB	CIRC	Fusion total
Cost per patient achieving ODI success	$34,883 (AIDR more costly but more effective)	$35,373 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	AIDR less costly, more effective	$73,662 (AIDR less costly and less effective)

COMB: combination fusion (PLF+PLIF); CIRC: circumferential fusion (PLF+ALIF).
Legend:
AIDR less effective, no decision threshold necessary
AIDR less effective, decision threshold necessary
AIDR more effective, no decision threshold necessary
AIDR more effective, decision threshold necessary

QALYs

PLIF and PLF were estimated to be more effective in terms of QALYs gained compared to AIDR. PLF was also less costly and thus PLF was considered to dominate AIDR. PLIF was more costly and the incremental cost per QALY gained with PLIF was estimated to be $598,794. No data was available for ALIF, combination or circumferential fusion or all fusion approaches overall.

Table 37 Incremental cost per QALYs gained (Fusion - AIDR)

	ALIF	PLIF	PLF	COMB	CIRC	Fusion Total
Cost per QALYs gained	NA	$598,794 (AIDR less costly and less effective)	(AIDR more costly and less effective)	NA	NA	NA

COMB: combination fusion (PLF+PLIF); CIRC: circumferential fusion (PLF+ALIF).
Legend:
AIDR less effective, no decision threshold necessary
AIDR less effective, decision threshold necessary
AIDR more effective, no decision threshold necessary
AIDR more effective, decision threshold necessary

Summary

Overall the results are mixed depending on the clinical outcome of interest. It should be noted that the estimates of cost-effectiveness were based on point estimates of efficacy. This may not be appropriate if MSAC considers AIDR to be non-inferior in terms of the clinical outcome measures or the rates of re-operations.

If MSAC considers that AIDR is non-inferior compared to the fusion approaches in terms of success but not in terms of the rate of re-operations, then the total costs

accounting for the rate of re-operations should be considered and thus ALIF was the least costly approach (Table 33).

If MSAC considers that AIDR is non-inferior compared to the fusion approaches in terms of both success and the rate of re-operations, only the initial costs of surgery (Table 30) should be considered and thus ALIF was the least costly approach.

Implication to the extended safety net

The impact on the Extended Medicare Safety Net (EMSN) is unknown. The majority of MBS items are for procedures undertaken in the inpatient setting; therefore these do not contribute to the EMSN. Some MBS items, such as the initial and follow-up consultations, will occur in the outpatient setting and may therefore contribute toward the patients out–of-pocket expenses. However, it is unknown whether these accumulative co-payment charges will be higher than the current EMSN threshold.

Sensitivity analysis

Sensitivity analysis was conducted on estimates of: the relative risk of overall success and ODI success (95% confidence intervals), the baseline probability of overall success with AIDR (higher and lower estimates based on the available RCTs), the proportion of patients on narcotics following successful surgery (95% confidence interval), the growth in QALYs gained with lumbar AIDR (95% confidence interval), direct use of QALY estimates, exclusion of the costs of re-operations, the proportion of fusion patients requiring BMP (varied from 0 to 60%) and the length of stay in hospital (hospitalisation costs with AIDR was assumed to be equal to that with fusion).

Overall the results were most sensitive to using the direct approach to apply utility weights, the time in hospital with AIDR and changes in the relative risk of overall or ODI success. The results were somewhat sensitive to the proportion of fusion patients requiring BMP.

When hospitalisation costs with AIDR were assumed to be equal to that with fusion, fusion became less costly compared to AIDR.

The model was not sensitive to the proportion of patients on narcotics following successful surgery, the baseline estimates of overall success with AIDR, or the inclusion of re-operation costs. Note that the cost per patient discontinuing narcotics was more sensitive to the relative risk of overall success rather than the proportion of patients on narcotics following successful surgery.

If the direct approach was used to apply utility weights, the average QALYs gained with lumbar AIDR and PLIF/PLF was 1.25 QALYs and 1.16 QALYs, respectively. Thus QALYs experienced increased by 0.10 QALYs with lumbar AIDR compared to PLIF/PLF. Using this approach AIDR was estimated to be less costly and more effective compared to PLIF and PLF. While compared to PLF, AIDR was estimated to be more costly and more effective, and had an additional cost per QALY of $8,443.

Table 38 Incremental cost-effectiveness (Fusion - AIDR)

	ALIF	PLIF	PLF	COMB	CIRC	Fusion Total
Cost per patient discontinuing narcotics						
Baseline (37%)	$46,439 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Lower CI of RR of achieving overall success (in favour of AIDR)	$21,868 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Upper CI of RR of achieving overall success (against AIDR)	AIDR more costly, less effective	NA	NA	NA	$352,507 (AIDR less costly and less effective)	$397,102 (AIDR less costly and less effective)
Upper baseline estimate of overall success with AIDR (57.1%)	$47,732 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Lower baseline estimate of overall success with AIDR (53.4%)	$45,492 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Lower CI of patients discontinuing narcotics after achieving overall success (29%)	$39,294 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Upper CI of patients discontinuing narcotics after achieving overall success (46%)	$58,380 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Exclusion of cost of re-operations	$57,843 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Proportion on BMP (0%) (against AIDR)	$98,237 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	$42,251 (AIDR more costly, more effective)
Proportion on BMP (60%) (in favour of AIDR)	AIDR less costly, more effective	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Hospitalisation costs of AIDR ($6,464.42)	$82,924 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	$5,263 (AIDR more costly, more effective)
Cost per patient achieving overall success						
Baseline	$20,433 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Lower CI of RR of achieving overall success (in favour of AIDR)	$9,622 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Upper CI of RR of achieving overall success (against AIDR)	AIDR more costly, less effective	NA	NA	NA	$155,103 (AIDR less costly and less effective)	$174,725 (AIDR less costly and less effective)
Upper baseline estimate of overall success with AIDR (57.1%)	$21,002 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Lower baseline estimate of overall success with AIDR (53.4%)	$20,016 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Exclusion of cost of re-operations	$25,451 (AIDR more costly but	NA	NA	NA	AIDR less costly, more	AIDR less costly, more

	ALIF	PLIF	PLF	COMB	CIRC	Fusion Total
	more effective)				effective	effective
Proportion on BMP (0%) (against AIDR)	$43,226 (AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	$18,591 (AIDR more costly, more effective)
Proportion on BMP (60%) (in favour of AIDR)	AIDR less costly, more effective	NA	NA	NA	AIDR less costly, more effective	AIDR less costly, more effective
Hospitalisation costs of AIDR ($6,464.42)	$36,487(AIDR more costly but more effective)	NA	NA	NA	AIDR less costly, more effective	$2,316 (AIDR more costly, more effective)
Cost per patient achieving ODI success						
Baseline	$34,883 (AIDR more costly but more effective)	$35,373 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	AIDR less costly, more effective	$73,662 (AIDR less costly and less effective)
Lower CI of RR of achieving ODI success (in favour of AIDR)	$11,051 (AIDR more costly but more effective)	AIDR less costly, more effective	$5,100 (AIDR more costly, more effective)	NA	AIDR less costly, more effective	AIDR less costly, more effective
Upper CI of RR of achieving ODI success (against AIDR)	AIDR more costly, less effective	$9,175 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	AIDR less costly, equally effective	$5,875 (AIDR less costly and less effective)
Exclusion of cost of re-operations	$42,119 (AIDR more costly but more effective)	$40,881 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	AIDR less costly, more effective	$54,626 (AIDR less costly and less effective)
Proportion on BMP (0%) (against AIDR)	$72,500 (AIDR more costly but more effective)	$17,610 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	AIDR less costly, more effective	AIDR more costly and less effective
Proportion on BMP (60%) (in favour of AIDR)	AIDR less costly, more effective	$53,135 (AIDR less costly and less effective)	$7,638 (AIDR less costly and less effective)	NA	AIDR less costly, more effective	$190,872 (AIDR less costly and less effective)
Hospitalisation costs of AIDR ($6,464.42)	$61,465 (AIDR more costly but more effective)	$22,082 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	AIDR less costly, more effective	AIDR more costly and less effective
Cost per QALYs gained						
Baseline	NA	$598,794 (AIDR less costly and less effective)	AIDR more costly and less effective	NA	NA	NA
Lower CI for growth with AIDR (against AIDR)	NA	$8,181 (AIDR less costly and less effective)	AIDR more costly and less effective	NA	NA	NA
Upper CI for growth with AIDR (in favour of AIDR)	NA	AIDR less costly, more effective	$1,463 (AIDR more costly, more effective)	NA	NA	NA
Direct Approach	NA	AIDR less costly, more effective	$8,443 (AIDR more costly, more effective)	NA	NA	NA
Exclusion of cost of re-operations	NA	$694,655 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	NA	NA
Proportion on BMP (0%) (against AIDR)	NA	$305,085 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	NA	NA
Proportion on BMP (60%) (in favour of AIDR)	NA	$892,396 (AIDR less costly and less effective)	$187,100 (AIDR less costly and less effective)	NA	NA	NA
Hospitalisation costs of AIDR ($6,464.42)		$380,340 (AIDR less costly and less effective)	AIDR more costly, less effective	NA	NA	NA

COMB: combination fusion (PLF+PLIF), CIRC; circumferential fusion (PLF+ALIF).
Legend:
AIDR less effective, no decision threshold necessary
AIDR less effective, decision threshold necessary
AIDR more effective, no decision threshold necessary
AIDR more effective, decision threshold necessary

Other considerations

There were a number of limitations with the approach.

A proportion of patients treated with AIDR may also be treated with lumbar fusion at the adjacent or multiple levels in the same procedure. This was not considered in this analysis due to a lack of clinical data. The cost-effectiveness results should not be considered to represent the cost-effectiveness of AIDR in combination with another fusion approach.

The lack of a standard definition of overall success across the RCTs hindered the analysis of the cost-effectiveness of lumbar AIDR compared to lumbar fusion. In particular, Zigler et al (2007) uses a more comprehensive definition of overall success compared to Blumenthal et al (2005). This may impact on the estimates of cost-effectiveness if a more comprehensive definition favours one treatment over another. Furthermore these definitions of success subsequently impact on the estimates of the proportion of patients who discontinue narcotics.

The proportion of patients who discontinue narcotics was indicated by the Advisory Panel to be a more appropriate indicator of treatment success. Unfortunately this outcome does not account for patients who use lower doses of narcotics following surgery, which may also be considered a measure of treatment effectiveness.

QALYs are often used by decision makers as ICERs are able to be compared across other uses of funding. Unfortunately there was a lack of data on utility weights following treatment success or failure, which limits the ability to estimate the cost per QALYs gained for all treatments. Further research on utility weights following surgery is required.

Only the costs incurred in the first 2 years were included in the analysis. This is due to the uncertainty in costs incurred after 2 years. In particular, the potential increased risk of re-operations at adjacent levels following fusion surgery.

Financial implications

In 2009 and 2010 the number of AIDR procedures was 263 and 258[23], respectively. After assuming the number of procedures is expected to grow in line with growth in the Australian Population (ABS 3222.0, Population Projections, Australia, 2006-2101, Series B).

The total cost of AIDR would be $6.23 million in 2013. If these patients instead received lumbar fusion the total cost would be $6.66 million. Hence the cost savings of performing lumbar AIDR as a direct replacement for lumbar fusion would be $0.43

[23] Based on MBS items 48691 48692, but not MBS item 48693 as this item is for claims by assisting surgeons.

million, assuming that patients who are treated with AIDR were previously likely to be treated with fusion using the same approach as the current distribution of fusion approaches.

As can be seen in Table 39 the bulk of the cost savings are due to the cost of consumables and other hospital costs. There would be an increase in the costs borne by the patient and the MBS.

Table 39 Total financial costs

	2010	2011	2012	2013
Number of patients	258	262	266	270
				AIDR
Total consumables	$2,553,145	$2,591,232	$2,629,359	$2,667,545
Total MBS fees	$801,773	$813,734	$825,707	$837,698
Total patient out-of-pocket	$1,310,743	$1,330,296	$1,349,870	$1,369,474
Total other hospital costs	$1,298,438	$1,317,808	$1,337,198	$1,356,618
Total financial implications	$5,964,101	$6,053,071	$6,142,135	$6,231,335
				Fusion
Total consumables	$2,884,506	$2,927,536	$2,970,612	$3,013,753
Total MBS fees	$777,688	$789,289	$800,902	$812,534
Total patient out-of-pocket	$934,628	$948,571	$962,528	$976,507
Total other hospital costs	$1,779,992	$1,806,545	$1,833,126	$1,859,748
Total financial implications	$6,376,814	$6,471,941	$6,567,168	$6,662,541
				Incremental costs (AIDR – Fusion)
Change in consumables	-$331,361	-$336,304	-$341,252	-$346,208
Change in MBS fees	$24,086	$24,445	$24,805	$25,165
Change in patient out-of-pocket	$376,114	$381,725	$387,342	$392,967
Change in other hospital costs	-$481,553	-$488,737	-$495,928	-$503,131
Change in financial implications	-$412,713	-$418,870	-$425,033	-$431,206

MBS: Medicare Benefits Schedule

What are the other considerations?

Consumer considerations

The clinical expert opinion of the Advisory Panel suggests that there are several issues that patients need to be aware of when considering the lumbar AIDR procedure:

- The procedure is highly specialised and technically demanding.
- The procedure is largely performed by neurosurgeons and orthopaedic surgeons who have specialised exclusively in spinal surgery.
- In Australia, the procedure is only performed in major private and public hospitals. In addition, it is important for patients who are considering the lumbar AIDR procedure to be aware that most public hospitals do not have a prosthetic budget that would enable them to offer this procedure. Therefore, patients who anticipate having their surgery in a public hospital will need to enquire about whether the hospital has a budget that would allow such a prosthesis to be used. Both of these factors raise the issue of equity of access for this procedure.
- The procedure is only applicable to a narrow band of patients, and has only been performed in a relatively small number of patients in Australia since it was listed on the MBS.
- Based on the studies included in this assessment, it is clear that patients can expect an improvement in pain as early as 6 weeks and up to 5 years after the procedure; however, the procedure may not necessarily eliminate pain. Therefore, it is important that patients discuss their expectations regarding pain relief with their treating surgeon prior to surgery, in order to determine if these expectations are realistic.

Discussion

Limitations of the evidence

This review examining the safety and effectiveness of lumbar AIDR was limited by both the quantity and quality of the available studies.

In terms of comparative evidence, only four RCTs (comprising 12 studies) and one nonrandomised comparative study were identified for inclusion in this assessment. The eligibility criteria used to recruit patients was similar across studies, and most studies included patients who had undergone previous spinal surgery, which may impact on patient outcomes following lumbar AIDR or lumbar fusion procedures. Although subgroup analyses conducted in one of the included RCTs showed that the rate of adverse events, as well as a variety of clinical outcomes including ODI scores, pain scores, rate of reoperation, work status and patient satisfaction with the procedure, were not significantly different in lumbar AIDR and lumbar fusion patients who had undergone previous lumbar decompressive surgery (including microdiscectomy, laminectomy, or minimal medial facetectomy), compared with those who had not undergone previous surgery.

Most studies utilised well known, validated instruments for the assessment of patient outcomes; however, patients and investigators were not blinded to the treatment, which may have led to bias in the reporting of results. A further limitation of the studies included in this assessment was the length of follow-up reported. Certain adverse events and problems associated with the durability of the prosthesis may only become apparent after many years of follow-up. However, the majority of studies in this assessment reported short- to medium-term (2-5 years) follow-up of patients. In addition, a variety of different prostheses and lumbar fusion techniques were used across studies. Importantly, two of the four included RCTs compared lumbar AIDR to cicumferential fusion; however, this approach represents only 1 per cent of all spinal fusion procedures that are performed in Australia.

An overall evaluation of the body of evidence for lumbar AIDR is presented in Table 40.

Table 40 Body of evidence assessment matrix

Component	A Excellent	B Good	C Satisfactory	D Poor
Evidence base	Several level I or II studies with low risk of bias			
Consistency		Most studies consistent and inconsistency may be explained		
Clinical impact		Substantial		
Generalisability		Population/s studied in the body of evidence are similar to the target population		
Applicability		Applicable to Australian health care context with few caveats		

Source: NHMRC (2008)

Safety

Overall, safety data was not reported as comprehensively as effectiveness outcomes in the included comparative studies, with only two studies reporting statistical comparisons between lumbar AIDR and lumbar fusion procedures. This may represent study bias where the primary concern of the authors was to present data on effectiveness, rather than safety.

For the majority of adverse events reported, there were no obvious differences in incidence rates between the lumbar AIDR and lumbar fusion groups, with two studies reporting no statistical differences in the rate of overall complications between the two groups. Wound infection was the most commonly reported adverse event, and demonstrated an incidence rate of 3.2 per cent in the lumbar AIDR population, and 5.1 per cent in the lumbar fusion population. Prosthesis-related adverse events were those relating to movement of the device, including collapse or subsidence (3%), and displacement (0.78%). Fusion-related adverse events included nonunion/pseudarthrosis (6.4%) and bone graft donor-site pain (11.1%). The rate of adjacent segment problems appeared higher following lumbar fusion (8.3%) compared with lumbar AIDR (1.3%).

Major adverse events such as major vessel injury, neurologic damage and nerve root injury were rare in both the lumbar AIDR and fusion groups. There was one reported death following lumbar AIDR which was narcotic-related, while no deaths were reported following lumbar fusion.

Overall, the safety of lumbar AIDR appears to be comparable to that of lumbar fusion.

Effectiveness

Clinical outcomes were the focus of the majority of comparative studies; however, a number of studies also reported radiographic outcomes following lumbar AIDR and lumbar fusion procedures.

All of the included comparative studies utilised the Oswestry Disability Index (ODI), one of the principal condition specific measures used in the management of spinal disorders, and the gold standard for assessing the extent to which a patient's functional level is limited by low back pain. Three studies reported that patients in the lumbar AIDR group showed statistically greater improvements in ODI scores than lumbar fusion patients at various time points up to 1 year follow-up; however, none of the studies reported significant differences between the groups at 2- or 5-year follow-up. Similarly, two studies reported that at 2-year follow-up, overall clinical success was significantly higher in the lumbar AIDR group compared with the lumbar fusion group, while the rate of re-operation was similar in both groups.

In two studies, patient satisfaction at 2-year follow-up was significantly higher in lumbar AIDR patients compared with lumbar fusion patients, with up to 81 per cent of AIDR patients saying they would have the procedure again, compared with 69 per cent of fusion patients. This may have reflected the fact that lumbar AIDR patients experienced significantly less pain and required less narcotic medication, reported better sexual function, and returned to work at higher rates, when compared with lumbar fusion patients up to 2 years after surgery.

Radiographic outcomes were reported in several studies; however, outcomes were reported differently across studies, and no statistical comparisons between the lumbar AIDR and lumbar fusion groups were reported, making it difficult to draw firm conclusions.

Overall, in the short to medium term, the effectiveness of lumbar AIDR appears to be comparable to that of lumbar fusion.

Cost-effectiveness

The economic evaluation adopted a cost-effectiveness analysis and a cost-utility analysis framework. For AIDR compared to fusion the incremental costs, incremental costs per patient discontinuing narcotic medication at 2 years, incremental costs per additional overall clinical success at 2 years and incremental costs per additional ODI success at 2 years were presented. For AIDR compared to PLF/PLIF the incremental cost per QALY gained was presented. This mixed approach was undertaken due to uncertainty in the outcome of most clinical relevance and whether the results were statistically significant.

The results are mixed depending on the outcome considered most clinically relevant. It should be noted that the estimates of effectiveness were based on point estimates. This may not be appropriate if MSAC considers AIDR to be non-inferior in terms of either overall success or the rate of re-operations. If MSAC considers that AIDR is non-inferior compared to the fusion approaches in terms of success but not in terms of the rate of re-operations, then the total costs accounting for the rate of re-operations should be considered. In this case, ALIF is the least costly approach followed by PLF. If MSAC considers that AIDR is non-inferior compared to the fusion approaches in terms of both success and the rate of re-operations, only the initial costs of surgery should be considered. In this case, ALIF is the least costly approach followed by PLF.

There were a number of limitations with the approach to the analysis including: a proportion of AIDR procedures may be in combination with other fusion approaches, which was not considered due to a lack of clinical data; there is a lack of a standard

definition of overall success; the proportion of patients who discontinue narcotics does not account for lower doses of narcotics following surgery; utility weights were only available for a small number of approaches; and only the costs incurred in the first 2 years were included in the analysis – there is a potential increased risk of re-operations at adjacent levels following fusion surgery which has not been considered.

Conclusions

The aim of the review was to evaluate the safety, effectiveness and economic implications of lumbar AIDR for patients suffering from significant axial back pain and/or radicular (nerve root) pain, secondary to disc degeneration or prolapse, who have failed non-operative treatment. The conclusions that could be drawn from this review were limited by the quantity and quality of the available evidence. Based on these studies, it appears that the lumbar AIDR procedure is relatively safe, and is not associated with serious adverse events. In the short to medium term, the effectiveness of lumbar AIDR in terms of ODI scores, success of the procedure, pain, patient satisfaction, workstatus, quality of life and sexual function, appears to be comparable to lumbar fusion procedures. While the number of patients who remained on narcotics was comparable following lumbar AIDR and lumbar fusion procedures, the clinical expert opinion of the Advisory Panel suggests that this proportion is significantly higher than that observed in clinical practice in Australia.

In 2009 and 2010 the number of AIDR procedures was 263 and 258[24], respectively. Using the analysis of costs in the economic evaluation, the total cost of AIDR would be $6.23 million in 2013. If these patients instead received lumbar fusion the total cost would be $6.66 million. Hence the cost savings of performing lumbar AIDR as a direct replacement for lumbar fusion would be $0.43 million. The bulk of the cost savings are due to the cost of consumables and other hospital costs. There would be an increase in the costs borne by the patient and a small increase to the MBS.

[24] Based on MBS items 48691 48692, but not MBS item 48693 as this item is for claims by assisting surgeons.

Appendix A MSAC terms of reference and membership

The Medical Services Advisory Committee (MSAC) is an independent scientific committee comprising individuals with expertise in clinical medicine, health economics and consumer matters. It advises the Minister for Health and Ageing on whether a new medical service should be publicly funded based on an assessment of its comparative safety, effectiveness, cost-effectiveness and total cost, using the best available evidence. In providing this advice, MSAC may also take other relevant factors into account. This process ensures that Australians have access to medical services that have been shown to be safe and clinically effective, as well as representing value for money for the Australian health care system.

MSAC is to:

- Advise the Minister for Health and Ageing on medical services including those that involve new or emerging technologies and procedures, in relation to:
    - the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;
    - whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
    - the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;
    - the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
    - other matters related to the public funding of health services referred by the Minister.
- Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.

MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

The membership of MSAC at the 52nd meeting held April 2011 comprised a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	**Expertise or Affiliation**
Professor Robyn Ward (Chair)	Medical Oncology
Dr Frederick Khafagi (Deputy Chair)	Nuclear Medicine
Professor Jim Butler (Chair, Evaluation Sub-committee)	Health Economics
Associate Professor John Atherton	Cardiology
Associate Professor Michael Bilous	Anatomical Pathology
Professor Chris Baggoley	Interim Commonwealth Chief Medical Officer (*ex officio*)
Associate Professor Kirsty Douglas	General Practice/Research
Professor Kwun Fong	Thoracic Medicine
Professor Paul Glasziou	Evidence-based health care
Dr Scott Jansson	Pathology
Professor David Little	Orthopaedics
Mr Russell McGowan	Consumer Health Representative
Professor David Roder	Health medicine/epidemiology
Associate Professor Bev Rowbotham	Haematology
Dr Graeme Suthers	Genetics/Pathology
Professor Ken Thomson	Radiology
Dr Christine Tippett	Obstetrics/Gynaecology
Associate Professor David Winlaw	Paediatric Cardiothoracic Surgery
Dr Caroline Wright	Colorectal Cancer/Surgery
Vacant	AHMAC Representative (*ex officio*)

Appendix B Advisory Panel and evaluators

Advisory Panel for MSAC Application 1090.1: Lumbar artificial intervertebral disc replacement

Member	Nomination/expertise or affiliation
Professor Ken Thomson	Chair, member of MSAC
Mr Russell McGowan	Deputy Chair, member of MSAC and Consumers Health Forum of Australia nominee
Dr Graeme Brazenor	Spine Society Nominee
Dr Peter Wilde	Spine Society Nominee
Dr Chris Poulos	Pain and Rehabilitation Specialist
Dr Mark Davies	Royal Australasian College of Surgeons nominee
Professor Bryan Stokes	Neurosurgeon
Dr Myron Rogers	Royal Australasian College of Surgeons nominee
Professor Nick Fazzalari	Head, Bone and Joint Research

Evaluation Sub-committee input

Name	
A/Professor Kirsty Douglas (until September 2010)	Member of MSAC Evaluation Sub-Committee Primary Healthcare
A/Professor Rachael Moorin (from September 2010)	Member of MSAC Evaluation Sub-Committee Nuclear Medicine and Health Economics

Evaluators

Name	Organisation
Dr Prema Thavaneswaran	ASERNIP-S
Dr Meegan Vandepeer	ASERNIP-S
Ms Bonny Parkinson	CHERE
Dr Stephen Goodall	CHERE

Appendix C Approach to assessment

Search strategy

Table 41 Bibliographic databases searched

Electronic database	Time period & search limits
Cochrane Library – including, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database	January 2005 – April 2010
EMBASE	January 2005 – April 2010
PubMed	January 2005 – April 2010

Table 42 Electronic internet databases searched

Electronic database	Internet address
Centre for Reviews and Dissemination (CRD) / International Network of Agencies for Health Technology Assessment (INAHTA) databases – including: NHS Economic Evaluation Database (NHS EED) / Database of Abstracts of Reviews of Effect (DARE) / Heath Technology Assessment (HTA) Database	http://www.york.ac.uk/inst/crd/
National Health and Medical Research Council (NHMRC) (Australia)	http://www.health.gov.au/nhmrc/
Australian Department of Health and Ageing	http://www.health.gov.au/
Scirus – for Scientific Information Only	http://www.scirus.com
Trip database	http://www.tripdatabase.com
Current Controlled Trials metaRegister	http://controlled-trials.com/
National Library of Medicine Health Services / Technology Assessment Text	http://text.nlm.nih.gov/
National Library of Medicine Locator Plus database	http://locatorplus.gov
New York Academy of Medicine Grey Literature Report	http://www.nyam.org/library/pages/grey_literature_report
US Department of Health and Human Services (reports and publications)	http://www.os.dhhs.gov/

Table 43 Health technology assessment internet sites

Argentina
Institute for Clinical Effectiveness and Health Policy (IECS) http://www.iecs.org.ar/iecs-visor-publicaciones-ing.php
Australia
Adelaide Health Technology Assessment (AHTA) http://www.health.adelaide.edu.au/publichealth/consult/health_techn_assess.html
Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) http://www.surgeons.org/asernip-s.htm
Centre for Clinical Effectiveness, Monash University http://www.mihsr.monash.org/cce/
Health Economics Unit, Monash University http://chpe.buseco.monash.edu.au
Medical Services Advisory Committee (MSAC) http://www.msac.gov.au
Austria
Institute of Technology Assessment (ITA) http://www.oeaw.ac.at/ita/e1-3.htm
Brazil
Departamento de Ciência e Tecnologia (DECIT) http://portal.saude.gov.br/portal/saude/area.cfm?id_area=1088
Canada
Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) http://www.aetmis.gouv.qc.ca/site/index.php?home
Alberta Heritage Foundation for Medical Research (AHFMR) http://www.ahfmr.ab.ca/publications/
Canadian Agency for Drugs and Technologies in Health (CADTH) http://www.cadth.ca/index.php/en/home
Canadian Association for Health Services and Policy Research (CAHSPR) http://www.cahspr.ca
Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org
Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca
Health Utilities Index (HUI) http://www.fhs.mcmaster.ca/hug/index.htm
Institute for Clinical and Evaluative Studies (ICES) http://www.ices.on.ca
Institute of Health Economics (IHE) http://www.ihe.ca/
Ministry of Health and Long-Term Care – Medical Advisory Secretariat http://www.health.gov.on.ca/english/providers/program/mas/mas_mn.html
Denmark
Danish Centre for Evaluation and Health Technology Assessment (DACEHTA) http://www.dacehta.dk
Danish Institute for Health Services Research (DSI) http://www.dsi.dk/engelsk.html
Finland
Finnish Office for Health Technology Assessment (FinOHTA) http://finohta.stakes.fi/EN/index.htm
France
Committee for Evaluation and Diffusion of Innovative Techniques (CEDIT) http://cedit.aphp.fr/english/index_present.html
French National Authority for Health (HAS) http://www.has-sante.fr
Germany
German Agency for Health Technology Assessment (DAHTA) http://www.dimdi.de/dynamic/en/hta/db/index.htm
Hungary
Unit of Health Economics and Technology Research Assessment (HunHTA) http://hecon.uni-corvinus.hu/corvinus.php?lng=en
The Netherlands
Health Council of the Netherlands Gezondheidsraad http://www.gr.nl/adviezen.php?phpLang=en
Netherlands Organisation for Health Research and Development (ZonMw) http://www.zonmw.nl/en/home.html
New Zealand
New Zealand Health Technology Assessment (NZHTA) http://nzhta.chmeds.ac.nz/

Table 43 continued Health technology assessment internet sites

Norway
Norwegian Knowledge Centre for the Health Services http://www.kunnskapssenteret.no
Spain
Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud Carlos III / Health Technology Assessment Agency (AETS) http://www.isciii.es/htdocs/en/investigacion/Agencia_quees.jsp
Andalusian Agency for Health Technology Assessment (AETSA) http://www.juntadeandalucia.es/index.html
Catalan Agency for Health Technology Assessment (CAHTA) http://www.gencat.cat/salut/depsan/units/aatrm/html/en/dir394/index.htm
Sweden
Swedish Council on Technology Assessment in Healthcare (SBU) http://www.sbu.se/en/
Center for Medical Health Technology Assessment http://www.cmt.liu.se/?l=en
Switzerland
Swiss Network on Health Technology Assessment (SNHTA) http://www.snhta.ch/
United Kingdom
NHS Quality Improvement Scotland http://www.nhshealthquality.org/nhqis/CCC_FirstPage.jsp
National Health Service Health Technology Assessment (UK) / National Coordinating Centre for Health Technology Assessment (NCCHTA) http://www.ncchta.org/
University of York NHS Centre for Reviews and Dissemination (NHS CRD) http://www.york.ac.uk/inst/crd/
National Institute for Clinical Excellence (NICE) http://www.nice.org.uk
United States
Agency for Healthcare Research and Quality (AHRQ) http://www.ahrq.gov/clinic/techix.htm
Harvard School of Public Health – Cost-Utility Analysis Registry http://www.tufts-nemc.org/cearegistry/
U.S. Blue Cross/ Blue Shield Association Technology Evaluation Centre (TEC) http://www.bcbs.com/betterknowledge/tec/
Veterans' Affairs Technology Assessment Program (VATAP) http://www.va.gov/vatap/publications.htm

Inclusion criteria

Table 44 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	*Effectiveness* Systematic reviews and clinical studies including randomised and non-randomised comparative studies will be included. Case series studies with a follow-up period of 5 years or more and consecutive patient enrolment will also be included. Non-systematic reviews, case reports, letters, editorials, and animal and laboratory studies will be excluded. *Safety* Systematic reviews and clinical studies including randomised and non-randomised comparative studies and case series will be included. Non-systematic reviews, case reports, letters, editorials, and animal, cadaver and laboratory studies will be excluded.
Patient	Patients with significant axial back pain with changes secondary to degeneration of the disc or disc prolapsed with or without radiculopathy or myelopathy who have failed operative treatment. Patients with significant axial back pain due to major disc prolapse who have failed non-operative treatment.
Intervention/test	Lumbar AIDR
Comparator	Lumbar spinal fusion
Outcome	*Effectiveness* • Reduction in pain (eg use of pain medication, rating scales) • Adjacent segment degeneration • Quality of life (including SF-36) • Length of hospital stay • Unplanned readmission within 30 days • Ability to perform activities of daily living (work and/or recreation) • Return to work • Improvement in positional tolerance (motion, strength and endurance) • Disability (disability rating scales, back specific scales eg ODI, Waddell, Roland-Morris) • Emotional wellbeing (depression scales) • Device failure (revision, re-operation or removal) *Safety* • Complication (eg pain, spinal infection, vascular damage, neurological damage or nerve root injury) • Migration or dislocation of disc • Device failure (revision, re-operation or removal) • Adjacent segment degeneration • Polyethylene wear
Language	Non-English language articles will be excluded unless they appear to provide a higher level of evidence than English language articles. Translation of such articles will significantly increase the timeframe of the review. The Advisory Panel has stated that the majority of published evidence in this field will be available through the English language; therefore it is unlikely that translation of non-English language publications will be needed.

Search terms

The following search strategy was used:

1 (artificial OR flexible OR mobile OR kinematic OR endoprosth$ OR replac$)

2 prostheses and implants/ OR implants, experimental/

3 prosthesis implantation/

4 arthroplasty, replacement/

5 arthroplasty

6 1 OR 2 OR 3 OR 4 OR 5

7 lumbar vertebrae/

8 (spine OR spinal OR lumbar)

9 vertebra$

10 (disc OR discs OR disk OR disks)

11 Intervertebral Disk/

12 7 OR 8 OR 9 OR 10 OR 11

13 6 AND 12

14 'intervertebral disc arthroplasty'

15 'intervertebral disc replacement'

16 'intervertebral disk arthroplasty'

17 'intervertebral disk replacement'

18 'total disc replacement'

19 'total disc arthroplasty'

20 'total disk replacement'

21 'total disk arthroplasty'

22 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21

23 13 OR 22

Appendix D Critical appraisal of comparative studies

Table 45 Critical appraisal summary of comparative studies: study design details

Study	Sample size	Participants	Randomisation details	Blinding	Interventions and outcomes
Level II studies					
Blumenthal 2005 *Includes:* McAfee 2005 McAfee 2006 Geisler 2008a Geisler 2008b Geisler 2009 Guyer 2009	Total: 304 CHARITÉ™: 205 Male/Female: 113/92 Age: 39.6 (19-60) Level: L4L5 (61), L5S1 (144) ALIF: 99 Male/Female: 44/55 Age: 39.6 (20-60) Level: L4L5 (32), L5S1 (67)	Inclusion criteria provided. Exclusion criteria provided. There was no significant difference between the two groups with respect to gender, age, race, height, BMI, incidence of prior surgery, activity level before onset of symptoms, activity level at time of enrolment, or preoperative working status or treatment level (p>0.05); however, patients in the ALIF group were slightly heavier at the time of surgery (p=0.0349).	Patients were randomly assigned in a 2:1 ratio (CHARITÉ™: ALIF) to one of two groups. A contract reserach organisation generated the random allocation sequence using SAS software. A fixed blocking method of randomisation was used with 6 assignments per block. Each site was provided with sequentially numbered sealed envelopes that contained the treatment assignments for their site. Compliance with the sequential assignment of treatments was monitored throughout the study.	The investigator, key office staff, and operating room staff were nonblinded to group assignment. Patients were not blinded throughout their 2-year course within the study because blinding all patient records would have been very difficult, and patients experiencing postoperative bone graft donor site pain would have been unblinded.	Lumbar AIDR was adequately detailed and ALIF was poorly detailed. Outcome measures reported were: *Operative outcomes* • Operative time • Blood loss • Length of hospital stay *Clinical outcomes* • ODI scores • VAS pain scores • Patient satisfaction • Clinical success rates • Narcotic medication use • Work status *Radiographic outcomes* • Operative level ROM • Disc space height and subsidence Adverse events were reported.
Zigler 2007 *Includes:* Auerbach 2009	Total: 236 ProDisc®-L: 161 Male/Female: 82/79 Age: 38.7 [8] Level: L3L4(3), L4L5 (54), L5S1 (104) Circumferential spinal fusion:	Inclusion criteria provided. Exclusion criteria provided. There was no significant difference between the two groups with respect to gender, age, race, BMI, smoking status, incidence of prior surgery, or	Patients were randomly assigned in a 2:1 ratio (ProDisc®-L: Circumferential spinal fusion) to one of two groups. Using a fixed randomization blocking method of 6 assignments per block, random allocations were generated in a 2:1 ratio. The	Treatment was unblinded to the patient after surgery. The surgeon and surgical staff were not blinded due to preparation requirements for each procedure, as well as the difference in postoperative management (brace	Lumbar AIDR was poorly detailed and circumferential spinal fusion was not detailed. Outcome measures reported were: *Operative outcomes* • Operative time • Blood loss

	75 Male/Female: 34/41 Age: 40.4 [7.6] Level: L3L4(3), L4L5 (22), L5S1 (50)	treatment level.	randomisation was held by the sponsor and disclosed to the site only after individual patient enrollment.	immobilisation for the fusion patients *vs.* early mobilization for the arthroplasty patients).	• Length of hospital stay *Clinical outcomes* • ODI scores • VAS pain scores • Patient satisfaction • Clinical success rates • Neurologic success • Narcotic medication use • Work and recreation status • Quality of life *Radiographic outcomes* • ROM Adverse events were reported.
Berg 2009a *Includes:* Berg 2009b	Total: 152 CHARITÉ™, ProDisc®-L or Maverick™: 80 Male/Female: 32/48 Age: 40.2 [8.1] PLF or PLIF: 72 Male/Female: 30/42 Age: 38.5 [7.8]	Inclusion criteria provided. Exclusion criteria provided. There was no significant difference between the two groups with respect to gender, age, race, smoking status, baseline ODI, prior surgical treatment, back pain or function, or treatment level (p>0.05); however, patients in the PLIF/PLF group suffered more leg pain at baseline (p=0.016).	Patients were randomised by means of a sealed envelope technique. The planning staff drew the envelope when the surgeon's inclusion form and the patient's informed consent had reached the planning office via internal mail.	Patients were not blinded to the treatment assignment. No other details on blinding were reported.	Lumbar AIDR and PLIF/PLF surgical techniques adequately detailed. *Operative outcomes* • Operative time • Blood loss • Length of hospital stay *Clinical outcomes* • ODI scores • VAS pain scores • Patient satisfaction • Quality of life • Sexual function • Work status Adverse events were reported.
Sasso 2008	Total: 76 FlexiCore™: 50 Male/Female: 23/21 Age: 36 Level: L4L5 (12), L5S1 (32) Circumferential spinal fusion: 26	Inclusion criteria provided. Exclusion criteria provided. Both treatment groups were comparable with regard to male/female ratio, age and BMI.	No details of randomisation were reported.	No details on blinding were reported.	Lumbar AIDR and circumferential spinal fusion were well detailed. *Operative outcomes* • Operative time • Blood loss • Length of hospital stay *Clinical outcomes*

	Male/Female: 10/13 Age: 41 Level: L4L5 (5), L5S1 (17), L4L5 and L5S1 (1)				• ODI scores • VAS pain scores *Radiographic outcomes* • ROM Adverse events were reported.
Level III-2 studies					
Schroven and Dorofey 2006	Total: 24 ProDisc®-L: 14 Male/Female: 8/6 Age: 43.5 (31-57) Level: L3L4 (1), L4L5 (2), L5S1 (11) ALIF: 10 Male/Female: 6/4 Age: 44.6 (29-60) Level: L3L4 (0), L4L5 (4), L5S1 (6)	Inclusion criteria provided. Exclusion criteria not provided. Both treatment groups were comparable with regard to male/female ratio, age spinal level and preoperative ODI score.	Not applicable.	No details on blinding were reported.	Lumbar AIDR and ALIF surgical techniques adequately detailed. Outcome measures reported were ODI (expressed in absolute values, with 60 reflecting the worst possible condition) calculated before the operation and at 6 and 12 months postoperatively, duration of hospitalisation, blood loss and operative time. Adverse events were reported.

Table 46 Critical appraisal summary of comparative studies: results details

Study	Numbers analysed	Statistical methods	Outcomes and estimation	Ancillary analyses	Adverse events	Follow-up
Level II studies						
Blumenthal 2005 *Includes:* McAfee 2005 McAfee 2006 Geisler 2008a Geisler 2008b Geisler 2009 Guyer 2009	The sample size was computed using the Blackwelder methodology, assuming that 70% of the patients in both the investigational and control groups would have a successful result and that a clinically insignificant difference in success rates between groups (delta) was 15%. Choosing a type I error of 5% (one-sided) and 80% power, the sample size in the investigational group was 174 patients, and the sample size in the control group was 87 patients, for a total of 261. Allowing for a potential dropout rate of 10% resulted in approximately 194 patients in the treatment group and 97 patients in the control group, for a total of 291 patients. Intention-to-treat analysis not defined.	For categorical variables, *p* values were generated using the Fisher exact test. A *t* test was used to test means. The Blackwelder test was used to test for treatment equivalence based on the assumption that a difference of 0.15 was clinically significant. The test was performed on the pooled population. Covariate analyses were done to assess the impact of various factors (age, baseline ODI, gender, operative level, use of hormone replacement therapy, use of pain medication at any time, body mass index (BMI), and baseline activity level). Sensitivity analyses were performed to evaluate the potential impact of incomplete subjects (eg, lost to follow-up).	Means, standard deviations, and ranges, as well as percentages were presented for reported outcomes. *P*-values were provided for differences between treatment groups. Adverse events: discussion of individual incidents only.	Statistical analysis was conducted to compare clinical success in patients who underwent revision surgery with those who did not. The clinical results of the study were analysed to assess the effect of previous surgery on clinical outcomes following either treatment. Statistical analysis was conducted to determine the incidence of, and reasons for, reoperation in all patients.	Adverse events detailed.	Follow-up occurred at 6 weeks, and 3, 6, 12, 24 and 60 months postsurgery. At 12 months, the follow-up rate was 95.8% in the investigational group and 94.2% in the control group. At 24 months, the rate of follow-up within the time window described in the protocol was 91.5% in the investigational group and 89.2% in the control group. At 60 months, a total of 160 patients completed the 5-year study, including 27 nonrandomised training cases and 133 randomised cases (90 CHARITE´ and 43 BAK patients). Thus, the follow-up rates reached 57% of eligible randomised patient population and 44% of the total patient cohort.
Zigler 2007 *Includes:* Auerbach 2009	The sample size, based on a noninferiority design, was computed using the Blackwelder methodology, assuming that 85% of patients in both the investigational and control groups would have a	Continuous and ordinal variables were analysed by a Wilcoxon rank sum test, and categorical variables were analysed using Fisher's exact test between the fusion and	Means and standard deviations, as well as percentages were presented for reported outcomes. *p*-values were provided for differences between	Data from patients with L4/5 and L5/S1 operative levels were analysed separately in order to assess for differential effects on ROM based on operative level. Withinsubjects	Adverse events detailed.	Clinical status of each patient was evaluated before and after surgery, at 6 weeks, and 3, 6, 12, 18 and 24 months. Patient accountability reveals that follow-up at 24

	successful result and that a clinically insignificant difference in success rates between groups (delta) was 12.5%. Choosing a type I error of 5% (1-sided) and 80% power, the sample size in the investigational group was 144 and 72 in the control group for a total of 216. Allowing for a potential dropout rate of 15%, total possible enrollment was 170 in the investigational group and 85 in the control group, for a total of 255 patients. Intention-to-treat analysis not defined.	ProDisc-L patients.	treatment groups. Adverse events: discussion of individual incidents only.	comparisons of ROM, changes 24 months after surgical intervention were assessed for both TDR and fusion subgroups, using the paired *t* test. The significance of the between-subjects effect of the type of surgical intervention (TDR *vs.* fusion) on ROM was assessed by repeated measures analysis of variance (ANOVA).		months was 98.2%. There was no significant difference at 24 months between the investigational (98.6%) and control (97.1%) groups. Follow-up of patients with complete data for the purpose of calculating overall study success was 91% (investigational) and 88.5% (control) at 24 months.
Berg 2009a *Includes:* Berg 2009b	The Lehr formula was used to provide crude estimates of sample size. With 80% power at 5% significance level, the size of each group was estimated at 64 patients, which was increased o 72 to allow for potential dropout. Intention-to-treat analysis not defined.	Statistical analysis was made using Statistica version 7 (StatSoft Inc. Tulsa, OK, USA). For comparison between the treatment groups, and for some sub-group analyses, two-tailed Mann–Whitney U test and Wilcoxon rank sum tests were used. For ordinal data, Student's t test was used, and for categorical data, eg global assessment, Spearman R, Fisher's exact and *v*2 tests were used. Multivariate statistics were used to analyse predictors.	Means and standard deviations were presented for reported outcomes. *p*-values were provided for differences between treatment groups. Adverse events: The grading of complications from ''The Swedish Spine Study'' was used.	Multiple regression analyses were performed separately for men and women and for those who underwent each surgical technique.	Adverse events detailed.	Follow-up occurred at 1 and 2 years postsurgery. For the main clinical outcomes, all patients appeared at check-ups and answered questionnaires at both the 1- and 2-year follow-up, resulting in a 100% follow-up rate.

		Statistical significance was defined as $p<0.05$.				
Sasso 2008	No power calculations reported Intention-to-treat analysis not defined.	No statistical methods reported.	Mean values were presented for ODI scores, VAS pain scores, length of hospitalisation, blood loss and operative time. Adverse events: Adverse events were recorded for each study subject, and were classified as serious adverse events (SAEs) if they were life threatening, required hospitalisation, or required medical intervention to preclude permanent impairment. SAEs were further classified as either requiring surgical intervention (SI) or not requiring SI.	No subgroup analyses performed.	Adverse events detailed.	Follow-up occurred at 6 weeks, 3 months, 6 months, 1 year and 2 years postsurgery. No description of patients lost to follow-up.
Level III-2 studies						
Schroven and Dorofey 2006	No power calculations reported. Intention-to-treat analysis not defined. Per-protocol analysis not defined.	Authors reported that statistical analysis was not done, given the small size of the groups.	Both individual patient values and mean (range) values were presented for ODI scores, length of hospitalisation, blood loss and operative time. Adverse events: discussion of individual incidents only.	No subgroup analyses performed.	Adverse events detailed.	Total follow-up period was 1 year. Losses to follow-up: at 1 year no patient had been lost to follow-up.

Appendix E Studies included in the review

Systematic reviews and health technology assessments

Blue Cross Blue Shield Association, 2007. Artificial lumbar disc replacement, Chicago IL: Blue Cross Blue Shield Association (BCBS), 24.

California Technology Assessment Forum, 2007. Artificial Disc Replacement for Degenerative Disc Disease of the Lumbar Spine, February.

Chou R, Baisden J et al, 2009. 'Surgery for low back pain: a review of the evidence for an American Pain Society Clinical Practice Guideline', *Spine (Phila Pa 1976)*, 34 (10), 1094-1109.

Freeman BJ, Davenport J, 2006. 'Total disc replacement in the lumbar spine: a systematic review of the literature', *Eur Spine J*, 15 Suppl 3, S439-S447.

Harrop JS, Youssef JA et al, 2008. 'Lumbar adjacent segment degeneration and disease after arthrodesis and total disc arthroplasty', *Spine (Phila Pa 1976)*, 33 (15), 1701-1707.

Ontario Ministry of Health and Long-Term Care (MAS), 2006. Artificial disc replacement for lumbar and cervical degenerative disc disease- update: an evidence-based analysis, Toronto: Medical Advisory Secretariat, 6(10), 105.

Vlayen J, Camberlin C, Paulus D, Ramaekers D, 2006. Rapid assessment of emerging spine technologies: intervertebral disc replacement and vertebro/balloon kyphoplasty, Belgian Federal Health Care Knowledge Centre (KCE), KCE reports 39.

Washington Health Technology Assessment, 2008. Washington State Health Care Authority, HTA Final Report - Artificial Discs Replacement (ADR), September 19.

Yajun W, Yue Z et al, 2010. 'A meta-analysis of artificial total disc replacement versus fusion for lumbar degenerative disc disease', *Eur Spine J*, Epub 4 April.

