Artificial intervertebral disc replacement

(Total disc arthroplasty)

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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 recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.***

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The procedure

Artificial intervertebral disc replacement (AIDR), also known as total disc arthroplasty, involves removal of the entire endogenous, damaged intervertebral disc and the implantation of a prosthetic device in its place. Implantation of the device in the lumbar region involves a transperitoneal or retroperitoneal approach. As the approach used for implantation of the device in the lumbar region differs from that of spinal fusion (which is usually performed posteriorly), spinal surgeons may require the assistance of an "access surgeon" to minimise rare but serious approach-related complications. Implantation in the cervical region is performed anteriorly. The anterior approach is also used for spinal fusion of the cervical spine and all spinal surgeons would be familiar with the technique. The endogenous vertebral endplates and surrounding spinal ligaments are preserved in both the cervical and lumbar spine and these help to maintain the stability of the implant. Single or multiple discs can be replaced during the same surgical procedure. All AIDR surgery is performed under general anaesthetic.

Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) is a key element of a measure taken by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Australian Government 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.

A rigorous assessment of the available evidence is thus the basis of decision making when funding is sought under Medicare. A team from Monash University was engaged to conduct a systematic review of literature on AIDR. An Advisory Panel with expertise in this area then evaluated the evidence and provided advice to MSAC.

MSAC's assessment of artificial intervertebral disc replacement

This assessment was undertaken to provide the broadest possible advice regarding the safety, effectiveness and cost-effectiveness of cervical and lumbar AIDR. Evidence was sought for the effectiveness of the procedure in adults with cervical radiculopathy and/or myelopathy with changes secondary to degeneration of the disc or disc prolapse, and in adults with significant lumbar axial back pain with changes secondary to degeneration of the disc or disc prolapse with or without radiculopathy and myelopathy or due to major disc prolapse, who are assessed as refractory to other conservative, non-surgical treatments.

Clinical need

There is considerable uncertainty regarding the prevalence and incidence of:

- cervical radiculopathy and/or myelopathy with changes secondary to degeneration of the disc or disc prolapse; and/or
- axial lumbar back pain with changes secondary to degeneration of the disc or disc prolapse.

Therefore, there is uncertainty in estimates of 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) and The National Health Survey of Australia conducted in 1995. The definition of back problems used in this survey included cases in which episodes of back pain resulted in at least moderate pain, and moderate or greater limitations in walking and/or undertaking usual activities (Mathers 1999).

Data from the AIHW (based on self-reporting), estimated that back problems affected 5.4 per cent of the total population of Australia in 1998. The prevalence of chronic back pain in the Australian setting has been estimated from another source to be one in five (20%). The National Health Survey of Australia conducted in 1995 estimated the burden of disease arising from back problems in Australia as 2,065 years lived with disability (YLD) for males and 1,903 YLD for females. Years lived with disability is a measure of the number of healthy life years lost as a result of developing a non-fatal disease.

The incidence of back problems in Australia was estimated to be 65,938 per 100,000 from the 1995 National Health Survey. For comparison, the burden of disease arising from osteoarthritis was estimated at 23,603 YLD for males and 34,764 YLD for females with an incidence of 465 per 100,000 (Mathers 1999). The relatively low YLD and relatively high incidence of back problems suggest that most cases are acute and the duration of symptoms is minimal. In contrast, the relatively high YLD and relatively low incidence of osteoarthritis indicate that individuals with osteoarthritis experience a significant burden of disease from this chronic condition. There is uncertainty about the prevalence of cervical or lumbar back pain in the Australian setting. A study in Switzerland found that approximately 14 per cent of the population had chronic back pain (defined as pain for greater than six months). Data from a US study indicated that lumbar back pain affects one in three individuals at some time.