Studies included for safety

Comparative studies

Berg ST, 2009. 'Total disc replacement compared to lumbar fusion: A randomised controlled trial with 2-year follow-up', *European Spine Journal*, 18 (10), 2009.

Blumenthal S, Regan JJ, 2005. 'A prospective, randomized, multicenter Food and Drug Administration Investigational Device Exemptions study of lumbar total disc replacement with the CHARITEartificial disc versus lumbar fusion - Part I: Evaluation of clinical outcomes', *Spine*, 30 (14), 15.

Sasso RC, Foulk DM, Hahn M, 2008. 'Prospective, randomized trial of metal-on-metal artificial lumbar disc replacement: initial results for treatment of discogenic pain', *Spine (Phila Pa 1976)*, 33 (2), 123-131.

Schroven I, Dorofey D, 2006. 'Intervertebral prosthesis versus anterior lumbar interbody fusion: one-year results of a prospective non-randomised study', *Acta Orthop Belg*, 72 (1), 83-86.

Zigler J, Delamarter R et al, 2007. 'Results of the prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease', *Spine (Phila Pa 1976)*, 32 (11), 1155-1162.

Case series

Aunoble S, Meyrat R et al, 2010. 'Hybrid construct for two levels disc disease in lumbar spine', *Eur Spine J*, 19 (2), 290-296.

Bertagnoli R, Yue JJ et al, 2005a. 'The treatment of disabling multilevel lumbar discogenic low back pain with total disc arthroplasty utilizing the ProDisc prosthesis: a prospective study with 2-year minimum follow-up', *Spine (Phila Pa 1976)*, 30 (19), 2192-2199.

Bertagnoli R, Yue JJ et al, 2005b. 'The treatment of disabling single-level lumbar discogenic low back pain with total disc arthroplasty utilizing the Prodisc prosthesis: a prospective study with 2-year minimum follow-up', *Spine (Phila Pa 1976)*, 30 (19), 2230-2236.

Bertagnoli R, Yue JJ et al, 2006a. 'Lumbar total disc arthroplasty in patients older than 60 years of age: A prospective study of the ProDisc prosthesis with 2-year minimum follow-up period', *Journal of Neurosurgery: Spine*, 4 (2), 85-90.

Bertagnoli R, Yue JJ et al, 2006b. 'Lumbar total disc arthroplasty utilizing the prodisc prosthesis in smokers versus nonsmokers: A prospective study with 2-year minimum follow-up', *Spine*, 31 (9), 992-997.

Bertagnoli R, Yue JJ et al, 2006c. 'Treatment of symptomatic adjacent-segment degeneration after lumbar fusion with total disc arthroplasty by using the prodisc prosthesis: a prospective study with 2-year minimum follow up', *J Neurosurg Spine*, 4 (2), 91-97.

Cakir B, Richter M et al, 2006. 'Dynamic stabilization of the lumbar spine', *Orthopedics*, 29 (8), 716-722.

Chung SS, 2006. 'Lumbar total disc replacement using ProDisc II: A prospective study with a 2-year minimum follow-up', *Journal of Spinal Disorders and Techniques*, 19 (6), 411-415.

David T, 2007. 'Long-term results of one-level lumbar arthroplasty: Minimum 10-year follow-up of the CHARITE artificial disc in 106 patients', *Spine*, 32 (6), 661-666.

Di Silvestre M, Bakaloudis G et al, 2009. 'Two-level total lumbar disc replacement', *Eur Spine J*, 18 Suppl 1, 64-70.

Gioia G, 2007. 'The Charite III Artificial Disc lumbar disc prosthesis: Assessment of medium-term results', *Journal of Orthopaedics and Traumatology*, 8 (3), 134-139.

Guyer RD, Geisler FH et al, 2008. 'Effect of age on clinical and radiographic outcomes and adverse events following 1-level lumbar arthroplasty after a minimum 2-year follow-up', *J Neurosurg Spine*, 8 (2), 101-107.

Hannibal M, Thomas DJ et al, 2007. 'ProDisc-L total disc replacement: a comparison of 1-level versus 2-level arthroplasty patients with a minimum 2-year follow-up', *Spine (Phila Pa 1976)*, 32 (21), 2322-2326.

Huang RC, 2006. 'Range of motion and adjacent level degeneration after lumbar total disc replacement', *Spine Journal*, 6 (3), 242-247.

Kim DH, Ryu KS et al, 2007. 'Factors influencing segmental range of motion after lumbar total disc replacement using the ProDisc II prosthesis', *J Neurosurg Spine*, 7 (2), 131-138.

Le Huec JC, 2005. 'Clinical results of Maverick lumbar total disc replacement: Two-year prospective follow-up', *Orthopedic Clinics of North America*, 36 (3 SPEC. ISS.), 315-322.

Lemaire JP, Carrier H et al, 2005. 'Clinical and radiological outcomes with the Charite artificial disc: a 10-year minimum follow-up', *J Spinal Disord Tech*, 18 (4), 353-359.

Marshman LAG, 2008. 'Subsidence and malplacement with the Oblique Maverick Lumbar Disc Arthroplasty: technical note', *Spine Journal*, 8 (4), 650-655.

Mirovsky Y, Shalmon E et al, 2008. 'Lumbar disk replacement with the ProDisc prosthesis', *Orthopedics*, 31 (2), 133.

Neal CJ, Rosner MK, Kuklo TR, 2005. 'Magnetic resonance imaging evaluation of adjacent segments after disc arthroplasty', *J Neurosurg Spine*, 3 (5), 342-347.

Ogon M, Howanietz N et al, 2007. 'Implantation of the ProDisc intervertebral disk prosthesis for the lumbar spine', *Oper Orthop Traumatol*, 19 (2), 209-230.

Park CK, Ryu KS, Jee WH, 2008. 'Degenerative changes of discs and facet joints in lumbar total disc replacement using ProDisc II: minimum two-year follow-up', *Spine (Phila Pa 1976)*, 33 (16), 1755-1761.

Patel VV, 2006. 'Computed tomography assessment of the accuracy of in vivo placement of artificial discs in the lumbar spine including radiographic and clinical consequences', *Spine*, 31 (8), 948-953.

Pimenta L, 2010. 'Clinical performance of an elastomeric lumbar disc replacement: Minimum 12 months follow-up', *SAS Journal* , 4 (1), 16-25.

Putzier M, Funk JF et al, 2006. 'Charite total disc replacement--clinical and radiographical results after an average follow-up of 17 years', *Eur Spine J*, 15 (2), 183-195.

Regan JJ,Maxwell JH, 2006. 'Evaluation of surgical volume and the early experience with lumbar total disc replacement as part of the investigational device exemption study of the Charite Artificial Disc', *Spine*, 31 (19), 2270-2276.

Ross R, 2007. 'Survival and clinical outcome of SB Charite III disc replacement for back pain', *Journal of Bone and Joint Surgery - Series B*, 89 (6), 785-789.

Schluessmann E, Diel P et al, 2009. 'SWISSspine: a nationwide registry for health technology assessment of lumbar disc prostheses', *Eur Spine J*, 18 (6), 851-861.

Shim CS, 2007. 'CHARITI versus ProDisc: A comparative study of a minimum 3-year follow-up', *Spine*, 32 (9), 1012-1018.

Siepe CJ, 2006. 'Clinical results of total lumbar disc replacement with ProDisc II: Three-year results for different indications', *Spine*, 31 (17), 1923-1932.

Siepe CJ, Wiechert K et al, 2007. 'Total lumbar disc replacement in athletes: Clinical results, return to sport and athletic performance', *European Spine Journal*, 16 (7), 1001-1013.

Siepe CJ, Mayer HM et al, 2007. 'Total lumbar disc replacement: different results for different levels', *Spine (Phila Pa 1976)*, 32 (7), 782-790.

Sinigaglia R, 2009. 'Comparison of single-level L4-L5 versus L5-S1 lumbar disc replacement: Results and prognostic factors', *European Spine Journal*, 18 (SUPPL. 1), S52-S63.

Tropiano P, Marnay T, 2005. 'Lumbar total disc replacement: Seven to eleven-year follow-up', *Journal of Bone and Joint Surgery - Series A*, 87 (3), 490-496.

Trouillier H, Kern P et al, 2006. 'A prospective morphological study of facet joint integrity following intervertebral disc replacement with the CHARITE Artificial Disc', *Eur Spine J*, 15 (2), 174-182.

Warachit P, 2008. 'Results of Charite artificial lumbar disc replacement: experience in 43 Thais', *J Med Assoc Thai*, 91 (8), 1212-1217.

Wenger M, Markwalder TM, 2005. 'A novel surgical treatment of lumbar disc herniation in patients with long-standing degenerative disc disease', *J Neurosurg Spine*, 2 (5), 515-20.

Zeh A, Becker C et al, 2009. 'Time-dependent release of cobalt and chromium ions into the serum following implantation of the metal-on-metal Maverick type artificial lumbar disc (Medtronic Sofamor Danek)', *Arch Orthop Trauma Surg*, 129 (6), 741-746.

Studies included for effectiveness

Comparative studies

Auerbach JD, Jones KJ et al, 2009. 'Segmental contribution toward total lumbar range of motion in disc replacement and fusions: a comparison of operative and adjacent levels', *Spine (Phila Pa 1976)*, 34 (23), 2510-2517.

Berg S, 2009. 'Total disc replacement compared to lumbar fusion: A randomised controlled trial with 2-year follow-up', *European Spine Journal*, 18 (10), 1512-1519.

Berg S, Fritzell P, Tropp H, 2009. 'Sex life and sexual function in men and women before and after total disc replacement compared with posterior lumbar fusion', *Spine J*, 9 (12), 987-994.

Blumenthal SM, Regan JJ, 2005. 'A prospective, randomized, multicenter Food and Drug Administration Investigational Device Exemptions study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion - Part I: Evaluation of clinical outcomes', *Spine*, 30 (14), 1565-1575.

Geisler FH, Guyer RD et al, 2008a. 'Effect of previous surgery on clinical outcome following 1-level lumbar arthroplasty', *J Neurosurg Spine*, 8 (2), 108-114.

Geisler FH, Guyer RD, et al, 2008b. 'Patient selection for lumbar arthroplasty and arthrodesis: The effect of revision surgery in a controlled, multicenter, randomized study', *Journal of Neurosurgery: Spine*, 8 (1), 13-16.

Geisler FH, 2009. 'Prospective, Randomized, Multicenter FDA IDE Study of CHARITE Artificial Disc versus Lumbar Fusion: Effect at 5-year Follow-up of Prior Surgery and Prior Discectomy on Clinical Outcomes Following Lumbar Arthroplasty', *SAS Journal*, 3 (1), 16-24.

Guyer RD, 2009. 'Prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion: Five-year follow-up', *Spine Journal*, 9 (5), 374-386.

McAfee PC, 2005. 'A prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion - Part II: Evaluation of radiographic outcomes and correlation of surgical technique accuracy with clinical outcomes', *Spine*, 30 (14), 1576-1583.

McAfee PC, Geisler FH et al, 2006. 'Revisability of the CHARITE artificial disc replacement: analysis of 688 patients enrolled in the U.S. IDE study of the CHARITE Artificial Disc', *Spine (Phila Pa 1976)*, 31 (11), 1217-1226.

Sasso RC, Foulk DM, Hahn M, 2008. 'Prospective, randomized trial of metal-on-metal artificial lumbar disc replacement: initial results for treatment of discogenic pain', *Spine (Phila Pa 1976)*, 33 (2), 123-131.

Schroven, Dorofey D, 2006. 'Intervertebral prosthesis versus anterior lumbar interbody fusion: one-year results of a prospective non-randomised study', *Acta Orthop Belg*, 72 (1), 83-86.

Zigler J, Delamarter R et al, 2007. 'Results of the prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease', *Spine (Phila Pa 1976)*, 32 (11), 1155-1162.

Appendix F Studies providing level IV safety data

Table 47 Characteristics of studies providing level IV safety evidence

Study ID and country	Design	Patient allocation	Inclusion/ exclusion criteria	No. of patients	Age in years (mean ± SD)	Male/ female	Prior lumbar surgery	Length of follow-up after surgery (mean ± SD)	Losses to follow-up
Aunoble et al 2010 France	Prospective	NR	Yes	80	43[a] [Range: 31-60[a]]	17/25[a]	All patients underwent a hybrid fusion (an ALIF at one level and a TDA at the other). 32 patients had prior lumbar procedures - 11 had at least one discectomy, 10 had at least one nucelotomy, 9 had at least one treatment of facet rhizolysis, 1 patient had a bilateral L4 & L5 nerve root decompression,1 patient underwent an L5 isthmic repair for a grade I spondylolisthesis.	26.3 months [Range: 21-50 months]	38 Reasons for losses: only 42 of 80 patients were followed up for at least 2 years – reasons why not provided.
Bertagnoli et al 2005a[b] Germany	Prospective	NR	Yes	29	51[a] [Range: 30-60[a]]	15/10[a]	70% of the patients entered in the study had greater than 50% disc height loss and advanced lumbar spondylosis at least 2 levels between L1-S1 and one had at least 1 prior surgical procedure excluding fusion.	31 months [Range: 25-41 months]	4 Reasons for losses: 4 patients lost to FU as their addresses were outside of Germany.
Bertagnoli et al 2005b[b] Germany	Prospective	NR	Yes	118	47.5[a] [Range: 36-60[a]]	47/57[a]	5 cases were performed in patients that had either a missing rib at T12 or a lumbarised S1 vertebra. 57% of patients had prior posterior surgery at the affected levels.	31 months [Range: 24-45 months]	14 Reasons for losses: 7 patients could not be examined after surgery because their permanent addresses were outside of Germany, 2 patients did not comply with appropriate FU visits, 1 patient's preoperative data was lost, no reasons were provided for 4 patients.
Bertagnoli et al	Prospective	NR	Yes	22	63	9/13	3 patients had undergone prior lumbar	34.6 months	0

2006a Germany					[Range: 61-71]		surgery at the same site of ADR (1 laminectomy and 2 discectomies).	[Range: 24-56 months]	
Bertagnoli et al 2006b[b] Germany	Prospective	NR	Yes	110	Mean: NR [Range: 29-60]	NR	60 patients had prior posterior surgery at the affected levels.	Mean: NR [Range: 24-49 months]	6 Reasons for losses: Complete FU was not possible because of distance of patients.
Bertagnoli et al 2006c Germany	Prospective	NR	Yes	20	Median = 50[a] [Range: 35-67[a]]	9/9[a]	56% of patients had undergone prior 2 level (8 cases) or 3 level (2 cases) fusion. The remaining 45% had undergone single level fusion. In one case a ProDisc was placed into a prior non-union and an additional level of ADR was performed. 2 patients had previously undergone ALIF. In these patients a standard retroperitoneal exposure was performed.	27 months [Range: 24-48 months]	2 Reasons for losses: 2 patients could not be examined postoperatively because they moved.
Cakir et al 2006 Germany	NR	NR	Inclusion not exclusion	29	40.8 [Range: 29-56]	10/19	8 of 29 patients had previous disc surgery.	15.3 months [Range:12-35 months]	0
Chung et al 2006 Korea	NR	Consecutive	Yes	38	43[a] Range: 25-58[a]	16/20[a]	7 patients had prior discectomies.	37 months [Range: 25-42]	2 Reasons for losses: Could not be contacted.
David 2007[b] France	Retrospective	NR	Inclusion not exclusion	108	36.4 [Range: 23-50]	45/63	44 patients had a prior lumbar procedure performed at the index level including 20 who had one microdiscectomy, 10 who had either a percutaneous nucleotomy or injection of chymopapain and 14 who had 2 procedures.	13.2 years [Range: 10-16.8 years]	2 Reasons for losses: 2 patients died due to causes unrelated to the surgery.
Di Silvestre et al 2009 Italy	Retrospective	NR	Inclusion not exclusion	32	38.5	11/21		Minimum of 3 years	0
Gioia et al	NR	Consecutive	No	56	39.5[a]	13/23[a]		6.9 years	20

2007 Italy					[Range: 32-39[a]]			[Range: 5-9 years]	Reasons for losses: Authors only presented results for first 36 patients operated before October 2002.
Guyer et al 2008[c] USA	Prospective	NR	Yes	276	Mean: NR [Range: 18-60]	NR		Maximum of 2 years	0
Hannibal et al 2007 USA	Prospective	Consecutive	Yes	59	39	38/21	9 of the 1-level and 13 of the 2-level patients had a previous surgery, which included IDET, microdiscectomy, or partial laminectomy.	Minimum of 2 years	0
Huang et al 2006[d] USA	Retrospective	NR	Inclusion not exclusion	64	45.2 ± 8.6[a] [Range: 25-65[a]]	23/19[a]	21 patients[a] had a history of prior spine surgery which included 21 discectomies, 2 decompresssions for lumbar stenosis & 14 other procedures (including thermocoagulation & chemonucleolysis).	8.7 ± 1.0 years [Range: 25-65]	22 Reasons for losses: 3 deceased, 3 lost to FU, 16 excluded because complete radiographic documentation was unavailable.
Kim et al 2007	Prospective	Consecutive	Yes	32	38.9[a] [Range: 24-60[a]]	12/18[a]		30.2 months [Range: 24-41 months]	1 Reasons for losses: patient could not be located for the FU evaluation.
Le Huec et al 2005 France	Prospective	NR	Yes	64	44 ± 7	25/39	18 patients underwent previous spinal treatment including 3 isolated rhyzolyses of the posterior facets and 4 disc annuloplasties, 1 of which was followed by a discectomy. Eight patients had received disc nucleolysis with chemopapain, 1 of which was followed by a discectomy.	18 months [Range: 12-36 months]	0
Lemaire et al 2005 France	NR	Consecutive	Yes	107	39.6[a] [Range: 23.9-50.8[a]]	41/59[a]	3 patients required a concomitant posterior instrumented fusion above the level of TDR for kyphosis correction prior to implantation of the disc. The author	11.3 years [Range: 10-13.4 years]	7 Excluded as not followed up for minimum of 10 years.

							stated that normally this would be a contraindication to TDR but the amount of correction was small.		
Marshman et al 2008[e, f] England	NR	Consecutive	Yes	14	NR [Range: 28-59]	9/5		Early postoperative	0
Mirovsky et al 2008 Israel	NR	NR	No	21	43 [Range: 33-56]	10/11	5 patients had disc degeneration following previous discectomy and 2 had disc degeneration at a level adjacent to a previous fusion.	3.1 years [Range: 17-49 months]	0
Neal et al 2005 USA	NR	Consecutive	No	10	36 [Range: 26-49]	6/4		5.3 months	0
Ogon et al 2007 Austria	NR	NR	Yes	34	44.3 [Range: 30-60]	8/26		Minimum of 1 year, maximum of 2 years	0
Park et al 2008[g] Korea	Retrospective	Consecutive	Yes	46	42.3[a] Range: 26-60[a]	12/20[a]		32.2 months [Range: 26 to 42 months]	14 Reasons for losses: 1 died, 1 was pregnant, 4 were lost, 1 refused the radiologic examinations, 7 were excluded because parts of the preoperative imaging studies had been lost.
Patel et al 2006 USA	Prospective	Consecutive	No	52	41.6	NR		41.5 weeks [Range: 26-69 weeks]	0
Pimenta et al 2010 Brazil	Prospective	NR	Yes	12	40.6 ± 8.4 [Range: 25-55]	11/1		Maximum of 12 months	0

Putzier et al 2006 Germany	Retrospective	Consecutive	Inclusion not exclusion	71	44[a] [Range: 30-59[a]]	20/33[a]	8 patients had had previous disc surgery and 3 patients suffered from additional spondylolisthesis grade I.	17.3 years [Range: 14.5-19.2 years]	18
Regan et al 2006b USA	Prospective	NR	Yes	71[h]	38.5 ± 7.81 [Range: 18-57]	41/30		Maximum of 24 months	10 (at 24 months) Reasons for losses not stated.
Ross et al 2007[i] England	NR	NR	Yes	160	46 [Range: 27-73]	62/98		79 months [Range: 31-161 months]	37 Reasons for losses: 24 lost to FU, 2 died postoperatively from unrelated. causes, 1 declined to participate, 10 had 12 implants removed
Schluessmann et al 2009 Switzerland	Prospective	NR	NR	427	Females: 41 [Range: 18.5-64.7] Males: 43.4 [Range: 19.6-?]	186/241		NR? [Range: 11 to 915 days]	30-40 Reasons for losses: No FU information recorded on either the NASS and/or EQ-5D and/or surgeon based FU forms.
Shim et al 2007	Retrospective	NR	Inclusion not exclusion	61	Charité group = 44.4[a] [Range: 31-63[a]] ProDisc group = 44[a] [Range: 31-66[a]]	30/27[a]		Charité group = 41 months [Range: 36-48] ProDisc group = 38 months [Range: 36-40]	4 Reasons for losses not stated
Siepe et al 2006[b] Germany	Prospective	Consecutive	Yes	192	42.5[a] [Range: 21.9-66.1[a]]	33/59[a]	17 patients had previous discectomies but none had marked scar tissue formation in the spinal canal.	34.2 months [Range: 24-62 months]	100 Reason for losses: 98 patients were excluded as they did not meet the criteria of a minimum FU time of 24 months. 2 patients were lost to FU but seen at the 3 months postoperative evaluation with an excellent result in 1 and satisfactory in the other.

Siepe et al 2007a[j,k] Germany	Prospective	NR	Yes	39	39.8 [Range: 26.2-58]	21/18	9 patients had previous discectomies; in 1 patient disc replacement was performed at L5-S1 due to adjacent degeneration in the lumbosacral junction 4.5 years after a previous fusion procedure at L4-L5.	26.3 months [Range: 9-50.7 months]	1 Reason for losses: Lost to FU.
Siepe et al 2007b[l] Germany	Prospective	NR	Yes	218	43.2[a] [Range: 21.9-65.8[a]]	39/60[a]		25.8 months [Range: 12.1-57.5]	119 Reasons for losses: The patients did not qualify for the study.
Sinigaglia et al 2009 Italy	Prospective	NR	Inclusion not exclusion	62	41.17 ± 7.14 [Range: 30-56]	12/24		38.67 ± 17.34 months Minimum of 12 months	26 Reason for losses: 5 lost to FU, 21 excluded due to multiple level or hybrids implants.
Tropiano et al 2005[m,n] France	NR	NR	Yes	64	46 [Range: 25-65]	36/25	10 patients had one prior operation, and 18 patients had two, three or four prior operations including – discectomy, laminotomy, percutaneous nucleotomy, chemonucleolysis and thermocoagulation. 7 patients underwent additional surgical procedures during the same surgical session; these operations included an L5-S1 arthrodesis with an L4-L5 lumbar TDR in 6 patients and and L5-S1 arthrodesis adjacent to L3-L4 & L4-L5 lumbar TDR in 1 patient.	8.7 years [Range: 85 to 128 months]	9 Reasons for losses: 3 had died from causes unrelated to the implantation surgery, 2 could not be located, 2 refused to return for the FU examination, 2 did not complete all items in the questionnaire.
Trouillier et al 2006[o] Germany	Prospective	NR	Yes	13	39 [Range: 27-49]	3/10	5 patients had prior nucleotomy at operating level.	Maximum 12 months	0
Wenger et al 2005 Switzerland	NR	NR	Yes	14	40 [Range: 22-56.1]	5/9		12.5 months [Range: 3.9-21.1 months]	0
Warachit 2008 Thailand	Prospective	NR	Inclusion not exclusion	43	42.3 [Range: 23-54]	26/17		NR	0

Zeh et al 2009 Germany	NR	NR	Yes	10	36.5 [Range: 18.8-49.4]	7/3			36.7 months [Range: 32-43.1 months]	0

NOTES: In this table all procedures were performed using an anterior retroperitoneal approach unless otherwise indicated in the study ID; ADR = artificial disc replacement; ALIF = anterior lumbar interbody fusion; EQ-5D = Euroqol-5D patient assessment; FU = follow-up; IDET = intradiscal electrothermal therapy; NASS = patient assessment; NR = not reported; SD = standard deviation; TDA = total disc arthroplasty; TDR = total disc replacement; [a]Data does not include those patients lost to FU; [b]One or more of the authors has/have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of the manuscript; [c]All authors received research funding for the investigational device exemption study and benefits for consulting work from DePuy Spine, Inc., the manufacturer of the Charité artificial disc. Four of the authors also received royalties from DePuy Spine; [d]Authors acknowledge financial relationships which may indirectly relate to the manuscript; [e]One or more authors are a consultant for the company producing the artificial disc; [f]Half of the patients had the Oblique Maverick prosthesis, the other half had the standard Anterior Maverick prosthesis; [g]Corporate/Industry fund were received in support of this work; [h]Although the study included another 205 TDR patients the results for these patients is not included as they are reported in Blumenthal et al 2005; [i]The majority of the surgery was carried out via a transperitoneal approach; [j]Patient population may possibly be represented in Siepe et al 2006; [k]Access to the disc space was achieved through an anterior retroperitoneal access in 32 patients (82.1%) and transperitoneal approach in 7 patients (17.9%); [l]Disc spaces were approached through a mini-open laparotomy; [m]45 patients were treated through a retroperitoneal approach and 10 through a transperitoneal approach; [n]In support of their research or preparation of the manuscript, one or more of the authors received grants or outside funding from Spine Solutions. In addition, one more of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity (Spine Solutions); [o]Disc was implanted via a ventral, retroperitoneal access.

Table 48 Adverse events reported in studies providing level IV safety evidence

Study ID	No. and type of implants	Implant levels, no. of each level, location and no. at each location	No. of patients	Adverse events (number of events) (resolution of adverse event, where reported)	Total adverse events
Aunoble et al 2010	44 (excludes losses to FU) All Maverick	All TDR were implanted in conjunction with ALIF at another level L5-S1 ALIF/L4-L5 prosthesis = 35 L4-L5 ALIF/L3-L4 prosthesis = 3 L5-S1 ALIF/L4-L5 prosthesis/L3-L4 prosthesis = 2 L5-S1prosthesis L4-L5 ALIF = 1 L5-S1 ALIF/L4-L5 ALIF/L3-L4 prosthesis = 1	80 (42 after exclusion of losses to FU)	Approach-related warmth and dryness of the left lower extremity (4) Device-related None Outcome-related complications reoperation (1) (after failing conservative treatment for worsening left L5 pain, including foraminal injections, an L5-S1decompression and posterior fusion was performed with an excellent outcome)	5
Bertagnoli et al 2005a	72 (60 after exclusion of losses to FU) All ProDisc	<u>2 level</u> L4-L5 & L5-S1 = 8 L3-L4 & L4-L5 = 5 L2-L3 & L4-L5 = 1 L3-L4 & L5-S1 = 1 <u>3 level</u> L3-L4 & L4-L5 & L5-S1 = 10	29 (25 after exclusion of losses to FU)	Approach-related subcutaneous sterile inflammatory suture reaction (1) (the suture was debrided and the skin closed primarily) temporary retrograde ejaculation (1) (recovered spontaneously at 5.5 months after surgery) Device-related partial implant subsidence (1) (found on a postoperative radiograph 3 days following the index surgical procedure, after the initial subsidence no increase in subsidence was noted and the patient returned to normal activity without pain at approximately 5 months after surgery) anterior extrusion of polyethylene component (1) (identified at 2 year FU visit – the complication was treated with removal of the entire prosthesis and anterior fusion with a femoral ring allograft and Pyramid plate)	4
Bertagnoli et al 2005b	118 (104 after exclusion of losses to FU) All ProDisc	All single level L5-S1 = 80 L4-L5 = 17 L3-L4 = 7	118 (104 after exclusion of losses to FU)	Approach-related retroperitoneal haematomae (2) (treated with decompressions) subcutaneous haematoma (1) (evacuated percutaneously) retrograde ejaculation (1) (recovered spontaneously at 6.5 months after surgery) persistent leg pain (1) (required posterior exploration and decompression which revealed posterior subarticular stenosis – the patient was still unsatisfied with her outcome at 32 months post index procedure) posterior subarticlular stenosis (1) Device-related None	6

Bertagnoli et al 2006a	28 All ProDisc	1 level – 17 2 level – 4 3 level – 1 Location: L2 to S1 segments	22	Device-related complications implant subsidence (2) 9 in one case subsidence occurred in the inferior endplate of L-4 in a single segment (L3-4) ADR. In the second case subsidence occurred after a 3 level (L3-S1) ADR). Approach-related complications None Neurological changes unilateral foot drop (2) (in both cases there was preoperative evidence of circumferential spinal stenosis. One patient who had undergone L3-S1 ADR also experienced loss of proprioception and vibration sensation bilaterally and required a posterior decompressive procedure following ADR; postoperatively the patient regained ambulatory status with the assistance of a single cane. The other patient who had undergone L4-L5 ADR recovered anti gravity strength without requiring any other surgical intervention). Vascular status/complications None	4
Bertagnoli et al 2006b	110 (104 after exclusion of losses to FU) All ProDisc	All single level[a] L3-L4 = 7 L4-L5 = 17 L5-S1 = 76 L5-L6 = 5	110 (104 after exclusion of losses to FU)	iatrogenic bladder laceration (1)	1
Bertagnoli et al 2006c	20 or 21 (excludes losses to FU) All ProDisc	<u>1 level</u> L5-S1 = 2 L3-L4 = 6 L4-L5 = 5 L3-L5 = 2 L2-L3 = 1 <u>2 level</u> L4-L5 & L5 –S1 = 1 L1-L2 & L2-L3 = 1	20 (18 after exclusion of losses to FU)	delayed onset elevated liver function parameters and jaundice (1) (the cause was thought to be secondary to a transfusion reaction, recovery was spontaneous) No device or approach-related complications occurred.	1
Cakir et al 2006	29 All ProDisc	All single level Location: NR	29	NA	0

Chung et al 2006	47 (excludes losses to FU) All ProDisc II	1 level – 25 2 level – 11 L5-S1 = 21 L4-L5 = 24 L3-L4 = 2	38 (36 after exclusion of losses to FU)	Approach-related complications major vein injury (2) (repaired primarily) Postoperative complications increased radicular pain postoperatively (3) (treated with medication or by epidural injection; in all 3 pain had resolved at the time of 6 week FU) residual back pain at 2 years postoperatively (2) (both patients had undergone a double TDR, one of the patients was managed with an oral nonsteroidal anti-inflammatory drug on a daily basis)	7
David 2007	108 (106 after exclusion of losses to FU) All Charité III	All single level L5-S1 = 82 L4-L5 = 25 L3-L4 = 1	108 (106 after exclusion of losses to FU)	Index level with secondary fusion procedure symptomatic facet arthrosis (5) (posterior fusion) continued axial low back pain (nonfacet) (1) (posterior fusion) subsidence of prosthesis (1) (posterior fusion) axial back pain (1) sciatica with drop foot (1) (prosthesis removal and 360º fusion – both the drop foot and sciatica resolved following the fusion) Index level with prosthesis replacement early core subluxation due to prosthesis positioning (2) (prosthetic replacement) late core failure related to oxidation of the polyethylene (1) (prosthetic replacement with good clinical result) Index level without reoperation complete ossification, spontaneous fusion (2) subsidence with spontaneous fusion (1) Adjacent level disc herniation (2) (successfully treated with microdiscectomy) spinal stenosis (1) (posterior decompression and fusion)	19
Di Silvestre et al 2009	32 All Charité III	1 level - 16 2 level - 16 Location: NR	32	1 level TDR persistent postoperative sciatica (2) (resolved after 2 weeks of steroid treatment) partial subsidence of the superior component of a monosegmental L5-S1 (1) (remained stable at FU without clinical consequence persistent lower back pain (1) (resolved completely after a cast worn for 2 weeks – treated with a pedicular screw fixation and fusion at the same level) 2 level TDR intraoperative tear in the iliac vein (1) (repaired) ileus (1) (successfully treated with drugs) severe post operative anemia (2) (required blood transfusions)	13 (4 in 1 level TDR & 9 in 2 level TDR)

				persistent sciatica (1) (required steroid treatment for continued radiculopathy) partial implant subsidence (1) (remained stable at FU without pain) partial extrusion of the polyethylene core (1) (remained stable at the last visit 39 months later without clinical consequences) persistent lower back pain (1) (resolved after a cast worn for 2 weeks – treated by pedicular instrumentation & fusion at the same levels of TDR laparocele of the abdominal wall (1) (required surgical repair)	
Gioia et al 2007	45 (excludes losses to FU) All Charité III	1 level – 28 2 level - 7 3 level - 1 L5-S1 = 15 L4-L5 = 11 L3-L4 = 2	56 (36 after exclusion of losses to FU	persistent nerve root pain (1) (posterior bone fusion 5 years after disc replacement) Surgical complications left iliac vein injury (1) (sutured uneventfully) pre-sacral nerve injury leading to retrograde ejaculation (1) (patient was unsatisfied and lost to FU) malposition with excessive posterior subsidence (1) (required immediate revision surgery because of sciatic compression, a second revision surgery at another institution was perfomed 4 years after disc replacement where the implant was removed and circumferential bone fusion performed) scrotal edema (1) (resolved uneventfully) ileus (3) (resolved spontaneously within 48 hours)	8
Guyer et al 2008	276 All Charité	All single level L4-L5 = 80 L5-S1 = 196	276	Major neurological event burning/leg pain (8) motor deficit (4) nerve root injury (1) Approach-related event venous injuries (19) retrograde ejaculation (6) ileum (5) thrombosis (2) blood loss >1500 mL (1) hernia (3) epidural haematoma (1) dural tear (1) Technique-related event subsidence (7) migration (5) Other adjacent level disease (2) reoperation (16)	81
Hannibal et al	59	1 level	59	1 level TDR	10

2007	All ProDisc	L5-S1 = 17 L4-L5 = 10 2 level L4-L5 & L5-S1 = 29 L3-L4 & L4-L5 = 3		tear in the iliac vein (1) (repaired) continued radiculopathy (2) (required epidural steroid injection) laminotomy (1) 2 level TDR left external iliac thrombosis (1) (required thrombectomy) left foot drop (2) (1 resolved spontaneously & the other had fully resolved at 6 week visit) femoral artery thrombosis (1) (treated with thrombectomy) microdiscectomy (1) vertebral body fracture (1) (caused prosthesis subsidence and was subsequently treated by removal of the L5-S1 ProDisc and replaced with 360º fusion at that level)	(4 in 1 level TDR & 6 in 2 level TDR)
Huang et al 2006	93 (60 after exclusion of losses to FU) All ProDisc	1 level - 27 2 level - 12 3 level - 3 L2-L3 = 1 L3-L4 = 5 L4-L5 = 32 L5-S1 = 22	64 (42 after exclusion of losses to FU)	adjacent level degeneration (10) - 4 had loss of disc space height, 3 had anterior osteophyte formation & 3 had both loss of disc space height and anterior osteophyte formation	10
Kim et al 2007	42 (excludes 1 loss to FU) ProDisc II	1 level – 20 2 level – 11	32 (31 after exclusion of loss to FU)	dislocation of polyethylene underlay (1) (revision surgery – unsuccessful due to uncontrollable bleeding in the inferior vena cava and left iliac vein during dissection. The surgeon had to eventually ligate the left iliac artery and vein. The patient died of complications from the revision surgery approximately 1 year later)	1
Le Huec et al 2005	64 All Maverick	All single level L5-S1 = 35 L4-L5 = 27[b] L3-L4 = 2	64	postoperative root pain (4) spinal pain other than in the lumber region (3) superficial infection treated with debridement (1) visceral lesion due to surgical incision (1) (damage was successfully repaired) minor intraoperative complications due to the surgical approach (11) axial device migration (5) (subsidence was stable at 1 year FU, the outcome was satisfactory in 3 patients, poor in one and very poor in another in terms of Oswestry improvement) heterotopic ossification (3) (all were mobile on dynamic radiographs)	28
Lemaire et al 2005	147 (excludes losses to FU)	1 level - 54 2 level - 45 3 level - 1 L3-L4 = 6 L4-L5 = 69	107 (100 after exclusion of losses to FU)	patients requiring secondary arthrodesis (5) posterior articular arthritis (4)[b] periprosthetic ossification affecting prosthesis mobility (2) (3 cases were exhibited but one did not affect mobility of the prosthesis) adjacent level degeneration (2)[d] neurologic (2) (a posterior ligamentoplasty was perfomed on 1 patient and yielded a complete	21

	All Charité	L5-S1 = 72		neurologic recovery in the 3rd month but with a poor overall result) subsidence (2) (no further surgery required, did not affect clinical outcome) perioperative vascular injury (2) (repaired without sequelae) sexual dysfunction (1) (spontaneous recovery occurred 1 year after surgery with an excellent clinical result and resumption of high-level athletic activities) acute leg ischemia (1) (required endarterecotomy with good result)	
Marshman et al 2008	14 7 A-Mav & 7 O-Mav	All single level L4/5 = 14	14	postoperative ileus (2) (1 in A-Mav insertion group, 1 in O-Mav insertion group)[e]	2
Mirovsky et al 2008	22 All ProDisc II	1 level L5-S1 = 18 L4-L5 = 2 2 level L4-L5 & L5-S1 = 1	21	dislocation of the polyethylene insert (1) (patient was satisfied with their result and refused revision surgery) heterotrophic calcification of the annulus fibrosus at the implanted level (1) (patient was satisfied with their result and refused revision surgery) subcutaneous seroma (2) (wound revision was unnecessary as it resolved spontaneously) postoperative incisional hernia (1) (repaired 2 months later) superficial wound infection (1) (treated by oral administration of cephalosporin)	6
Neal et al 2005	10 All Maverick	All single level L4/5 = 3 L5-S1 = 7	10	NA	0
Ogon et al 2007	36 All ProDisc	1 level L4-L5 = 10 L5-S1 = 22 2 level L4-L5 & L5-S1 = 2	34	fall 4 months postoperatively with subsequent treatment resistant ischialgic pain in the right thigh (1) (laminotomy performed microscopically on the right at L5/S1 which ameliorated the symptoms) postoperative subileus (1) (symptoms were relieved after 2 days of conservative therapy) effects of sympathectomy whereby the right leg felt colder and the left leg warmer (2) (the effect had completely disappeared within the first 6 months in both patients subsidence of the prosthesis of > 2 mm into the coverplate (15) spontaneous fusion at the operated segment (1)	20
Park et al 2008	41 (excludes losses to FU) All ProDisc II	1 level - 23 2 level - 9 L3-L4 = 3 L4-L5 = 20 L5-S1 = 18	46 (32 after exclusion of losses to FU)	increase in disc degeneration (1 out of 33 upper segments from grade 2 to grade 3 & 1 out of 14 lower segments from grade 1 to grade 2 progression of facet arthrosis at index levels (9) (12 segments: 7 cases (7 of 20, 35%) at L4-L5; 5 cases (5 of 18, 27.8%) at L5-S1) progression of facet arthrosis at adjacent segments (1 of 33 upper segments; 2 of 14 lower segments)	9
Patel et al 2006	Number NR All ProDisc	NR	52	NA	0

Pimenta et al 2010	16 All Physio-L	1 level L5-S1 = 8 2 level L4-L5 & L5-S1 = 4	12	clinically significant blood loss (1) (resolved without further incident) retrograde ejaculation between 3 & 6 months (1) (resolved spontaneously by 12 month FU) mild radiolucency at 3 & 6 month FU (2) (resolved in 1 patient by 12 months) moderate radiolucency (1)	5
Putzier et al 2006	84 (63 after exclusion of losses to FU) All Charité - 16 type I, 25 type II, 22 had type III	L3-L4 = 2 patients L4-L5 = 25 patients L5-S1 = 16 patients L4-S1 = 10 patients	71 (53 after exclusion of losses to FU)	implant fracture (8) (7 fusion & 1 secondary operative instrumented sponylodesis) subsidence (5) (3 fusion & 2 secondary operative instrumented spondylodesis) dislocation (2) (1 fusion & 1 secondary operative instrumented sponylodesis) persisting pain (1) (fusion) persistant leg pain (1) (secondary operative instrumented spondylodesis) possible or likely motion impairment (7) definitive signs of ankylosis (32) significant degeneration of adjacent segments (9)	65
Regan et al 2006	71 All Charité	All single level L4-L5 = 19 L5-S1 = 52	71	neurologic (24) superficial wound infections (5) approach-related (8) device-related – implant migrations (4)	41
Ross et al 2007	226 (189 after exclusion of losses to FU) All Charité III	All single level L5-S1 = 114 L4-L5 = 92 L3-L4 = 20	160 (123 after exclusion of losses to FU)	deep vein thrombosis (4) pulmonary embolism (2) paralytic ileus (4) infection (9) incisional hernia (17) retrograde ejaculation (5) displacement (3) (implant removal) fracture S1 (1) (implant removal) spondylolisthesis (1) (implant removal) chronic infection (1) (implant removal) implant failure (4) (implant removal) pain (2) (implant removal)	53
Schluessmann et al 2009	497 Type: NR	1 level – 357 2 level – 70 Location: NR	427	Intraoperative complications/revisions blood vessel injury (13) (10 in monosegmental TDR; 3 in bisegmental TDR) ureter injury (1) (all in monosegmental TDR) vertebral body fracture (2) (1 in monosegmental TDR; 1 in bisegmental TDR) sintering of implant (2) (1 in monosegmental TDR; 1 in bisegmental TDR) dura lesion (2) (1 in monosegmental TDR; 1 in bisegmental TDR) revision during hospitalisation (16) (7 in monosegmental TDR; 8 in bisegmental TDR)	94

				Complications/revisions during FU delayed wound healing/wound infection (3) (all in monosegmental TDR) incision hernia/abdominal hernia (2) (all in monosegmental TDR) cutaneal nerve irritation (1) (in monosegmental TDR) abdominal pain (2) (1 in monosegmental TDR; 1 in bisegmental TDR) testicular pain (1) (in monosegmental TDR) recurring pain (2) (both in monosegmental TDR) sympathectomy effects (8) (6 in monosegmental TDR; 2 in bisegmental TDR) retrograde ejaculation (2) (1 in monosegmental TDR; 1 in bisegmental TDR) urethral problem (1) (in monosegmental TDR) radiculopathy (7) (6 in monosegmental TDR; 1 in bisegmental TDR) drop foot (2) (in bisegmental TDR) psychogenic foot paralysis (1) (in monosegmental TDR) OA facet joint (1) (in bisegmental TDR) residual disc sequester (1) (in monosegmental TDR) Fx endplate (2) (all in monosegmental TDR) dislocation (3) (1 in monosegmental TDR; 2 in bisegmental TDR) spondylolisthesis (1) (in monosegmental TDR) foot pain intermittent (1) (in bisegmental TDR) functional foot paralysis (1) (in monosegmental TDR) unspecified (5) (4 in monosegmental TDR; 1 in bisegmental TDR) revision after discharge (12) (11 in monosegmental TDR; 1 in bisegmental TDR)	
Shim et al 2007	64 (excludes losses to FU) ProDisc & Charité	<u>1 level</u> L4-L5 = 36 L5-S1 = 14 <u>2 level</u> n = 7 (levels not stated)	61 (57 after exclusion of losses to FU)	tears of the great vein during surgical approach (2) (immediately repaired without any adverse sequelae in the intraoperative or postoperative period) subsidence (3) (1 patient was treated with percutaneous vertebroplasty to prevent further sinking of the prosthesis and this patient was grouped as a failure because of persistent back pain; the other 2 patients were simply followed without any further intervention and had no significant pain or disability. Incisional hernia (1) (required repair)	6
Siepe et al 2006	108 (excludes losses to FU) All ProDisc II	1 level – 77 2 level – 14 3 level – 1 L5-S1 = 57 L5-L6 = 5 L4-L5 = 12 L4-L5-S1 = 13 L2-L3 = 1 L5-L6-S1 = 1 L4-S1 = 2 L3-L4-L5-S1 = 1	192 (92 after exclusion of losses to FU)	Intraoperative complications retrograde ejaculation (2)†‡ (1 persisting, 1 temporary) sympathectomy related dysesthesia (1)† Postoperative complications *General* DVT + LAE + lysis (1)‡ (patient with known coagulopathy) superficial wound healing impaired (1) ‡ *Surgery related* extraforaminal disc protrusion following TDR (1) † (spontaneous improvement upon conservative therapy) neuropathy (1)† heterotopic ossification (1)‡ (type III McAfee classification)	18 12 in 1 level TDR & 6 in 2 level TDR)

				primary suboptimal implantation (1)† (secondary dislocation + fusion) inlay dislocation (1)† (implant replaced) implant subsidence (2)† (secondary operation - fusion) segmental hyperlordosis; persisting problems (1)† (posterior dynamic fixation – Dynesis) persisting facet joint problems (2)† (secondary fusion) secondary spinal canal stenosis (same segment) (1)‡ (microsurgical decompression) reoperations (non index level), adjacent segment disc herniation (2)†‡ (microsurgical discectomy) †complication occurred in monosegmental TDR ‡complication occurred in bisegmental TDR	
Siepe et al 2007a	42 (includes 1 lost to FU after 3 months post op) All ProDisc II	1 level L5-S1 = 26 L4-L5 & L5-L6 = 10 2 level L4-L5 & L5-S1 = 3	39 (38 after exclusion of losses to FU)	Intraoperative complications lesion of superior hypogastric plexus (1) Postoperative complications L5 radiculopathy due to extraforaminal disc protrusion following TDR (1) L5 radiculopathy of unknown reason (1) Reoperations haematoma of the abdominal wall (1) Reoperations (non index level) adjacent segment disc herniation (1) Device-related complications subsidence (13)	18
Siepe et al 2007b	119 (excludes losses to FU) All Prodisc II	1 level L5-S1 = 57 L4-L5 = 22 2 level L4-L5 & L5-S1 = 20	218 (99 after exclusion of losses to FU)	Complications following TDR at level L4-L5 *Intraoperative, access-related* Sympathectomy-related dysesthesia (1) *Postoperative surgery related* L5 neuropathy (2) haematoma of the abdominal wall (1) Complications following TDR at level L5-S1 *Intraoperative, access-related* superior hypogastric plexus lesion (1) *Postoperative, surgery-related* heterotopic ossification (1) inlay dislocation (1)† persisting facet joint problems (1)† primary suboptimal implantation (1)† segmental hyperlordosis, persisting problems (1)†	47

				adjacent segment disc herniation (1) Complications following TDR at level L4-L5 & L5-S1 *Intraoperative access-related* superior hypogastric plexus lesion (1) Postoperative, surgery-related secondary spinal canal stenosis (same segment) (1)† adjacent level disc herniation (bisegmental L2-L3, L3-L4) (1)† superficial wound healing impaired (1)† seroma, retroperitoneal (1) persisting facet joint complaints (1)† †Complications requiring revision surgery Summary of revision surgery reoperations (index level) (6) reoperations (non-index level) (1) reoperations following L4-L5 TDR (0) reoperations following L5-S1 TDR (4) reoperations following L4-L5 & L5-S1 TDR (4) Overall rate of reoperations (8) Posterior joint pain (30)	
Sinigaglia et al 2009	84 (36 after exclusion of losses to FU) 17 ProDisc II, 19 Maverick	All single level L4/5 = 12 L5-S1 = 24	62 (36 after exclusion of losses to FU)	Surgical approach laparocele (4) persistent abdominal pain (2) wound dehiscence (2) transitory urinary disorders (1) L1-L2 paresthesia (1) Prosthesis junctional pathology (5) (1 required surgery) persistent radiculitis (6) (4 required surgery) facet degeneration (4) persistent back pain (2) transitory radiculitis (2)	29
Tropiano et al 2005	78 (excludes losses to FU) All ProDisc	1 level L3-L4 = 2 L4-L5 = 17 L4-L5 with concomitant L5-S1 arthrodesis = 6 L5-S1 = 10	64 (55 after exclusion of losses to FU)	Surgical complications deep venous thrombosis (1) iliac vein laceration (1) (repaired primarily) transient retrograde ejaculation (1) incisional hernias (2) Other	10

		2 level L3-L4/L4-L5 = 1 L4-L5/L5-S1 = 15 L3-L4/L4-L5 with concomitant L5-S1 arthrodesis = 1 L3-L4/L4-L5/L5-S1 = 3		increased radicular pain postoperatively (5) (all had previous discectomies and were treated with medication – the radicular pain had resolved by 3months postoperatively in all patients) No complication was related to the prosthesis itself	
Troullier et al 2006	13 All Charité	All single level L4/L5 = 9 L5/S1 = 4	13	ileus (1) (successfully treated with a gastrograph) [f] postoperative sympathicus lesions (2) (one of patients fully recovered after 3 months) [f] malposition (7) significant decreases in bone density at the operated level (10)[g] significant decreases in subchondral bone density at the level above the operated segment (6)[g, h] significant decreases in subchondral bone density at the level below the operated segment (3)[g, i]	29
Wenger et al 2005	14 All ProDisc II	All single L5-S1 = 13 L4-L5 = 1	14	radicular pain for 2 days (1)	1
Warachit 2008	50 All Charité	1 level - 36 2 level - 7 L3-L4 = 1 L4-L5 = 33 L5-S1 = 16	43	malalignment (1) loosening (1) (patient underwent reoperation by retrograde peritoneal approach on the right side to avoid adhesion. Finally interbody fusion with cage and pedicular screw fixation posterior was performed with clinical improvement) inadequate removal of degenerative ruptured disc from anterior discectomy (1)	3
Zeh et al 2009	15 All Maverick	1 level L5-S1 = 5 2 level L4-L5 & L5-S1 = 5	10	damage to the dura mater resulting in cerebral spine fluid loss syndrome caused by insertion of a peridual catheter (1) (treated with postoperative blood patch)	1

NOTES: ADR = artificial disc replacement; ALIF = anterior lumbar interbody fusion; DVT = deep vein thrombosis; FU = follow-up; LAE = arterial pulmonary embolism; NR = not reported; TDR = total disc replacement; [a]It appears there is an error in the table listing the number of TDRs at each level in the paper. The number of TDRs for the smoking group should tally up to 34 not 35. This has resulted in a total of 105 instead of 104 TDRs; [b]13 of these cases were in combination with L5-S1 arthrodesis; [c]All 11 patients had non-ideal positioning of the prosthesis, which was too far anterior in the sagittal plane. Of these 11 patients, 4 became symptomatic. The 7 non symptomatic cases presented a progressive after-effect of Scheuermann disease. The authors did not believe these cases were due to the implant but rather the natural history of a degenerative spinal column and poor positioning of the prosthesis; [d]The two cases could be explained by an underlying functional overload compensating for a kyphosis of the dorsolumbar hinge joint of about 25°, concomitant in one case with the appearance of T12-L3 degenerative lumbar scoliosis after 10 years; [e]A-Mav = oblique Maverick prosthesis; O-Mav = anterior Maverick prosthesis; [f]Complications were said to be related to the anterior approach and not the insertion of the Charité Artificial Disc; [g]Any changes in bone density ≥3% were considered significant; [h]Out of 12 patients; [i]Out of 5 patients.