Further estimates have been derived from the 1995 National Health Survey, where 2.2 per cent of the Australian population self-reported disorders of the intervertebral disc, approximately half of whom may have had degenerative disc disease (DDD). However, there is a degree of uncertainty in these data since it has been shown that approximately one-third of women have been diagnosed with disc degeneration pathology but have no symptoms of pain, demonstrating the lack of correlation between the anatomical diagnosis and the experience of back pain. Therefore, there is still a large degree of uncertainty regarding the prevalence and incidence of DDD.

The true incidence and prevalence in the Australian setting of cervical and lumbar radiculopathy and/or myelopathy and lumbar disc prolapse are unknown.

An alternative approach to estimate the number of individuals who may be eligible to undergo AIDR is to observe the number of individuals currently undergoing spinal fusion. All MBS item numbers relating to spinal fusion map to Diagnosis Related Groups (DRGs) I09A and I09B. The number of DRGs for the 2002/2003 financial year was 4,992 (combining public and private hospital contributions). The numbers of individuals who may be eligible for cervical or lumbar AIDR is unknown.

Safety

Cervical AIDR

The safety of cervical AIDR was assessed from one randomised controlled trial (RCT) comparing cervical AIDR and cervical spinal fusion, 11 case series and one health technology assessment (HTA) report. The trial compared cervical AIDR using the Prestige cervical disc to anterior cervical fusion using iliac crest autograft, for the treatment of single level cervical symptomatic DDD. No statistically significant differences in the total number of adverse events experienced by participants allocated to cervical AIDR and those randomised to cervical spinal fusion were observed (relative risk [RR]=0.93, 95% confidence interval [CI]: 0.63, 1.36). The long-term (>5 years) comparative safety of cervical AIDR and cervical spinal fusion is unknown.

Safety results for 578 participants who underwent cervical AIDR (701 discs) were reported in 11 case series. Reported adverse events included new or worsening pain, haematomas, temporary dysphonia or other transient vocal cord problems, revision decompression surgery, migration or suspected migration of the prosthesis, adjacent level surgery and removal of the prosthesis with or without subsequent cervical spinal fusion. Each of these adverse events occurred at a rate of less than 14 per cent in each of the individual case series, with the exception of one study in which all participants were reported to experience transient dysphagia. The longest period of follow-up of in the case series was 65 months. Similar adverse events and rates of adverse events were reported in the identified HTA report.

Lumbar AIDR

Two multicentre RCTs comparing lumbar AIDR and lumbar spinal fusion have been conducted. One trial enrolled participants with single level disease at L4-L5 or L5-S1. Participants in the second trial had DDD at no more than two adjacent vertebral levels between L3 and S1. No significant differences in the rates of any of the adverse events were observed between the 205 participants treated by lumbar AIDR with the SB Charité™ disc or those of the 99 participants treated with the BAK Interbody Fusion Device (BAK Cage) (RR=0.98; 95% CI: 0.86, 1.11). Infection rates in this trial were reported to be 12.2 and 6.1 per cent for participants randomised to lumbar AIDR and lumbar fusion, respectively. Severe or life-threatening infections were reported in 1.5 and 2.0 per cent of participants randomised to lumbar AIDR and lumbar fusion, respectively. No statistically significant differences were observed in the rates of infection between the treatment groups.

Another publication reporting adverse events occurring in an RCT comparing lumbar AIDR with ProDisc II (55 participants) and circumferential lumbar spinal fusion (23 participants) reported disc-related problems, minor intraoperative complications, episodes of pain and mild infections, which cleared with minimal intervention.

The long-term (>5 years) comparative safety of lumbar AIDR and lumbar spinal fusion is unknown.

Adverse event data from the 15 case series (553 participants who underwent lumbar AIDR, 706 discs) reported that revision surgery was required in a total of 30 participants from nine of the 15 studies. For studies in which revision surgery was reported, the proportion of participants undergoing the additional procedure ranged from 2.9 to 28.6 per cent. The artificial disc was replaced in four participants. In the remaining participants, lumbar spinal fusion was required. The artificial disc was removed before fusion in five cases. Revision was required as a result of disc migration, persistent symptoms of pain or bone complications such as vertebral fractures and periprosthetic ossifications. Some cases of pain were managed with medication and analgesics. The longest period of follow-up of these case series was 157 months. Similar adverse events and adverse event rates were reported in the identified HTA reports and systematic reviews.