Appendix G Excluded studies

Non-English language articles

2000. 'Artificial intervertebral disk: Mobile again with high tech', *Kompendium Orthopadie, Unfallchirurgie und Rheumatologie*, 1 (1), April.

2000. 'From yesterday to today: The advances of prosthetic disc nucleus replacement', *Journal of Clinical Rehabilitative Tissue Engineering Research*, 13 (39), 24.

Alpizar-Aguirre A, Mireles-Cano JN. et al, 2008. 'Clinical and radiological follow-up of Nubac disc prosthesis. Preliminary report', *Cir Cir*, 76 (4), 317-321.

Baur-Melnyk A, 2006. 'Lumbar disc arthroplasty: Indications, biomechanics, types, and radiological criteria', *Radiologe*, 46 (9), Sep.

Birnbaum K, Phoa T et al, 2009. 'Biomechanical analysis of lumbar spine after implantation of a disk prosthesis and supplementary spinal fusion for management of complications', *Z Orthop Unfall*, 147 (4), 493-500.

Bordes-Monmeneu M, Bordes-Garcia V et al, 2005. 'System of dynamic neutralization in the lumbar spine: experience on 94 cases', *Neurocirugia (Astur)*, 16 (6), 499-506.

Boskovic K, 2008. 'Critical approach to diagnostics and treatment of lumbar radiculopathy', *Med Pregl*, 61 (11-12), 553-556.

de Jonghe JF, 2007. 'Complaints after implantation of a disc prosthesis for low back pain]', *Ned Tijdschr Geneeskd*, 151 (39), 2183-2184.

Gravius SW, 2000. 'Lumbar intervertebral total disc replacement: A narrative review', *Deutsches Arzteblatt*, 104 (38), 21.

Grob D, 2009. 'Lumbar total disc replacement', *Orthopade*, 38 (1), January.

He Z-S, 2000. 'Artificial total disc replacement for lumbar degenerative disc disease: A systematic review', *Chinese Journal of Evidence-Based Medicine*, 5 (2), Feb.

Hopf C, 2008. 'Revision surgery after implantation of a vertebral disc prosthesis', *Orthopade*, 37 (4), Apr.

Huang DS, Liang AJ et al, 2006. 'The risk factors and preventive strategies of heterotopic ossification after artificial disc replacement in lumbar spine', *Zhonghua Wai Ke Za Zhi*, 44 (4), 242-245.

Karatoprak O, Aydogan M et al, 2007. 'Total disc prosthesis for painful degenerative lumbar disc disease', *Acta Orthop Traumatol Turc*, 41 (4), 281-285.

Konovalov NA, Shevelev IN et al, 2008. 'Replacement of lumbosacral intervertebral disks using artificial prostheses: surgical tactics and technique', *Zh Vopr Neirokhir.Im N N Burdenko*, (3), 25-30.

Kramer J, 2000. 'Artificial discs: Review, current status, outlook', *Zeitschrift fur Orthopadie und Ihre Grenzgebiete*, 143 (3), May.

Lacombe M, 2000. 'Vascular complications of lumbar disk surgery', *Annales de Chirurgie*, 131 (10), Dec.

Lange U, 2006. 'Titanium vertebral body replacement of adjustable size: A prospective clinical trial', *Unfallchirurg*, 109 (9), 733-742.

Li Y, 2000. 'Anesthetic characteristics and complication of artificial joint arthroplasty', *Journal of Clinical Rehabilitative Tissue Engineering Research*, 11 (36), 09.

Liu S-L, 2000. 'The role of artificial disc replacement in restoring lumbar segment motion and intervertebral height', *National Medical Journal of China*, 85 (1), 05.

Lu SB, Wang QY et al, 2008. 'Total lumbar disc replacement with SB Charite III prosthesis: Chinese experience with more than two years follow-up', *Zhonghua Wai Ke Za Zhi*, 46 (5), 342-345.

Madi K, 2000. 'Incidence of the anatomic situation of the iliocaval junction for disc prosthesis implantation', *Revue de Chirurgie Orthopedique et Reparatrice de l'Appareil Moteur*, 92 (2), Apr.

Matejka J, 2000. 'Mid-term results of 360-degree lumbar spondylodesis with the use of a tantalum implant for disc replacement', *Acta Chirurgiae Orthopaedicae et Traumatologiae Cechoslovaca*, 76 (5), October.

Mayer HM, 2005. 'Degenerative disorders of the lumbar spine. Total disc replacement as an alternative to lumbar fusion?', *Orthopade*, 34 (10), 1007-1020.

Miao J, 2000. 'Mini-invasive extraperitoneal approach for anterior lumbar surgery', *Zhonghua Yi Xue Za Zhi*, 89 (23), 16.

Molenaar JC, 2007. '[Complaints after implantation of a disc prosthesis for low back pain]', *Ned Tijdschr Geneeskd*, 151 (39), 2184.

Morales JF, Palacios JL, Soriano JC, 2008. 'Twelve cases of total arthroplasty of lumbar disc. Preliminary results at 6 months', *Acta Ortop Mex*, 22 (2), 97-102.

Moreno P, Boulot J, 2008. 'Comparative study of short-term results between total artificial disc prosthesis and anterior lumbar interbody fusion', *Rev Chir Orthop Reparatrice Appar Mot*, 94 (3), 282-288.

Muller-Wille R, Feuerbach S, Zorger N, 2008. 'Arteriovenous fistula after intervertebral disc operation: fistula occlusion by percutaneous stent graft implantation', *Rofo*, 180 (8), 757-758.

Pfeiffer F, 2000. 'Spine arthroplasty society in Miami Beach USA from May 6-9, 2008', *Zeitschrift fur Orthopadie und Unfallchirurgie*, 146 (4), July/August.

Pieler-Bruha E, 2000. 'News-screen orthopadie', *Journal fur Mineralstoffwechsel*, 16 (1), 2009.

Qiu GX, 2006. 'Non-fusion technique on the surgical treatment of spinal degenerative disease', *Zhonghua Wai Ke Za Zhi*, 44 (16), 1081-1083.

Renckens CN, 2007. 'Complaints after implantation of a disc prosthesis for low back pain', *Ned Tijdschr Geneesk*, 151 (39), 2182-2183.

Rognsvag T, Strand LI, Skouen JS, 2007. 'Pain and functional ability in patients with total disc replacement in the lumbar spine', *Tidsskr Nor Laegeforen*, 127 (9), 1188-1191.

Rollinghoff M, Sobottke R et al, 2008. 'Minimally invasive surgery of the lumbar spine', *Z Orthop Unfall*, 146 (3), 395-408.

Schulte TL, 2005. 'Lumbar disc arthroplasty. Established technique or experimental procedure?', *Orthopade*, 34 (8), 801-813.

Stulik J, 2000. 'Injury to major blood vessels in anterior thoracic and lumbar spinal surgery', *Acta Chirurgiae Orthopaedicae et Traumatologiae Cechoslovaca*, 73 (2), 2006.

Thome C, 2000. 'Chronic back pain: Operative therapy approach for chronic back pain', *Anasthesiologie Intensivmedizin Notfallmedizin Schmerztherapie*, 44 (1), 2009.

Tian W, 2005. 'Artificial disc replacement promises the end of spinal fusion technology', *Zhonghua Yi Xue Za Zhi*, 85 (1), 9.

Tulik J, 2000. 'ProDisc-C mobile replacement of an intervertebral disc. A prospective mono-centric two-year study', *Acta Chirurgiae Orthopaedicae et Traumatologiae Cechoslovaca*, 75 (4), August.

van Duppen D, 2007. 'Complaints after implantation of a disc prosthesis for low back pain', *Ned Tijdschr Geneesk*, 151 (39), 2181-2182.

van Ooij A, 2000. 'Findings in 67 patients with recurrent or persistent symptoms after implantation of a disc prosthesis for low back pain', *Nederlands Tijdschrift voor Geneeskunde*, 151 (28), 14.

Wang P, 2005. 'The relation of artificial intervertebral disc replacement and spondylodesis', *Zhonghua Yi Xue Za Zhi*, 85 (1), 10-11.

Welke B, 2000. 'Spinal column: Fusion or spinal disk prosthetic replacement?', *Zeitschrift fur Orthopadie und Unfallchirurgie*, 146 (6), November/December.

Wiedenhofer B, Ewerbeck V et al, 2008. 'Current short- and long-term results of lumbar disc replacement : update 2008', *Chirurg*, 79 (10), 937-943.

Wu G, 2000. 'Current situation and principle for design of artificial lumbar disc prostheses', *Journal of Clinical Rehabilitative Tissue Engineering Research*, 11 (1), 07.

Xiao R-C, 2000. 'Biomechanical characteristics after artificial intervertebral disc implantation', *Journal of Clinical Rehabilitative Tissue Engineering Research*, 12 (13), 25.

Zeilstra DJ, 2007. 'Complaints after implantation of a disc prosthesis for low back pain', *Ned Tijdschr Geneesk*, 151 (39), 2179-2180.

No relevant data reported

Acosta FL, Jr, Aryan HE, Ames CP, 2005. 'Emerging directions in motion preservation spinal surgery', *Neurosurg Clin N Am*, 16 (4), 665-669.

Ahrens M, 2009. 'Nucleus replacement with the DASCOR disc arthroplasty device: Interim two-year efficacy and safety results from two prospective, non-randomized multicenter european studies', *Spine*, 34 (13), 1376-1384.

Auerbach JD, Johannessen W et al, 2006. 'In vivo quantification of human lumbar disc degeneration using T(1rho)-weighted magnetic resonance imaging', *Eur Spine J*, 15 Suppl 3 S338-S344.

Auerbach JD, 2000. 'Lumbar instability adjacent to a previous fusion', *Seminars in Spine Surgery*, 17 (4), Dec.

Auerbach JD, 2000. 'Radiographic Evaluation in Lumbar Total Disc Replacement: Assessment of Potential Candidacy and Range of Motion', *Seminars in Spine Surgery*, 19 (2), Jun.

Bendo JA, 2008. 'A comparison of two retroperitoneal surgical approaches for total disc arthroplasty of the lumbar spine', *Spine*, 33 (2), 205-209.

Bertagnoli R, Karg A, Voigt S, 2005. 'Lumbar partial disc replacement', *Orthop Clin North Am*, 36 (3), 341-347.

Cakir B, Carazzo C et al, 2009. 'Adjacent segment mobility after rigid and semirigid instrumentation of the lumbar spine', *Spine (Phila Pa 1976)*, 34 (12), 1287-1291.

Chelly JE & Schilling D, 2008. 'Thromboprophylaxis and peripheral nerve blocks in patients undergoing joint arthroplasty', *J Arthroplasty*, 23 (3), 350-354.

Crawford NR, 2005. 'Biomechanics of lumbar arthroplasty', *Neurosurg Clin N Am*, 16 (4), 595-602.

de Maat GH, Punt IM et al, 2009. 'Removal of the Charite lumbar artificial disc prosthesis: surgical technique', *J Spinal Disord Tech*, 22 (5), 334-339.

Gstoettner M, Heider D et al, 2008. 'Footprint mismatch in lumbar total disc arthroplasty', *Eur Spine J*, 17 (11), 1470-1475.

Gumbs AA, Hanan S et al, 2007. 'Revision open anterior approaches for spine procedures', *Spine J*, 7 (3), 280-285.

Hansson T, Hansson E, Malchau H, 2008. 'Utility of spine surgery: a comparison of common elective orthopaedic surgical procedures', *Spine (Phila Pa 1976)*, 33 (25), 2819-2830.

Harper ML, 2009. 'The fundamentals of biotribology and its application to spine arthroplasty', *SAS Journal*, 3 (4), 125-132.

Huang RC, Girardi FP et al, 2005. 'Correlation between range of motion and outcome after lumbar total disc replacement: 8.6-year follow-up', *Spine (Phila Pa 1976)*, 30 (12), 1407-1411.

Kowalski TJ, Berbari EF et al, 2007. 'The management and outcome of spinal implant infections: contemporary retrospective cohort study', *Clin Infect Dis*, 44 (7), 913-920.

Kurtz SM, van Ooij A et al, 2007. 'Polyethylene wear and rim fracture in total disc arthroplasty', *Spine J*, 7 (1), 12-21.

Kurtz SM, MacDonald D et al, 2009. 'The natural history of polyethylene oxidation in total disc replacement', *Spine (Phila Pa 1976)*, 34 (22), 2369-2377.

Kurtz SM, Patwardhan A et al, 2008. 'What is the correlation of in vivo wear and damage patterns with in vitro TDR motion response?', *Spine (Phila Pa 1976)*, 33 (5), 481-489.

Labler L, Keel M et al, 2006. 'Wound conditioning by vacuum assisted closure (V.A.C.) in postoperative infections after dorsal spine surgery', *Eur Spine J*, 15 (9), 1388-1396.

Lange U, 2007. 'Anterior vertebral body replacement with a titanium implant of adjustable height: A prospective clinical study', *European Spine Journal*, 16 (2), 161-172.

Leivseth G, Braaten S et al, 2006. 'Mobility of lumbar segments instrumented with a ProDisc II prosthesis: a two-year follow-up study', *Spine (Phila Pa 1976)*, 31 (15), 1726-1733.

Lim MR, Loder RT et al, 2006. 'Measurement error of lumbar total disc replacement range of motion', *Spine (Phila Pa 1976)*, 31 (10), E291-E297.

Mariottini, A., Pieri, S. et al, 2005. 'Preliminary results of a soft novel lumbar intervertebral prothesis (DIAM) in the degenerative spinal pathology', *Acta Neurochir Suppl*, 92, 129-131.

Markel DC, Doerr T et al, 2007. 'Observational study on intrathecal and peridural changes after routine spinal and epidural anesthesia in patients undergoing total joint arthroplasty', *J Arthroplasty*, 22 (6), 844-848.

Marshman LA, Strong G et al, 2010. 'Minimizing ferromagnetic artefact with metallic lumbar total disc arthroplasty devices at adjacent segments: technical note', *Spine (Phila Pa 1976)*, 35 (2), 252-256.

Marshman LA, Friesem T et al, 2007. 'Significantly improved lumbar arthroplasty placement using image guidance: technical note', *Spine (Phila Pa 1976)*, 32 (18), 2027-2030.

Marshman LA, Trewhella M et al, 2007. 'The accuracy and validity of "routine" X-rays in estimating lumbar disc arthroplasty placement', *Spine (Phila Pa 1976)*, 32 (23), E661-E666.

Sasso RC, Smucker JD et al, 2007. 'Artificial disc versus fusion: a prospective, randomized study with 2-year follow-up on 99 patients', *Spine (Phila Pa 1976)*, 32 (26), 2933-2940.

Tortolani PJ, Cunningham BW et al, 2007. 'Prevalence of heterotopic ossification following total disc replacement. A prospective, randomized study of two hundred and seventy-six patients', *J Bone Joint Surg Am*, 89 (1), 82-88.

Winter RB, Lonstein JE, Denis F, 2007. 'How much correction is enough?', *Spine (Phila Pa 1976)*, 32 (24), 2641-2643.

Economic data only

'Expect price decline for intervertebral discs as products increase, but don't expect reimbursement boost soon', 2008. *Hosp Mater Manage*, 33 (5), 4-6.

'Little back pain: key spinal product prices remain steady while spine surgeries continue upward path. Increased use of BMP, not internal fixation products, pushes hospital budgets', 2008. *Hosp Mater Manage*, 33 (9), 6-8.

'New manufacturers, materials should slash prices of intervertebral discs', 2007. *Hosp Mater Manage*, 32 (4), 1, 4-1, 7.

'Spinal surgery: beyond the total disc', 2006. *OR Manager*, 22 (2), 10-11.

'Strategies for managing spinal implant costs', 2006. *OR Manager*, 22 (2), 9.

Fayssoux R, Goldfarb NI et al, 2010. 'Indirect costs associated with surgery for low back pain - a secondary analysis of clinical trial data', *Popul Health Manag*, 13 (1), 9-13.

Guyer RD, Tromanhauser SG, Regan JJ, 2007. 'An economic model of one-level lumbar arthroplasty versus fusion', *Spine J*, 7 (5), 558-562.

Hiatt C, 2006. 'Spinal implant pricing model at work', *Mater Manag Health Care*, 15 (10), 48.

Kurtz SM, Lau E et al, 2010. 'National Revision Burden for Lumbar Total Disc Replacement in the United States: Epidemiologic and Economic Perspectives', *Spine (Phila Pa 1976)*, 35(6), 690-696.

Levin DA, Bendo JA et al, 2007. 'Comparative charge analysis of one- and two-level lumbar total disc arthroplasty versus circumferential lumbar fusion', *Spine (Phila Pa 1976)*, 32 (25), 2905-2909.

Mathias JM & Patterson P, 2006. 'FDA approves second lumbar artificial disc', *OR Manager*, 22 (11), 23, 25.

Mathias JM, 2005. 'New artificial spinal disc has a learning curve, payment issues', *OR Manager*, 21 (1), 16-18.

Mendenhall S, 2005. 'Spine costs: a bigger problem than joints', *OR Manager*, 21 (4), 21-22.

Patel VV, Estes S et al, 2008. 'Lumbar spinal fusion versus anterior lumbar disc replacement: the financial implications', *J Spinal Disord Tech*, 21 (7), 473-476.

Patterson P & Mathias JM, 2006. 'Getting a grip on costs and usage of spinal implant technologies', *OR Manager*, 22 (2), 20-23.

Patterson P, 2009. 'Meeting challenges for spine costs', *OR Manager*, 25 (1), 10-13.

Review article

Alander DH, 2005. 'Innovations in the treatment of low back pain', *Mo.Med*, 102 (3), 225-229.

Bajnoczy S, 2005. 'Artificial disc replacement--evolutionary treatment for degenerative disc disease', *AORN J*, 82 (2), 192-196.

Balderston RA, 2000. 'The definition of lumbar spinal instability and its clinical significance', *Seminars in Spine Surgery*, 17 (4), Dec.

Bertagnoli R, Zigler J et al, 2005. 'Complications and strategies for revision surgery in total disc replacement', *Orthop Clin North Am*, 36 (3), 389-395.

Bono CM, 2007. 'Interspinous process devices in the lumbar spine', *Journal of Spinal Disorders and Techniques*, 20 (3), 255-261.

Carragee EJ, 2007. '(ii) The role of surgery in low back pain', *Current Orthopaedics*, 21 (1), 9-16.

Clouet J, Vinatier C et al, 2009. 'The intervertebral disc: from pathophysiology to tissue engineering', *Joint Bone Spine*, 76 (6), 614-618.

Errico TJ, 2008. 'Looking ahead: what long-term outcomes can we expect from spinal devices for degenerative disc disease', *J Long Term Eff Med Implants*, 18 (4), 309-319.

Errico TJ, 2005. 'Lumbar disc arthroplasty', *Clinical Orthopaedics and Related Research*, 435, 106-117.

Fekete TF, Porchet F, 2010. 'Overview of disc arthroplasty-past, present and future', *Acta Neurochir (Wien)*, 152 (3), 393-404.

Frelinghuysen P, 2005. 'Lumbar total disc replacement part I: Rationale, biomechanics, and implant types', *Orthopedic Clinics of North America*, 36 (3 SPEC. ISS.), 293-299.

Galbusera F, Bellini CM et al, 2008. 'Design concepts in lumbar total disc arthroplasty', *Eur Spine J*, 17 (12), 1635-1650.

Gamradt SC, 2005. 'Lumbar disc arthroplasty', *Spine Journal*, 5 (1), 95-103.

Geisler FH, 2006. 'The CHARITE Artificial Disc: design history, FDA IDE study results, and surgical technique', *Clin Neurosurg*, 53, 223-228.

German JW, Foley KT, 2005. 'Disc arthroplasty in the management of the painful lumbar motion segment', *Spine (Phila Pa 1976)*, 30 (16 Suppl), S60-S67.

Guyer RD, 2000. 'Disc prosthesis for degenerative disease and axial instability - Charite[trademark] artificial disc', *Seminars in Spine Surgery*, 17 (4), Dec.

Hallab NJ, 2009. 'A review of the biologic effects of spine implant debris: Fact from fiction', *SAS Journal*, 3 (4), 143-160.

Hebela NM, 2000. 'Revision of Lumbar Total Disc Arthroplasty and Other Anterior Instrumentation', *Seminars in Spine Surgery*, 20 (1), Mar.

Huang RC, Girardi FP et al, 2005. 'Advantages and disadvantages of nonfusion technology in spine surgery', *Orthop Clin North Am*, 36 (3), 263-269.

Huang RC, Wright TM et al, 2005. 'Biomechanics of nonfusion implants', *Orthop Clin North Am*, 36 (3), 271-280.

Inamasu J, 2006. 'Vascular injury and complication in neurosurgical spine surgery', *Acta Neurochirurgica*, 148 (4), 375-387.

Jacobs JJ, Hallab NJ et al, 2006. 'Wear particles', *J Bone Joint Surg Am*, 88 (Suppl 2), 99-102.

Kishen TJ & Diwan AD, 2010. 'Fusion versus disk replacement for degenerative conditions of the lumbar and cervical spine: quid est testimonium?', *Orthop Clin North Am*, 41 (2), 167-181.

Kulkarni AG & Diwan AD, 2005. 'Prosthetic lumbar disc replacement for degenerative disc disease', *Neurol India*, 53 (4), 499-505.

Kurtz SM, 2009. 'Retrieval analysis of motion preserving spinal devices and periprosthetic tissues', *SAS Journal*, 3 (4), 161-177.

Lau S, 2007. 'Lumbar stabilisation techniques', *Current Orthopaedics*, 21 (1), 25-39.

Lin EL,Wang JC, 2006. 'Total disk arthroplasty', *J Am Acad Orthop Surg*, 14 (13), 705-714.

Madonia-Barr JR, 2007. 'Lumbar ADR: a triumph of technology over reason?', *JAAPA*, 20 (8), 30-33.

Marshman LA, Friesem T et al, 2008. 'Lumbar Total Disc Arthroplasty: Coronal Midline Definition and Optimal TDA Placement', *J Long Term Eff Med Implants*, 18 (4), 303-307.

Mayer HM, 2007. 'Total lumbar disc arthroplasty', *Current Orthopaedics*, 21 (1), 17-24.

Mayer HM, 2005. 'Total lumbar disc replacement', *Journal of Bone and Joint Surgery - Series B*, 87 (8), 1029-1037.

Murtagh RD, Quencer RM et al, 2009. 'Normal and abnormal imaging findings in lumbar total disk replacement: devices and complications', *Radiographics*, 29 (1), 105-118.

Nordin M, 2006. 'Nonspecific lower-back pain: Surgical versus nonsurgical treatment', *Clinical Orthopaedics and Related Research*, 443, 156-167.

Ohnmeiss DD, 2009. 'Twenty-four month follow-up for reporting results of spinal implant studies: Is this guideline supported by the literature?', *SAS Journal*, 3 (3), 100-107.

Patel AA, Brodke DS et al, 2008. 'Revision strategies in lumbar total disc arthroplasty', *Spine (Phila Pa 1976)*, 33 (11), 1276-1283.

Pazmino PR, 2008. 'Revision Strategies Involving Lumbar Artificial Disc Replacement', *Seminars in Spine Surgery*, 20 (1), 34-45.

Petersilge CA, 2006. 'Lumbar disc replacement', *Seminars in Musculoskeletal Radiology*, 10 (1), 22-29.

Raj PP, 2008. 'Intervertebral disc: anatomy-physiology-pathophysiology-treatment', *Pain Pract*, 8 (1), 18-44.

Randolph GB, 2006. 'Lumbar Total Disc Arthroplasty: State of the Data', *Seminars in Spine Surgery*, 18 (2), 61-71.

Regan JJ, 2005. 'Clinical results of Charite lumbar total disc replacement', *Orthopedic Clinics of North America*, 36 (3 SPEC. ISS.), 323-340.

Resnick DK & Watters WC, 2007. 'Lumbar disc arthroplasty: a critical review', *Clin Neurosurg*, 54 83-87.

Robinson Y & Sanden B, 2009. 'Spine imaging after lumbar disc replacement: pitfalls and current recommendations', *Patient Saf Surg*, 3 (1), 15.

Simpson AK, Cholewicki J, Grauer J, 2006. 'Chronic low back pain', *Curr Pain Headache Rep*, 10 (6), 431-436.

Singh K, An HS, 2006. 'Motion preservation technologies: alternatives to spinal fusion', *Am J Orthop (Belle Mead NJ)*, 35 (9), 411-416.

Tortolani PJ, 2006. 'Failures of Lumbar Disc Replacement', *Seminars in Spine Surgery*, 18 (2), 78-86.

Truumees E, 2008. 'Lumbar Disc Replacement: Where Are We in 2007?', *Seminars in Spine Surgery*, 20 (2), 132-145.

Zigler JE 2005. 'Disc prosthesis for lumbar degenerative disease and axial instability - Prodisc', *Seminars in Spine Surgery*, 17 (4), 285-296.

Zigler JE, 2006. 'Patient Selection for Lumbar Arthroplasty', *Seminars in Spine Surgery*, 18 (2), 40-46.

Zindrick MR, Tzermiadianos MN et al, 2008. 'An evidence-based medicine approach in determining factors that may affect outcome in lumbar total disc replacement', *Spine (Phila Pa 1976)*, 33 (11), 1262-1269.

Less than 5-years follow-up and no safety data

Auerbach JD, Wills BP et al, 2007. 'Evaluation of spinal kinematics following lumbar total disc replacement and circumferential fusion using in vivo fluoroscopy', *Spine (Phila Pa 1976)*, 32 (5), 527-536.

Cakir B, Schmidt R et al, 2009. 'Index level mobility after total lumbar disc replacement: is it beneficial or detrimental?', *Spine (Phila Pa 1976)*, 34 (9), 917-923.

Cakir B, Richter M et al, 2006. 'Reliability of motion measurements after total disc replacement: the spike and the fin method', *Eur Spine J*, 15 (2), 165-173.

Chung SS, Lee CS et al, 2006. 'The effect of lumbar total disc replacement on the spinopelvic alignment and range of motion of the lumbar spine', *J Spinal Disord Tech*, 19 (5), 307-311.

Delecrin J, 2009. 'Does core mobility of lumbar total disc arthroplasty influence sagittal and frontal intervertebral displacement? Radiologic comparison with fixed-core prosthesis', *SAS Journal*, 3 (3), 91-99.

Guyer RD, Siddiqui S et al, 2008. 'Lumbar spinal arthroplasty: analysis of one center's twenty best and twenty worst clinical outcomes', *Spine (Phila Pa 1976)*, 33 (23), 2566-2569.

Herkowitz HN, 2006. 'Total disc replacement with the CHARITE artificial disc was as effective as lumbar interbody fusion', *J Bone Joint Surg Am*, 88 (5), 1168.

Kafer W, Clessienne CB et al, 2008. 'Posterior component impingement after lumbar total disc replacement: a radiographic analysis of 66 ProDisc-L prostheses in 56 patients', *Spine (Phila Pa 1976)*, 33 (22), 2444-2449.

Le Huec J, Basso Y et al, 2005. 'The effect of single-level, total disc arthroplasty on sagittal balance parameters: a prospective study', *Eur Spine J*, 14 (5), 480-486.

Leahy M, Zigler JE et al, 2008. 'Comparison of results of total disc replacement in postdiscectomy patients versus patients with no previous lumbar surgery', *Spine*, 33 (15), 1690-1693.

Lim MR, Girardi FP et al, 2005. 'Measurement of total disc replacement radiographic range of motion: a comparison of two techniques', *J Spinal Disord Tech*, 18 (3), 252-256.

Nabhan A, Al Yhary A et al, 2007. 'Analysis of spinal kinematics following implantation of lumbar spine disc prostheses versus fusion: radiological study', *J Long Term Eff Med Implants*, 17 (3), 207-216.

Oetgen ME, 2008. 'Does Vertebral Endplate Morphology Influence Outcomes in Lumbar Total Disc Arthroplasty? Part II: Clinical and Radiographic Results as Evaluated Utilizing the Vertebral Endplate Yue-Bertagnoli (VEYBR) Classification', *SAS Journal*, 2 (2), 101-106.

Ordway NR, 2008. 'Twelve-Month Follow-up of Lumbar Spine Range of Motion Following Intervertebral Disc Replacement Using Radiostereometric Analysis', *SAS Journal*, 2 (1), 9-15.

Park SA, Ordway NR et al, 2009. 'Comparison of Cobb technique, quantitative motion analysis, and radiostereometric analysis in measurement of segmental range of motions after lumbar total disc arthroplasty', *J Spinal Disord Tech*, 22 (8), 602-609.

Rohan MX, Jr, Ohnmeiss DD et al, 2009. 'Relationship between the length of time off work preoperatively and clinical outcome at 24-month follow-up in patients undergoing total disc replacement or fusion', *Spine J*, 9 (5), 360-365.

SariAli e, Lemaire JP et al, 2006. 'In vivo study of the kinematics in axial rotation of the lumbar spine after total intervertebral disc replacement: long-term results: a 10-14 years follow up evaluation', *Eur Spine J*, 15 (10), 1501-1510.

Sasani M, Oktenoglu T et al, 2009. 'Total disc replacement in the treatment of lumbar discogenic pain with disc herniation: a prospective clinical study', *Turk Neurosurg*, 19 (2), 127-134.

Siepe CJ, Tepass A et al, 2009. 'Dynamics of improvement following total lumbar disc replacement: is the outcome predictable?', *Spine (Phila Pa 1976)*, 34 (23), 2579-2586.

Siepe CJ, Hitzl W et al, 2009. 'Interdependence between disc space height, range of motion and clinical outcome in total lumbar disc replacement', *Spine (Phila Pa 1976)*, 34 (9), 904-916.

Tournier C, Aunoble S et al, 2007. 'Total disc arthroplasty: consequences for sagittal balance and lumbar spine movement', *Eur Spine J*, 16 (3), 411-421.

Yaszay B, Bendo JA et al, 2008. 'Effect of intervertebral disc height on postoperative motion and outcomes after ProDisc-L lumbar disc replacement', *Spine (Phila Pa 1976)*, 33 (5), 508-512.

Contains combined data that cannot be separated

Chiriano J, Abou-Zamzam AM, Jr et al, 2009. 'The role of the vascular surgeon in anterior retroperitoneal spine exposure: preservation of open surgical training', *J Vasc Surg*, 50 (1), 148-151.

Gumbs AA, Shah RV et al, 2005. 'The open anterior paramedian retroperitoneal approach for spine procedures', *Arch Surg* , 140 (4), 339-343.

Ohnmeiss DD, Bodemer W, Zigler JE, 2010. 'Effect of adverse events on low back surgery outcome: twenty-four-month follow-up results from a Food And Drug Administration investigational device exemptiontrial', *Spine (Phila Pa 1976)*, 35 (7), 835-838.

Peng CW, Bendo JA et al, 2009. 'Perioperative outcomes of anterior lumbar surgery in obese versus non-obese patients', *Spine J*, 9 (9), 715-720.

Study protocol only

Yue JJ, Mo FF, 2010. 'Clinical study to evaluate the safety and effectiveness of the Aesculap Activ-LTM artificial disc in the treatment of degenerative disc disease', *BMC Surg*, 10 (1), 14.

Commentary / editorial / discussion / letter / interview or erratum

'Discussion', 2007. *Journal of Vascular Surgery*, 47 (2), 257.

'FDA approves artificial spine disc', 2005. *Health News*, 11 (1), 2.

'I have degenerative disk disease. Will Medicare cover the cost of an artificial disk replacement?', 2008. *Johns Hopkins Med Lett Health After 50*, 20 (8), 8.

'New disc bests fusion', 2007. *Duke.Med Health News*, 13 (1), 11.

Allen RT, 2009. 'Point of view', *Spine*, 34 (7), 647.

An HS, 2006. 'Artificial disc replacement: progress or hype?', *Am J Orthop (Belle Mead NJ)*, 35 (9), 405.

Blumenthal, 2005. 'Erratum: A prospective, randomized, Multicenter Food and Drug Administration investigational device exemptions study of lumbar total disc replacement with the CHARITE[trademark] artificial disc versus lumbar fusion: Part I - Evaluation of clinical outcomes (Spine (2005) 30 (1565-1575))', *Spine*, 30 (20), 15.

Boeree N, 2007. 'Controversial topics in surgery', *Annals of the Royal College of Surgeons of England*, 89 (1), 6-11.

Botelho RV, 2008. 'Re: Sasso R, Heller J, Hacker B, Smucker J. Artificial disc versus fusion. A prospective, randomized study with 2-years follow-up on 99 patients. Spine 2007;32:2933-40', *Spine (Phila Pa 1976)*, 33 (10), 1156-1157.

Brau SA, 2000. 'Exposure Issues in Lumbar Disc Replacement Surgery', *Seminars in Spine Surgery*, 18 (2), Jun.

Buttner-Janz K, 2006. 'Letter to the Editor concerning "Charite total disc replacement: Clinical and radiographical results after an average follow-up of 17 years" (M. Putzier et al.) [1]', *European Spine Journal*, 15 (4), 521-522.

Buttner-Janz K, 2006. 'Reply to the author's comment to the letters of K. Buttner-Janz and H. D. Link regarding "Charite total disc replacement - Clinical and radiographical results after an average follow-up of 17 years (M. Putzier et al.) [4]', *European Spine Journal*, 15 (4), Apr.

Carragee EJ, 2005. 'The surgical treatment of disc degeneration: is the race not to the swift?', *Spine J*, 5 (6), 587-588.

Cheung KM & Ito K, 2008. 'World Forum for Spine Research: the intervertebral disc: first Japanese meeting, Kyoto, Japan, 23-26 January 2008', *Eur Spine J*, 17 (Suppl 4), 419-420.

Ching AC, Birkenmaier C, Hart RA, 2010. 'Short segment coronal plane deformity after two-level lumbar total disc replacement', *Spine (Phila Pa 1976)*, 35 (1), 44-50.

Fairbank J, 2007. 'Re: Zigler J, Delamarter R, Spivak J, et al. Results of the prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease. Spine 2007;32:1155-62', *Spine (Phila Pa 1976)*, 32 (25), 2929-2930.

Gumbs AA, Bloom ND et al, 2007. 'Open anterior approaches for lumbar spine procedures', *Am J Surg*, 194 (1), 98-102.

Guyer RD, 2010. 'Re: "prospective, randomized multicenter Food and Drug Administration investigational device exemption study of lumbar tool disc replacement with the CHARITE artificial disc versus lumbar fusion: five-year follow-up"', *Spine J*, 10 (4), 360-363.

Guyer RD, 2007. 'Survival and clinical outcome of SB Charite III disc replacement for back pain [1]', *Journal of Bone and Joint Surgery - Series B*, 89 (12), Dec.

Hu S, 2007. 'Review: Surgery may be more effective than unstructured nonoperative treatment for chronic low-back pain - Commentary', *Journal of Bone and Joint Surgery - Series A*, 89 (11), 2558.

Khan SN & Stirling AJ, 2007. 'Controversial topics in surgery: degenerative disc disease: disc replacement. Against', *Ann R Coll Surg Engl*, 89 (1), 6-11.

Korovessis PG, 2008. 'Letters', *Spine*, 33 (16), 15.

Korovessis PG, 2008. 'Re: Sasso RC, Foulk DM, Hahn M. Prospective, randomized trial of metal-on-metal artificial lumbar disc replacement: initial results for treatment of discogenic pain. Spine 2008;33:123-31', *Spine (Phila Pa 1976)*, 33 (16), 1812.

Korovessis PG, 2000. 'To the Editor', *Spine*, 34 (23), November.

Kurtz SM & Walker PS, 2008. 'How have new designs and new types of joint replacement influenced wear behavior?', *J Am Acad Orthop Surg*, 16 (Suppl 1), S107-S110.

Laurent JJ, Bisson EF, Hadley MN, 2006. 'Spinal reconstruction: quo vadis?', *Clin Neurosurg*, 53 229-237.

Lee LA, 2009. 'Rare complications and national databases', *Anesthesia and Analgesia*, 109 (5), 1357-1359.

Lemaire J-P, 2005. 'Erratum: Clinical and radiological outcomes with the charite artificial disc: A 10-year minimum follow-up (Journal of Spinal Disorders and Techniques (August 2005) 18 (4) (353-359))', *Journal of Spinal Disorders and Techniques*, 19 (1), Feb.

Leonardi M, 2000. 'Editorial comment', *Interventional Neuroradiology*, 13 (2), Jun.

Link HD, 2006. 'Letter to the Editor concerning "Charite total disc replacement: Clinical and radiographical results after an average follow-up of 17 years" (M. Putzier et al.) [2]', *European Spine Journal*, 15 (4), 514-517.

Mayer M, 2005. 'Spine arthroplasty', *Expert Rev Med Devices*, 2 (1), 3-6.

McAfee P, 2009. 'Point of view', *Spine*, 34 (11), 1160-1161.

McAfee PC, 2005. 'Comments on the van Ooij article', *J Spinal Disord Tech*, 18 (1), 116-117.

McAfee PC, 2005. 'To the editor (multiple letters)', *Spine Journal*, 5 (1), 118.

McCormick PC, 2008. 'Lumbar disc arthroplasty compared with interbody fusion', *Journal of Neurosurgery: Spine*, 8 (1), Jan.

McCormick PC, 2007. 'The adjacent segment', *J Neurosurg Spine*, 6 (1), 1-4.

McCutchen TM, 9 A.D. 'With reply', *Regional Anesthesia and Pain Medicine*, 34 (1), January/February.

Meyer B, 2010. 'Spinal arthroplasty is here to stay: editorial', *Acta Neurochir (Wien)*, 152 (3), 405-407.

Mirza SK, 2005. 'Point of view: Commentary on the research reports that led to Food and Drug Administration approval of an artificial disc', *Spine (Phila Pa 1976)*, 30 (14), 1561-1564.

Monsey RD, 2007. 'Point of view', *Spine*, 32 (8), 891.

Morrow T, 2005. 'Spinal disc technology seeks to replace body's engineering marvel', *Manag Care*, 14 (6), 67-68.

Nakagawa H, 2000. 'Neurosurgery Review: Comments', *Neurosurgical Review*, 32 (2), April.

Orr RD, Postak PD et al, 2007. 'The current state of cervical and lumbar spinal disc arthroplasty', *J Bone Joint Surg Am*, 89 (Suppl 3), 70-75.

Phillips FM, 2009. 'Point of view', *Spine (Phila Pa 1976)*, 34 (4), 399.

Pierson DJ, 2000. 'Discussion', *Respiratory Care*, 51 (8), Aug.

Pinheiro-Franco JL, 2008. 'Letters', *Spine* , 33 (9), 1050.

Putzier M, 2006. 'Reply to the letters of Prof. K. Buettner-Janz and Mr. H.D. Link concerning "Charite total disc replacement: Clinical and radiographical results after an average follow-up of 17 years" by M. Putzier et al. [3]', *European Spine Journal*, 15 (4), Apr.

Rafael H, 2007. 'Low-back pain', *Journal of Neurosurgery: Spine*, 7 (1), 114-116.

Resnick DK, 2000. 'Comments', *Neurosurgery* , 64 (5 SUPPL. 2), May.

Roitberg B, 2009. 'Research news and notes', *Surgical Neurology*, 71 (4), 405-407.

Rose SM, 2006. 'Spinal body replacement and endoscopic reconstruction', *European Journal of Trauma*, 32 (3), 213-214.

Ross ER, 2009. 'Revision in artificial disc replacement', *Spine J*, 9 (9), 773-775.

Scott-Young MN, 2007. 'Survival and clinical outcome of SB Charite III disc replacement for back pain [3]', *Journal of Bone and Joint Surgery - Series B*, 89 (12), Dec.

Shedid D, Ugokwe KT, Benzel EC, 2005. 'Lumbar total disc replacement compared with spinal fusion: treatment choice and evaluation of outcome', *Nat Clin Pract Neurol*, 1 (1), 4-5.

Snell BE & Maiman DJ, 2005. 'Decompression, arthrodesis, and arthroplasty: decision making in the surgical treatment of lumbar disc disease', *Clin Neurosurg*, 52, 271-278.

Sonntag VKH, 2005. 'Surgical technique of lumbar artificial disc replacement with the Charite Artificial Disc: Comments', *Neurosurgery*, 56 (1 SUPPL.), Jan.

Stambough JL, 2008. 'Introduction', *Seminars in Spine Surgery*, 20 (1), 1.

Tropiano P, 2010. 'Expert's comment concerning Grand Rounds case entitled "Revision of a lumbar disc arthroplasty following late infection" (by Jeffrey M. Spivak and Anthony M. Petrizzo)', *Eur Spine J*, 19, 682-684.

Vaccaro A, 2006. 'Disk regeneration', *Orthopedics*, 29 (12), 1074.

Wilson-MacDonald J, Boeree N, 2007. 'Controversial topics in surgery: degenerative disc disease: disc replacement. For', *Ann R Coll Surg Engl*, 89 (1), 6-11.

Winter RB, 2009. 'Lessons from the past: pathways to the future', *J Orthop Sci*, 14 (1), 121-127.

Zdeblick TA, 2009. 'The second half', *Spine*, 34 (26), 2835-2837.

Zeller JL, 2006. 'Artificial spinal disk superior to fusion for treating degenerative disk disease', *JAMA*, 296 (22), 2665-2667.

Zindrick MR, 2008. 'Point of view', *Spine*, 33 (5), Mar.

Critique of another paper

Burkus JK, Polly DW, Jr, Gornet M, 2005. 'Artificial disc', J Neurosurg Spine, 2 (3), 395-397.

Non human / model or cadaver study

Anabtawi M, Beck P, Lemons J, 2008. 'Biocompatibility testing of simulated total joint arthoplasty articulation debris', *J Biomed Mater Res B Appl Biomater*, 84 (2), 478-485.

Anderson PA, 2000. 'Explant Analysis of Total Disc Replacement', *Seminars in Spine Surgery*, 18 (2), Jun.

Buttermann GR, 2009. 'Biomechanical characterization of an annulus-sparing spinal disc prosthesis', *Spine Journal*, 9 (9), 744-753.

Cakir B, Richter M et al, 2009. 'Resect or not to resect: the role of posterior longitudinal ligament in lumbar total disc replacement', *Eur Spine J*, Epub 31, October 2009.

Chen SH, Zhong ZC et al, 2009. 'Biomechanical comparison between lumbar disc arthroplasty and fusion', *Med Eng Phys*, 31 (2), 244-253.

Cunningham BW, Hu N et al, 2009. 'Bioactive titanium calcium phosphate coating for disc arthroplasty: analysis of 58 vertebral end plates after 6- to 12-month implantation', *Spine J*, 9 (10), 836-845.

Denoziere G & Ku DN, 2006. 'Biomechanical comparison between fusion of two vertebrae and implantation of an artificial intervertebral disc', *J Biomech*, 39 (4), 766-775.

Goel VK, Grauer JN et al, 2005. 'Effects of charite artificial disc on the implanted and adjacent spinal segments mechanics using a hybrid testing protocol', *Spine (Phila Pa 1976)*, 30 (24), 2755-2764.

Grauer JN, Biyani A et al, 2006. 'Biomechanics of two-level Charite artificial disc placement in comparison to fusion plus single-level disc placement combination', *Spine J*, 6 (6), 659-666.

Palissery V, Mulholland RC, McNally DS, 2009. 'The implications of stress patterns in the vertebral body under axial support of an artificial implant', *Med Eng Phys*, 31 (7), 833-837.

Petilon J, Hardenbrook M, Sukovich W, 2008. 'The effect of parallax on intraoperative positioning of the Charite artificial disc', *J Spinal Disord Tech*, 21 (6), 422-429.

Case reports

Bertagnoli R, 2005. 'Hybrid constructs', *Orthopedic Clinics of North America*, 36 (3 SPEC. ISS.), 379-388.

Daly KJ, Ross ER et al, 2006. 'Vascular complications of prosthetic inter-vertebral discs', *Eur Spine J*, 15 (Suppl 5), 644-649.

David T, 2005. 'Revision of a Charite artificial disc 9.5 years in vivo to a new Charite artificial disc: case report and explant analysis', *Eur Spine J*, 14 (5), 507-511.

Schulte TL, Lerner T et al, 2007. 'Acquired spondylolysis after implantation of a lumbar ProDisc II prosthesis: case report and review of the literature', *Spine (Phila Pa 1976)*, 32 (22), E645-E648.

Shim CS, Lee S et al, 2005. 'Vertical split fracture of the vertebral body following total disc replacement using ProDisc: report of two cases', *J Spinal Disord Tech*, 18 (5), 465-469.

van Ooij A, 2007. 'Polyethylene wear debris and long-term clinical failure of the Charite disc prosthesis: A study of 4 patients', *Spine*, 32 (2), 223-229.

Description of technique

Aryan HE, Acosta FL, Jr, Ames CP, 2005. 'The Charite Artificial Disc: insertion technique', *Neurosurg Clin N Am*, 16 (4), 637-650.

Aryan HE, Acosta FL, Jr, Ames CP, 2005. 'The ProDisc artificial disc: insertion technique', *Neurosurg Clin N Am*, 16 (4), 651-656.

Geisler FH, 2005. 'Surgical technique of lumbar artificial disc replacement with the Charite Artificial Disc', *Neurosurgery*, 56, Epub, January.

Pimenta L, Diaz RC, Guerrero LG, 2006. 'Charite lumbar artificial disc retrieval: use of a lateral minimally invasive technique. Technical note', *J Neurosurg Spine*, 5 (6), 556-561.

Revision / reoperation and original cohort not specified

Brau SA, 2008. 'Access strategies for revision in anterior lumbar surgery', *Spine*, 33 (15), 1662-1667.

Leary SP, Regan JJ et al, 2007. 'Revision and explantation strategies involving the CHARITE lumbar artificial disc replacement', *Spine (Phila Pa 1976)*, 32 (9), 1001-1011.

Punt IM, Visser VM et al, 2008. 'Complications and reoperations of the SB Charite lumbar disc prosthesis: experience in 75 patients', *Eur Spine J*, 17 (1), 36-43.

Punt IM, Cleutjens JP et al, 2009. 'Periprosthetic tissue reactions observed at revision of total intervertebral disc arthroplasty', *Biomaterials*, 30 (11), 2079-2084.

Rosen C, Kiester PD, Lee TQ, 2009. 'Lumbar disk replacement failures: review of 29 patients and rationale for revision', *Orthopedics*, 32 (8), Epub, August.

Wagner WH, Regan JJ et al, 2006. 'Access strategies for revision or explantation of the Charite lumbar artificial disc replacement', *J Vasc Surg*, 44 (6), 1266-1272.

Data reported in another study

Auerbach JD, 2005. 'Lumbar disc arthroplasty versus fusion for single-level degenerative disc disease: Two-year results from a randomized prospective study', *Seminars in Spine Surgery*, 17 (4), 310-317.

Cakir B, Richter M et al, 2005. 'The impact of total lumbar disc replacement on segmental and total lumbar lordosis', *Clin Biomech (Bristol, Avon)*, 20 (4), 357-364.

Cunningham BW, McAfee PC et al, 2008. 'Distribution of in vivo and in vitro range of motion following 1-level arthroplasty with the CHARITE artificial disc compared with fusion', *J Neurosurg Spine*, 8 (1), 7-12.

Delamarter RB, 2005. 'Clinical results of ProDisc-II lumbar total disc replacement: Report from the United States clinical trial', *Orthopedic Clinics of North America*, 36 (3 SPEC. ISS.), 301-313.

Le Huec JC, Basso Y et al, 2005. 'Influence of facet and posterior muscle degeneration on clinical results of lumbar total disc replacement: two-year follow-up', *J Spinal Disord Tech*, 18 (3), 219-223.

Siepe CJ, Korge A et al, 2008. 'Analysis of post-operative pain patterns following total lumbar disc replacement: results from fluoroscopically guided spine infiltrations', *Eur Spine J*, 17 (1), 44-56.

Tropiano P, Huang RC et al, 2006. 'Lumbar total disc replacement. Surgical technique', *J Bone Joint Surg Am*, 88A (Suppl 1 Pt 1), 50-64.

Zeh A, Planert M et al, 2007. 'Release of cobalt and chromium ions into the serum following implantation of the metal-on-metal Maverick-type artificial lumbar disc (Medtronic Sofamor Danek)', *Spine (Phila Pa 1976)*, 32 (3), 348-352.

Unable to obtain

Anon, 2005. 'Artificial disc replacement surgery', *Clin Privil White Pap*, (231), 1-12.

Appendix H Economic evaluation data

MBS claims data were provided by the Department of Health on patients who claimed any of the following MBS items from July 2005 through to August 2010: 48648, 48651, 48654, 48657, 48660, 48663, 48669, 48672, 48675, 48684, 48690, 48691 and 48692. For these patients, any other MBS item claimed by the same patient on the same day was also provided. Due to complexity, a maximum of 20 items for each same patient/same day procedure were extracted and MBS items relating to anaesthesia time were not extracted. Only 10.4 per cent of patients claimed 20 items or more.

Analysis of MBS data indicates that there were:

- 860 claims for MBS items associated with lumbar AIDR procedures.[25]
- 58,829 claims for MBS items associated with spinal fusion procedures.[26]

However, many procedures were performed for indications that are not linked to DDD, such as stenosis, scoliosis and spinal fracture. When patients who also claimed for items relating to stenosis, scoliosis and spinal fracture on the same day as their operation are removed[27] there were:

- 852 claims for MBS items associated with lumbar AIDR procedures
- 26,114 claims for MBS items associated with spinal fusion procedures.

It is important to note that many procedures may involve claims for more than one relevant MBS item (ie some patients may claim for MBS items associated with both AIDR and spinal fusion procedures, while other patients may claim for MBS items associated with different types of spinal fusion procedures).

When procedures involving claims for MBS items associated with AIDR procedures are removed there were 12,568 spinal fusion only procedures (same patient, same day) involving 25,101 claims for spinal fusion MBS items.

Some of these spinal fusion procedures can be identified as occurring in the lumbar or cervical region based on the MBS item claimed for initiation of anaesthesia[28]:

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[25] 819 claims for MBS item number 48691 of which one procedure charged for this item number twice, and 41 claims for MBS item number 48692. Note that MBS item number 49693 is the fee charged by an assisting surgeon associated with MBS item number 48692.

[26] MBS item numbers 48642, 48645, 48648, 48651, 48654, 48657, 48660, 48663, 48666, 48669, 48672, 48675, 48684, 48687, 48690, 40321, 40324.

[27] Any procedure involving a claim for MBS item numbers associated with scoliosis (48606, 48612, 48613, 48615, 48618, 48621, 48624, 48627, 48630, 48632, 50600, 50604, 50608, 50612, 50616, 50620, 50624, 50628, 50632, 50636, 50640, 50644), stenosis (40303, 40306) and spinal fracture (47702).

[28] Cervical procedures are indicated by MBS item number 20600 and lumbar procedures are indicated by MBS item number 20630.

- 4,331 spinal fusion only procedures also involved claims for initiation of anaesthesia in the cervical region (approximately 866 per year) and spinal fusion 2,418 in the lumbar region (approximately 484 per year).

Similarly, when procedures involving claims for MBS items associated with spinal fusion are removed there were:

- 346 AIDR only procedures (same patient, same day), of which none involved claims for initiation of anaesthesia in the cervical region and 219 in the lumbar region.

Note that this split between the lumbar and cervical region is an indication only as many involved claims for extensive spine/spinal cord procedures (20670) and therefore cannot be identified as occurring in a specific spinal region. Furthermore, many of these procedures may relate to revisions of earlier surgeries, and so cannot be taken as an indication of the number of patients.

Table 49 Calculation of initial surgery costs for lumbar AIDR

	Unit cost	Units	Multiple operations adjustment	Total
Consumables				
Artificial disc	$9,550.00	1		$9,550.00
Costs associated with procedure				
Pre operational				
Brief pre-anaesthesia consultation (MBS 17610)	$30.45	1		$30.45
MBS 17610 copayment	$43.73	1		$43.73
Operational				
AIDR procedure (MBS 48691)*	$1,271.40	1	100%	$1,271.40
MBS 48691 copayment	$3,228.63	1		$3,228.63
Spinal rhizolysis (MBS 40330)*	$676.95	0.23	50%^	$77.85
MBS 40330 copayment	$444.07	0.23		$102.14
Removal of intervertebral disc (MBS 40300)*	$676.95	0.24	50%^	$81.23
MBS 40300 copayment	$995.26	0.24		$238.86
Fluroscopy (MBS 60506)	$47.85	0.5		$23.93
MBS 60506 copayment	$47.79	0.5		$23.89
Fluroscopy (MBS 60509)	$74.20	0.34		$25.23
MBS 60509 copayment	$66.77	0.34		$22.70
Initiation of Anaesthesia (MBS 20630)	$112.20	1		$112.20
MBS 20630 copayment	$432.12	1		$432.12
Anaesthesia 2h0min to 2h10min (MBS 23091)	$126.25	1		$126.25
MBS 23091 copayment	$203.92	1		$203.92
Assistance (MBS 51303)	20%	0.91		$260.35
MBS 51303 copayment	$192.95	0.91		$175.59
Post operational				
Hospital stay	$1,261.55	3.79		$4,780.80
Total consumables				$9,550.00
Total MBS fees				$2,008.88
Total patient out-of-pocket				$4,471.59
Total other hospital costs				$4,780.80
Total cost of lumbar AIDR implant				$20,811.27

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 91% of procedures require assistance; ^It is unclear which MBS item would be the 2nd most costly procedure and only a small proportion would receive both. Consequently 50% is applied to both.

Table 50 Calculation of initial surgery for lumbar fusion, ALIF

	Unit cost	Units	Multiple operations adjustment	Total
Consumables				
Anterior interbody cage	$3,600.00	1		$3,600.00
Plate	$2,317.65	0.5		$1,158.82
BMP	$6,400.00	1 if BMP, else 0		$6,400.00 or $0
Graft Substitute	$1,390.00	1 if BMP, else 0		$1,390.00 or $0
Costs associated with procedure				
Pre operational				
Brief pre-anaesthesia consultation (MBS 17610)	$30.45	1		$30.45
MBS 17610 copayment	$43.73	1		$43.73
Operational				
Spinal fusion (anterior interbody) (MBS 48660)*	$767.45	1	100%	$767.45
MBS 48660 copayment	$1,130.76	1		$1130.76
Segmental internal fixation of spine (MBS 48684)*	$667.35	0.92	25%	$153.49
MBS 48684 copayment	$378.33	0.92		$348.07
Spinal rhizolysis(MBS 40330)*	$676.95	0.31	50%^	$104.93
MBS 40330 copayment	$444.07	0.31		$137.66
Removal of intervertebral disc(MBS 40300)*	$676.95	0.25	50%^	$84.62
MBS 40300 copayment	$995.26	0.25		$2480.82
Bone graft, harvesting, small amount (MBS 47726)	$100.15	0.15 if autograft, else 0	25%	$3.76 or $0
MBS 47726 copayment	$129.95	0.15 if autograft, else 0		$19.49 or $0
Bone graft, harvesting, large amount (MBS 47729)	$166.95	0.85 if autograft, else 0	25%	$35.48 or $0
MBS 47729 copayment	$191.18	0.85 if autograft, else 0		$162.50 or $0
Fluroscopy (MBS 60506)	$47.85	0.44		$21.05
MBS 60506 copayment	$47.79	0.44		$21.03
Fluroscopy (MBS 60509)	$74.20	0.39		$28.94
MBS 60509 copayment	$66.77	0.39		$26.04
Initiation of anaesthesia (MBS 20630)	$112.20	1		$112.20
MBS 20630 copayment	$432.12	1		$432.12
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	1		$182.35
MBS 23113 copayment	$292.35	1		$292.35
Assistance (MBS 51303)	20%	0.86		$191.00
MBS 51303 copayment	$192.95	0.86		$165.94
Post operational				
Hospital stay	$1,261.55	5.12		$6,464.42
Total consumables				$7,095.82
Total MBS fees				$1,684.33
Total patient out-of-pocket				$2,882.90
Total other hospital costs				$6,464.42
Weighted average cost**				$18,127.47

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 86% of procedures require assistance; ** Autograft = 20%, BMP = 30%, Autograft (locally obtained) = 50%; ^It is unclear which MBS item would be the 2nd most costly procedure and only a small proportion would receive both. Consequently 50% is applied to both.

Table 51 Calculation of initial surgery for lumbar fusion, PLIF

	Unit cost	Units	Multiple operations adjustment	Total
Consumables				
Screws and rods	$6,841.49	1		$6,841.49
Posterior interbody cage	$3,000.00	2		$6,000.00
BMP	$6,400.00	1 if BMP, else 0		$6,400.00 or $0
Graft substitute	$1,390.00	1 if BMP, else 0		$1,390.00 or $0
Costs associated with procedure				
Pre operational				
Brief pre-anaesthesia consultation (MBS 17610)	$30.45	1		$30.45
MBS 17610 copayment	$43.73	1		$43.73
Operational				
Spinal fusion (posterior interbody) (MBS 48654)*	$767.45	1	100%	$767.45
MBS 48654 copayment	$522.75	1		$522.75
Segmental internal fixation of spine (MBS 48684)*	$667.35	0.89	25%	$148.49
MBS 48684 copayment	$378.33	0.89		$336.72
Spinal rhizolysis(MBS 40330)*	$676.95	0.8	50%	$270.78
MBS 40330 copayment	$444.07	0.8		$355.26
Removal of intervertebral disc(MBS 40300)*	$676.95	0.37	25%	$62.62
MBS 40300 copayment	$995.26	0.37		$368.25
Bone graft, harvesting, small amount (MBS 47726)	$100.15	0.08 if autograft, else 0	25%	$2.09 or $0
MBS 47726 copayment	$129.95	0.08 if autograft, else 0		$10.83 or $0
Bone graft, harvesting, large amount (MBS 47729)	$166.95	0.92 if autograft, else 0	25%	$38.26 or $0
MBS 47729 copayment	$191.18	0.92 if autograft, else 0		$175.25 or $0
Fluroscopy (MBS 60506)	$47.85	0.43		$20.58
MBS 60506 copayment	$47.79	0.43		$20.55
Fluroscopy (MBS 60509)	$74.20	0.34		$25.23
MBS 60509 copayment	$66.77	0.34		$22.70
Initiation of anaesthesia (MBS 20630)	$112.20	1		$112.20
MBS 20630 copayment	$432.12	1		$432.12
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	1		$182.35
MBS 23113 copayment	$292.35	1		$292.35
Assistance (MBS 51303)	20%	0.76		$199.42
MBS 51303 copayment	$192.95	0.76		$146.64
Post-operational				
Hospital stay	$1,261.55	5.12		$6,464.42
Total consumables				$15,178.49
Total MBS fees				$1,814.88
Total patient out-of-pocket				$2,563.40
Total other hospital costs				$6,464.42
Weighted average cost**				$26,021.18

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 76% of procedures require assistance; ** Autograft = 12%, BMP = 30%, Autograft (locally obtained) = 58%.

Table 52 Calculation of initial surgery for lumbar fusion, PLF

	Unit cost	Units	Multiple operations adjustment	Total
Consumables				
Screws and rods	$6,841.49	1		$6,841.49
BMP	$6,400.00	1 if BMP, else 0		$6,400.00 or $0
Graft substitute	$1,390.00	1 if BMP, else 0		$1,390.00 or $0
Costs associated with procedure				
Pre operational				
Brief pre-anaesthesia consultation (MBS 17610)	$30.45	1		$30.45
MBS 17610 copayment	$43.73	1		$43.73
Operational				
Bone graft to spine (posterolateral fusion) (MBS 48648)*	$767.45	1	100%	$767.45
MBS 48648 copayment	$788.44	1		$788.44
Segmental internal fixation of spine (MBS 48684)*	$667.35	0.73	25%	$121.79
MBS 48684 copayment	$378.33	0.73		$276.18
Spinal rhizolysis(MBS 40330)*	$676.95	0.35	50%^	$118.47
MBS 40330 copayment	$444.07	0.35		$155.43
Removal of intervertebral disc(MBS 40300)*	$676.95	0.2	50%^	$67.70
MBS 40300 copayment	$995.26	0.2		$199.05
Bone graft, harvesting, small amount (MBS 47726)	$100.15	0.03 if autograft, else 0	25%	$0.70 or $0
MBS 47726 copayment	$129.95	0.03 if autograft, else 0		$3.61 or $0
Bone graft, harvesting, large amount (MBS 47729)	$166.95	0.97 if autograft, else 0	25%	$40.58 or $0
MBS 47729 copayment	$191.18	0.97 if autograft, else 0		$185.87 or $0
Fluroscopy (MBS 60506)	$47.85	0.39		$18.66
MBS 60506 copayment	$47.79	0.39		$18.64
Fluroscopy (MBS 60509)	$74.20	0.25		$18.55
MBS 60509 copayment	$66.77	0.25		$16.69
Initiation of Anaesthesia (MBS 20630)	$112.20	1		$112.20
MBS 20630 copayment	$432.12	1		$432.12
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	1		$182.35
MBS 23113 copayment	$292.35	1		$292.35
Assistance (MBS 51303)	20%	0.81		$174.22
MBS 51303 copayment	$192.95	0.81		$156.29
Post operational				
Hospital stay	$1,261.55	5.12		$6,464.42
Total consumables				$9,178.49
Total MBS fees				$1,626.69
Total patient out-of-pocket				$2,447.13
Total other hospital costs				$6,464.42
Weighted average cost**				$19,716.72

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 81% of procedures require assistance; ** Autograft = 36%, BMP = 30%, Autograft (locally obtained) = 34%; ^It is unclear which MBS item would be the 2nd most costly procedure and only a small proportion would receive both. Consequently 50% is applied to both.

Table 53 Calculation of initial surgery for lumbar fusion, combination (PLIF + PLF) approach

	Unit cost	Units	Multiple operations adjustment	Total
Consumables				
Screws and rods	$6,841.49	1		$6,841.49
Posterior interbody cage	$3,000.00	2		$6,000.00
BMP	$6,400.00	1 if BMP, else 0		$6,400.00 or $0
Graft substitute	$1,390.00	1 if BMP, else 0		$1,390.00 or $0
Costs associated with procedure				
Pre operational				
Brief pre-anaesthesia consultation (MBS 17610)	$30.45	1		$30.45
MBS 17610 copayment	$43.73	1		$43.73
Operational				
Spinal fusion (posterior interbody) (MBS 48654)*	$767.45	1	100%	$767.45
MBS 48654 copayment	$522.75	1		$522.75
Bone graft to spine (posterolateral fusion) (MBS 48648)*	$767.45	1	50%	$383.73
MBS 48648 copayment	$788.44	1		$788.44
Segmental internal fixation of spine (MBS 48684)*	$667.35	0.98	25%	$163.50
MBS 48684 copayment	$378.33	0.98		$370.77
Spinal rhizolysis(MBS 40330)*	$676.95	0.9	25%	$152.31
MBS 40330 copayment	$444.07	0.9		$399.67
Removal of intervertebral disc(MBS 40300)*	$676.95	0.27	25%	$45.69
MBS 40300 copayment	$995.26	0.27		$268.72
Bone graft, harvesting, small amount (MBS 47726)	$100.15	0.03 if autograft, else 0	25%	$0.66 or $0
MBS 47726 copayment	$129.95	0.03 if autograft, else 0		$3.40 or $0
Bone graft, harvesting, large amount (MBS 47729)	$166.95	0.97 if autograft, else 0	25%	$40.64 or $0
MBS 47729 copayment	$191.18	0.97 if autograft, else 0		$186.17 or $0
Fluroscopy (MBS 60506)	$47.85	0.3		$14.36
MBS 60506 copayment	$47.79	0.3		$14.34
Fluroscopy (MBS 60509)	$74.20	0.48		$35.62
MBS 60509 copayment	$66.77	0.48		$32.05
Initiation of anaesthesia (MBS 20630)	$112.20	1		$112.20
MBS 20630 copayment	$432.12	1		$432.12
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	1		$182.35
MBS 23113 copayment	$292.35	1		$292.35
Assistance (MBS 51303)	20%	0.86		$260.18
MBS 51303 copayment	$192.95	0.86		$165.94
Post operational				
Hospital stay	$1,261.55	5.12		$6,464.42
Total consumables				$15,178.49
Total MBS fees				$2,160.48
Total patient out-of-pocket				$3,388.90
Total other hospital costs				$6,464.42
Weighted average cost**				$27,192.28

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 86% of procedures require assistance; ** Autograft = 31%, BMP = 30%, Autograft (locally obtained) = 39%.

Table 54 Calculation of initial surgery for lumbar fusion, circumferential (ALIF + PLF) approach

	Unit cost	Units	Multiple operations adjustment	Total
Consumables				
Screws and rods	$6,841.49	1		$6,841.49
Anterior interbody cage	$3,600.00	1		$3,600.00
Plate	$2,317.65	0.3		$695.29
BMP	$6,400.00	1 if BMP, else 0		$6,400.00 or $0
Graft substitute	$1,390.00	1 if BMP, else 0		$1,390.00 or $0
Costs associated with procedure				
Pre operational				
Brief pre-anaesthesia consultation (MBS 17610)	$30.45	1		$30.45
MBS 17610 copayment	$43.73	1		$43.73
Operational				
Spinal fusion (anterior interbody) (MBS 48660)*	$767.45	1	100%	$767.45
MBS 48660 copayment	$1,130.76	1		$1,130.76
Bone graft to spine (posterolateral fusion) (MBS 48648)*	$767.45	1	50%	$383.73
MBS 48648 copayment	$788.44	1		$788.44
Segmental internal fixation of spine (MBS 48684)*	$667.35	0.93	25%	$155.16
MBS 48684 copayment	$378.33	0.93		$351.85
Spinal rhizolysis(MBS 40330)*	$676.95	0.31	25%	$52.46
MBS 40330 copayment	$444.07	0.31		$137.66
Removal of intervertebral disc(MBS 40300)*	$676.95	0.14	25%	$23.69
MBS 40300 copayment	$995.26	0.14		$139.34
Bone graft, harvesting, small amount (MBS 47726)	$100.15	0	25%	$0
MBS 47726 copayment	$129.95	0		$0
Bone graft, harvesting, large amount (MBS 47729)	$166.95	1 if autograft, else 0	25%	$41.74 or $0
MBS 47729 copayment	$191.18	1 if autograft, else 0		$191.18 or $0
Fluroscopy (MBS 60506)	$47.85	0.34		$16.27
MBS 60506 copayment	$47.79	0.34		$16.25
Fluroscopy (MBS 60509)	$74.20	0.59		$43.78
MBS 60509 copayment	$66.77	0.59		$39.39
Initiation of anaesthesia (MBS 20630)	$112.20	1		$112.20
MBS 20630 copayment	$432.12	1		$432.12
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	1		$182.35
MBS 23113 copayment	$292.35	1		$292.35
Assistance (MBS 51303)	20%	0.93		$257.14
MBS 51303 copayment	$192.95	0.93		$179.44
Post operational				
Hospital stay	$1,261.55	5.12		$6,464.42
Total consumables				$13,473.78
Total MBS fees				$2,046.38
Total patient out-of-pocket				$3,650.74
Total other hospital costs				$6,464.42
Weighted average cost**				$25,635.33

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 93% of procedures require assistance; ** Autograft = 52%, BMP = 30%, Autograft (locally obtained) = 18%.

Table 55 Calculation of re-operation costs, hardware replacement, AIDR

	Unit cost	Units	Multiple operations adjustment	Total
Initial surgery MBS costs	$2,008.88	1		$2,008.88
Copayments	$4,471.59	1		$4,471.59
Removal of device (MBS 48639)*	$967.60	1	50%	$483.80
MBS 48639 copayment	$783.80	1		$783.80
Spinal rhizolysis (MBS 40330)*	$676.95	-0.23	50%	-$77.85
MBS 40330 copayment	$444.07	-0.23		-$102.14
Removal of intervertebral disc (MBS 40300)*	$676.95	-0.24	50%	-$81.23
MBS 40300 copayment	$995.26	-0.24		-$238.86
Anaesthesia 2h0min to 2h10min (MBS 23091)	$126.25	-1		-$126.25
MBS 23091 copayment	$203.92	-1		-$203.92
Anaesthesia 3h01min to 3h01min (MBS 23115)	$210.40	1		$210.40
MBS 23115 copayment	$330.46	1		$330.46
Assistance (MBS 51303)	20%	0.91		$59.10
MBS 51303 copayment	No impact			$0.00
Total consumables				$9,550.00
Total MBS fees				$2,476.85
Total patient out-of-pocket				$5,040.92
Total other hospital costs				$4,780.80
Total				$21,848.57
Total minus consumables				$12,298.57

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 91% of procedures require assistance.

Table 56 Calculation of re-operation costs, hardware replacement, ALIF

	Unit cost	Units	Multiple operations adjustment	Total
Initial surgery costs	$1,684.33	1		$1,684.33
Copayments	$2,882.90	1		$2,882.90
Removal of device (MBS 48639)*	$967.60	1	100%	$967.60
MBS 48639 copayment	$783.80	1		$783.80
Spinal fusion (anterior interbody) (MBS 48660)*	$767.45	1	Decrease to 50%	-$383.73
MBS 48660 copayment	No impact	1		$0.00
Spinal rhizolysis (MBS 40330)*	$676.95	-0.31	50%	-$104.93
MBS 40330 copayment	$444.07	-0.31		-$137.66
Removal of intervertebral disc (MBS 40300)*	$676.95	-0.25	50%	-$84.62
MBS 40300 copayment	$995.26	-0.25		-$248.82
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	-1		-$182.35
MBS 23113 copayment	$292.35	-1		-$292.35
Anaesthesia 3h01min to 3h01min (MBS 23115)	$210.40	1		$210.40
MBS 23115 copayment	$330.46	1		$330.46
Assistance (MBS 51303)	20%	0.86		$67.82
MBS 51303 copayment	No impact			$0.00
Total consumables				$7,095.82
Total MBS fees				$2,174.53
Total patient out-of-pocket				$3,318.33
Total other hospital costs				$6,464.42
Total				$19,053.11
Total minus consumables				$11,957.28

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 86% of procedures require assistance.

Table 57 Calculation of re-operation costs, hardware replacement, PLIF

	Unit cost	Units	Multiple operations adjustment	Total
Initial surgery costs	$1,814.88	1		$1,814.88
Copayments	$2,563.40	1		$2,563.40
Removal of device (MBS 48639)*	$967.60	1	100%	$967.60
MBS 48639 copayment	$783.80	1		$783.80
Spinal fusion (posterior interbody) (MBS 48654)*	$767.45	1	Decrease to 50%	-$383.73
MBS 48654 copayment	No impact			$0.00
Spinal rhizolysis (MBS 40330)*	$676.95	-0.8	50%	-$270.78
MBS 40330 copayment	$444.07	-0.8		-$355.26
Removal of intervertebral disc (MBS 40300)*	$676.95	-0.37	25%	-$62.62
MBS 40300 copayment	$995.26	-0.37		-$368.25
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	-1		-$182.35
MBS 23113 copayment	$292.35	-1		-$292.35
Anaesthesia 3h01min to 3h01min (MBS 23115)	$210.40	1		$210.40
MBS 23115 copayment	$330.46	1		$330.46
Assistance (MBS 51303)	20%	0.76		$28.55
MBS 51303 copayment	No impact			$0.00
Total consumables				$15,178.49
Total MBS fees				$2,131.48
Total patient out-of-pocket				$2,661.80
Total other hospital costs				$6,464.42
Total				$26,436.18
Total minus consumables				$11,257.69

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 76% of procedures require assistance.

Table 58 Calculation of re-operation costs, hardware replacement, PLF

	Unit cost	Units	Multiple operations adjustment	Total
Initial surgery MBS costs	$1,626.69	1		$1,626.69
Copayments	$2,447.13	1		$2,447.13
Removal of device (MBS 47930)*	$186.90	1	25%	$46.73
MBS 47930 copayment	$191.16	1		$191.16
Segmental internal fixation of spine (MBS 48684)*	$667.35	1	Increase to 50%	$121.79
MBS 48684 copayment	No impact	1		$0.00
Spinal rhizolysis (MBS 40330)*	$676.95	-0.35	50%	-$118.47
MBS 40330 copayment	$444.07	-0.35		-$155.43
Removal of intervertebral disc (MBS 40300)*	$676.95	-0.2	50%	-$67.70
MBS 40300 copayment	$995.26	-0.2		-$199.05
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	-1		-$182.35
MBS 23113 copayment	$292.35	-1		-$292.35
Anaesthesia 3h01min to 3h01min (MBS 23115)	$210.40	1		$210.40
MBS 23115 copayment	$330.46	1		$330.46
Assistance (MBS 51303)	20%	0.81		-$2.86
MBS 51303 copayment	No impact			$0.00
Total consumables				$9,178.49
Total MBS fees				$1,634.23
Total patient out-of-pocket				$2,321.92
Total other hospital costs				$6,464.42
Total				$19,599.06
Total minus consumables				$10,420.57

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 81% of procedures require assistance.

Table 59 Calculation of re-operation costs, hardware replacement, Combination (PLF+PLIF)

	Unit cost	Units	Multiple operations adjustment	Total
Initial surgery costs	$2,160.48	1		$2,160.48
Copayments	$3,388.90	1		$3,388.90
Removal of device (MBS 48639)*	$967.60	1	100%	$967.60
MBS 48639 copayment	$783.80	1		$783.80
Removal of device (MBS 47930)*	$186.90	1	25%	$46.73
MBS 47930 copayment	$191.16	1		$191.16
Spinal fusion (posterior interbody) (MBS 48654)*	$767.45	1	Decrease to 50%	-$383.73
MBS 48654 copayment	No impact	1		$0.00
Bone graft to spine (posterolateral fusion) (MBS 48648)*	$767.45	1	Decrease to 25%	-$191.86
MBS 48648 copayment	No impact	1		$0.00
Spinal rhizolysis (MBS 40330)*	$676.95	-0.9	25%	-$152.31
MBS 40330 copayment	$444.07	-0.9		-$399.67
Removal of intervertebral disc (MBS 40300)*	$676.95	-0.27	25%	-$45.69
MBS 40300 copayment	$995.26	-0.27		-$268.72
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	-1		-$182.35
MBS 23113 copayment	$292.35	-1		-$292.35
Anaesthesia 3h01min to 3h01min (MBS 23115)	$210.40	1		$210.40
MBS 23115 copayment	$330.46	1		$330.46
Assistance (MBS 51303)	20%	0.86		$41.41
MBS 51303 copayment	No impact			$0.00
Total consumables				$15,178.49
Total MBS fees				$2,470.66
Total patient out-of-pocket				$3,733.58
Total other hospital costs				$6,464.42
Total				$27,847.14
Total minus consumables				$12,668.66

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 86% of procedures require assistance.

Table 60 Calculation of re-operation costs, hardware replacement, Circumferential (PLF+ALIF)

	Unit cost	Units	Multiple operations adjustment	Total
Initial surgery costs	$2,046.38	1		$2,046.38
Copayments	$3,650.74	1		$3,650.74
Removal of device (MBS 48639)*	$967.60	1	100%	$967.60
MBS 48639 copayment	$783.80	1		$783.80
Removal of device (MBS 47930)*	$186.90	1	25%	$46.73
MBS 47930 copayment	$191.16	1		$191.16
Spinal fusion (anterior interbody) (MBS 48660)*	$767.45	1	Decrease to 50%	-$383.73
MBS 48660 copayment	No impact			$0.00
Bone graft to spine (posterolateral fusion) (MBS 48648)*	$767.45	1	Decrease to 25%	-$191.86
MBS 48648 copayment	No impact			$0.00
Spinal rhizolysis (MBS 40330)*	$676.95	-0.31	25%	-$52.46
MBS 40330 copayment	$444.07	-0.31		-$137.66
Removal of intervertebral disc (MBS 40300)*	$676.95	-0.14	25%	-$23.69
MBS 40300 copayment	$995.26	-0.14		-$139.34
Anaesthesia 2h41min to 2h51min (MBS 23113)	$182.35	-1		-$182.35
MBS 23113 copayment	$292.35	-1		-$292.35
Anaesthesia 3h01min to 3h01min (MBS 23115)	$210.40	1		$210.40
MBS 23115 copayment	$330.46	1		$330.46
Assistance (MBS 51303)	20%	0.93		$67.44
MBS 51303 copayment	No impact			$0.00
Total consumables				$13,473.78
Total MBS fees				$2,504.46
Total patient out-of-pocket				$4,386.81
Total other hospital costs				$6,464.42
Total				$26,829.47
Total minus consumables				$13,355.69

MBS: Medicare Benefits Schedule May 2010; * 20% of fee plus 93% of procedures require assistance.

Table 61 Re-operation costs, hardware removal without replacement

	Unit cost	Units	Multiple operations adjustment	Total
Costs associated with procedure				
Pre operational				
Brief pre-anaesthesia consultation (MBS 17610)	$30.45	1		$30.45
MBS 17610 copayment	$43.73	1		$43.73
Operational				
Removal of device (MBS 47930)*	$186.90	1	100%	$186.90
MBS 47930copayment	$191.16	1		$191.16
Initiation of Anaesthesia (MBS 20630)	$112.20	1		$112.20
MBS 20630 copayment	$432.12	1		$432.12
Anaesthesia 1h01min to 1h05min (MBS 23051)	$70.15	1		$70.15
MBS 23051 copayment	$105.85	1		$105.85
Assistance (MBS 51300)	$61.20	0.81		$49.57
MBS 51300 copayment	$64.34	0.81		$52.12
Post operational				
Hospital stay	$1,261.55	1		$1,261.55
Total MBS fees				$449.27
Total patient out-of-pocket				$824.97
Total other hospital costs				$1,261.55
Total				$2,535.79

MBS: Medicare Benefits Schedule May 2010; * $61.20 * 81% of procedures require assistance (based on PLF).

References

Anderson PA & Rouleau JP, 2004. 'Intervertebral disc arthroplasty', *Spine*, 29 (23), 2779–2786.

Ann HS & Juarez KK, 2004. *Artificial Disc Replacement* [Internet]. Available from: www.spineuniverse.com/displayarticle.php/article1671.html [Accessed 21 January 2005].

Artificial disc replacement for lumbar and cervical degenerative disc disease- update: an evidence-based analysis, 2006. Toronto: Medical Advisory Secretariat, Ontario Ministry of Health and Long-Term Care (MAS), 6 (10), 105.

Auerbach JD, Jones KJ et al, 2009. 'Segmental contribution toward total lumbar range of motion in disc replacement and fusions: a comparison of operative and adjacent levels', *Spine (Phila Pa 1976)*, 34 (23), 2510-2517.

Aunoble S, Meyrat R et al, 2010. 'Hybrid construct for two levels disc disease in lumbar spine', *Eur Spine J*, 19 (2), 290-296.

Australian Institute of Health and Welfare, 2008. Australia's health 2008, Cat. no. AUS 99, Canberra: AIHW.

Berg S, 2009. 'Total disc replacement compared to lumbar fusion: A randomised controlled trial with 2-year follow-up', *European Spine Journal*, 18 (10), 2009.

Berg S, Fritzell P, Tropp H, 2009. 'Sex life and sexual function in men and women before and after total disc replacement compared with posterior lumbar fusion', *Spine J*, 9 (12), 987-994.

Bertagnoli R, Yue JJ et al, 2005a. 'The treatment of disabling multilevel lumbar discogenic low back pain with total disc arthroplasty utilizing the ProDisc prosthesis: a prospective study with 2-year minimum follow-up', *Spine (Phila Pa 1976)*, 30 (19), 2192-2199.

Bertagnoli R, Yue JJ et al, 2005b. 'The treatment of disabling single-level lumbar discogenic low back pain with total disc arthroplasty utilizing the Prodisc prosthesis: a prospective study with 2-year minimum follow-up', *Spine (Phila Pa 1976)*, 30 (19), 2230-2236.

Bertagnoli R, Yue,JJ et al, 2006a. 'Lumbar total disc arthroplasty in patients older than 60 years of age: A prospective study of the ProDisc prosthesis with 2-year minimum follow-up period', *Journal of Neurosurgery: Spine*, 4 (2), 85-90.

Bertagnoli R, Yue JJ et al, 2006b. 'Lumbar total disc arthroplasty utilizing the prodisc prosthesis in smokers versus nonsmokers: A prospective study with 2-year minimum follow-up', *Spine*, 31 (9), 992-997.

Bertagnoli R, Yue JJ et al, 2006c. 'Treatment of symptomatic adjacent-segment degeneration after lumbar fusion with total disc arthroplasty by using the prodisc prosthesis: a prospective study with 2-year minimum follow up', *J Neurosurg Spine*, 4 (2), 91-97.

Blue Cross Blue Shield Association. 'Artificial lumbar disc replacement', 2007. Chicago IL: Blue Cross Blue Shield Association (BCBS), 24.

Blumenthal S, Regan JJ, 2005. 'A prospective, randomized, multicenter Food and Drug Administration Investigational Device Exemptions study of lumbar total disc replacement with the CHARITE[trademark] artificial disc versus lumbar fusion - Part I: Evaluation of clinical outcomes', *Spine*, 30 (14), 15.

Cakir B, Richter M et al, 2006. 'Dynamic stabilization of the lumbar spine', *Orthopedics*, 29 (8), 716-722.

California Technology Assessment Forum, 2007. 'Artificial Disc Replacement for Degenerative Disc Disease of the Lumbar Spine', February.

CancerWeb, 1997. *Online Medical Dictionary* [Internet]. Department of Medical Oncology, Available from: http://cancerweb.ncl.ac.uk/cgi-bin/omd?action=Home&query= [Accessed 19 May 2005].

Chou R, Baisden J et al, 2009. 'Surgery for low back pain: a review of the evidence for an American Pain Society Clinical Practice Guideline', *Spine (Phila Pa 1976)*, 34 (10), 1094-1109.

Chung SS, 2006. 'Lumbar total disc replacement using ProDisc II: A prospective study with a 2-year minimum follow-up', *Journal of Spinal Disorders and Techniques*, 19 (6), 411-415.

David T, 2007. 'Long-term results of one-level lumbar arthroplasty: Minimum 10-year follow-up of the CHARITE artificial disc in 106 patients', *Spine*, 32 (6), 661-666.

Di Silvestre M, Bakaloudis G et al, 2009. 'Two-level total lumbar disc replacement', *Eur Spine J*, 18 Suppl 1, 64-70.

Eidelson SG, 1999, *Cervical Spine Anatomy* [Internet]. Available from: www.spineuniverse.com/displayarticle.php/article1021.html [Accessed 21 January 2005].

Freeman BJ & Davenport J, 2006. 'Total disc replacement in the lumbar spine: a systematic review of the literature', *Eur Spine J*, 15 Suppl 3, S439-S447.

Geisler FH, Guyer RD et al, 2008a. 'Effect of previous surgery on clinical outcome following 1-level lumbar arthroplasty', *J Neurosurg Spine*, 8 (2), 108-114.

Geisler FH, Guyer RD et al, 2008b. 'Patient selection for lumbar arthroplasty and arthrodesis: The effect of revision surgery in a controlled, multicenter, randomized study', *Journal of Neurosurgery: Spine*, 8 (1), 13-16.

Geisler FH, 2009. 'Prospective, Randomized, Multicenter FDA IDE Study of CHARITE Artificial Disc versus Lumbar Fusion: Effect at 5-year Follow-up of Prior Surgery and Prior Discectomy on Clinical Outcomes Following Lumbar Arthroplasty', *SAS Journal*, 3 (1), 16-24.

Gioia G, 2007. 'The Charite III Artificial Disc lumbar disc prosthesis: Assessment of medium-term results', *Journal of Orthopaedics and Traumatology*, 8 (3), 134-139.

Guyer RD, Geisler FH et al, 2008. 'Effect of age on clinical and radiographic outcomes and adverse events following 1-level lumbar arthroplasty after a minimum 2-year follow-up', *J Neurosurg Spine*, 8 (2), 101-107.

Guyer RD, 2009. 'Prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion: Five-year follow-up', *Spine Journal*, 9 (5), 374-386.

Hannibal M, Thomas DJ et al, 2007. 'ProDisc-L total disc replacement: a comparison of 1-level versus 2-level arthroplasty patients with a minimum 2-year follow-up', *Spine (Phila Pa 1976)*, 32 (21), 2322-2326.

Harrop JS, Youssef JA et al, 2008. 'Lumbar adjacent segment degeneration and disease after arthrodesis and total disc arthroplasty', *Spine (Phila Pa 1976)*, 33 (15), 1701-1707.

Huang RC, 2006. 'Range of motion and adjacent level degeneration after lumbar total disc replacement', *Spine Journal*, 6 (3), 242-247.

Kasper DL, Braunwald E et al, 2005, *Harrison's Principles of Internal Medicine* [Internet]. Available from: http://www.accessmedicine.com/resourceTOC.aspx?resourceID=4 [Accessed 19 May 2005].

Kim DH, Ryu KS et al, 2007. 'Factors influencing segmental range of motion after lumbar total disc replacement using the ProDisc II prosthesis', *J Neurosurg Spine*, 7 (2), 131-138.

Le Huec JC, 2005. 'Clinical results of Maverick lumbar total disc replacement: Two-year prospective follow-up', *Orthopedic Clinics of North America*, 36 (3 SPEC. ISS.), 315-322.

Lemaire JP, Carrier H et al, 2005. 'Clinical and radiological outcomes with the Charite artificial disc: a 10-year minimum follow-up', *J Spinal Disord Tech*, 18 (4), 353-359.

Marshman LAG, 2008. 'Subsidence and malplacement with the Oblique Maverick Lumbar Disc Arthroplasty: technical note', *Spine Journal*, 8 (4), 650-655.

McAfee PC, 2005. 'A prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITEtrade; artificial disc versus lumbar fusion - Part II: Evaluation of radiographic outcomes and correlation of surgical technique accuracy with clinical outcomes', *Spine*, 30 (14), 15.

McAfee PC, Geisler FH et al, 2006. 'Revisability of the CHARITE artificial disc replacement: analysis of 688 patients enrolled in the U.S. IDE study of the CHARITE Artificial Disc', *Spine (Phila Pa 1976)*, 31 (11), 1217-1226.

Mirovsky Y, Shalmon E et al, 2008. 'Lumbar disk replacement with the ProDisc prosthesis', *Orthopedics*, 31 (2), 133.

Neal CJ, Rosner MK, Kuklo TR, 2005. 'Magnetic resonance imaging evaluation of adjacent segments after disc arthroplasty', *J Neurosurg Spine*, 3 (5), 342-347.

NHMRC, 2009. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines, National Health and Medical Research Council, Canberra.

NHMRC, 2000. How to use the evidence: assessment and application of scientific evidence, National Health and Medical Research Council, Canberra.

Ogon M, Howanietz N et al, 2007. 'Implantation of the ProDisc intervertebral disk prosthesis for the lumbar spine', *Oper Orthop Traumatol*, 19 (2), 209-230.

Park CK, Ryu KS, Jee WH, 2008. 'Degenerative changes of discs and facet joints in lumbar total disc replacement using ProDisc II: minimum two-year follow-up', *Spine (Phila Pa 1976)*, 33 (16), 1755-1761.

Patel VV, 2006. 'Computed tomography assessment of the accuracy of in vivo placement of artificial discs in the lumbar spine including radiographic and clinical consequences', *Spine*, 31 (8), 948-953.

Pimenta L, 2010. 'Clinical performance of an elastomeric lumbar disc replacement: Minimum 12 months follow-up', *SAS Journal* , 4 (1), 16-25.

Putzier M, Funk JF et al, 2006. 'Charite total disc replacement--clinical and radiographical results after an average follow-up of 17 years', *Eur Spine J*, 15 (2), 183-195.

Regan JJ & Maxwell JH, 2006. 'Evaluation of surgical volume and the early experience with lumbar total disc replacement as part of the investigational device exemption study of the Charite Artificial Disc', *Spine*, 31 (19), 2270-2276.

Ross R, 2007. 'Survival and clinical outcome of SB Charite III disc replacement for back pain', *Journal of Bone and Joint Surgery - Series B*, 89 (6), 785-789.

Sasso RC, Foulk DM, Hahn M, 2008. 'Prospective, randomized trial of metal-on-metal artificial lumbar disc replacement: initial results for treatment of discogenic pain', *Spine (Phila Pa 1976)*, 33 (2), 123-131.

Schluessmann E, Diel P et al, 2009. 'SWISSspine: a nationwide registry for health technology assessment of lumbar disc prostheses', *Eur Spine J*, 18 (6), 851-861.

Schroven I & Dorofey D, 2006. 'Intervertebral prosthesis versus anterior lumbar interbody fusion: one-year results of a prospective non-randomised study', *Acta Orthop Belg*, 72 (1), 83-86.

Shim CS, 2007. 'CHARITI versus ProDisc: A comparative study of a minimum 3-year follow-up', *Spine*, 32 (9), 1012-1018.

Siepe CJ, 2006. 'Clinical results of total lumbar disc replacement with ProDisc II: Three-year results for different indications', *Spine*, 31 (17), 1923-1932.

Siepe CJ, Wiechert CJ et al, 2007a. 'Total lumbar disc replacement in athletes: Clinical results, return to sport and athletic performance', *European Spine Journal*, 16 (7), 1001-1013.

Siepe CJ, Mayer HM et al, 2007b. 'Total lumbar disc replacement: different results for different levels', *Spine (Phila Pa 1976)*, 32 (7), 782-790.

Sinigaglia R, 2009. 'Comparison of single-level L4-L5 versus L5-S1 lumbar disc replacement: Results and prognostic factors', *European Spine Journal*, 18 (SUPPL. 1), S52-S63.

Spine-health.com, 2005. *Spine anatomy and back pain* [Internet]. Available from: www.spine-health.com/print/topics/anat/a001.html [Accessed 17 February 2005].

Subach BR, 2004, *Spinal Structure and Body Mechanics* [Internet]. Available from: www.spineuniverse.com/displayarticle.php/article2683.html [Accessed 21 January 2005].

Tropiano P & Marnay T, 2005. 'Lumbar total disc replacement: Seven to eleven-year follow-up', *Journal of Bone and Joint Surgery - Series A*, 87 (3), 490-496.

Trouillier H, Kern P et al, 2006. 'A prospective morphological study of facet joint integrity following intervertebral disc replacement with the CHARITE Artificial Disc', *Eur Spine J*, 15 (2), 174-182.

Vlayen J, Camberlin C et al, 2006. 'Rapid assessment of emerging spine technologies: intervertebral disc replacement and vertebro/balloon kyphoplasty', Belgian Federal Health Care Knowledge Centre (KCE), report 39.

Walker BF, Muller R, Grant WW, 2003. 'Low back pain in Australian adults: the economic burden', *Asia Pacific Journal of Public Health*, 15 (2), 79-87.

Warachit P, 2008. 'Results of Charite artificial lumbar disc replacement: experience in 43 Thais', *J Med Assoc Thai*, 91 (8), 1212-1217.

Washington Health Technology Assessment (WHTA), 2008. Washington State Health Care Authority. Health Technology Assessment. HTA Final Report - Artificial Discs Replacement (ADR). September 19.

Wenger M & Markwalder TM, 2005. 'A novel surgical treatment of lumbar disc herniation in patients with long-standing degenerative disc disease', *J Neurosurg Spine*, 2 (5), 515-20.

Yajun W, Yue Z et al, 2010. 'A meta-analysis of artificial total disc replacement versus fusion for lumbar degenerative disc disease', *Eur Spine J*, Epub 4 April.

Zeh A, Becker C et al, 2009. 'Time-dependent release of cobalt and chromium ions into the serum following implantation of the metal-on-metal Maverick type artificial lumbar disc (Medtronic Sofamor Danek)', *Arch Orthop Trauma Surg*, 129 (6), 741-746.

Zigler J, Delamarter R et al, 2007. 'Results of the prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease', *Spine (Phila Pa 1976)*, 32 (11), 1155-1162.

Shortened forms

AIDR	artificial intervertebral disc replacement
ALIF	anterior lumbar interbody fusion
ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures - Surgical
BMP	bone morphogenetic proteins
CHERE	Centre for Health Economics Research and Evaluation
DDD	degenerative disc disease
EMSN	Extended Medicare Safety Net
ICER	incremental cost-effectiveness ratio
MASO	Medical Advisory Secretariat Ontario
MBS	Medicare Benefits Schedule
MSAC	Medical Services Advisory Committee
NHMRC	National Health and Medical Research Council
ODI	Oswestry Disability Index
PCS	Physical Component Scores
PLIF	posterior lumbar interbody fusion
QALY	quality-adjusted life year
RCT	randomised controlled trial
TLIF	transforaminal lumbar interbody fusion
WHTA	Washington Health Technology Assessment