Effectiveness

Cervical AIDR versus cervical spinal fusion

Evidence for the effectiveness of cervical AIDR versus cervical spinal fusion was derived from one RCT. The trial was designed to demonstrate equivalence between cervical AIDR and spinal fusion ie, that cervical AIDR is no worse than cervical spinal fusion.

At the level of the treated disc, participants undergoing cervical AIDR maintained the same range of motion (ROM) of 5.9° at the 12-month follow-up compared with baseline (5.9°), however participants undergoing cervical spinal fusion showed no significant preservation of motion at the 12-month follow-up (1.1°, which is considered to be no movement). At the adjacent level, there were no significant differences between the treatment groups in terms of ROM. Similarly, there were no significant differences between the treatment groups at 24 months follow-up for neck disability index (NDI), neck pain, arm pain and neurological status.

The trial concluded that the Prestige II disc is a viable alternative to cervical spinal fusion. However, the trial enrolled a limited number of participants, did not report full data and measures of variance at all time points and included relatively short-term follow-up. In addition, participants, investigators and outcome assessors were not blinded to treatment, which, when combined with the relatively subjective nature of many of the outcomes assessed, may have led to bias in the results obtained.

Lumbar AIDR versus lumbar spinal fusion

Evidence for the effectiveness of lumbar AIDR versus lumbar spinal fusion was derived from two RCTs. One trial was designed to demonstrate equivalence between lumbar AIDR and lumbar spinal fusion ie, that lumbar AIDR is no worse than lumbar spinal fusion. Data from the trials were reported inconsistently and the variance around the mean values for certain outcomes was not reported, precluding any meta-analyses.

The trial comparing lumbar AIDR using the Charité™ disc and lumbar spinal fusion reported that a statistically significantly greater number of participants undergoing lumbar AIDR achieved overall success compared with participants undergoing lumbar spinal fusion at the 24-month follow-up. Overall success was defined as at leat a 25 per

cent improvement in Oswestry disability index (ODI) scores, no device failures, no major complications and no neurological deterioration. Participants undergoing lumbar AIDR also showed statistically significantly reduced ODI scores at the six week, three and six month, but not at the 12- and 24-month follow-up compared with those undergoing lumbar spinal fusion in this trial.

The publications that reported limited results from the ProDisc II trial noted a statistically significantly reduced ODI score at the three-month follow-up in participants undergoing lumbar AIDR compared with those undergoing lumbar spinal fusion, but no differences in ODI scores were observed between treatment groups at the six-week or six-month follow-up. One publication reported that participants undergoing lumbar AIDR showed a statistically significantly greater ROM at six-months follow-up when the treated level was L4-L5, however no differences were observed between the treatment groups when the treated level was L5-S1. The other publication reported that participants undergoing lumbar AIDR had statistically significantly greater motion for forward, left lateral and right lateral bending at the six-month follow-up than those undergoing lumbar spinal fusion.

Data reported from the trials included relatively short-term follow-up of no more than 24 months. In addition, participants and investigators were not blinded to treatment, which, when combined with the relatively subjective nature of many of the outcomes assessed, may have led to bias in the results obtained. In addition, the results from the ProDisc II trial should be interpreted with caution as the two publications identified reported results from only two of 19 centres involved in the multicentre trial. This may have led to reporting bias if only centres with large populations or those with positive results reported their data.

Cost-effectiveness

On the assumption of equivalent short-term health outcomes, the economic evaluation considered only the comparative cost of AIDR and spinal fusion. Direct costs included in the cost comparison were health care costs, consisting of the costs of hospital care, prostheses and medical fees for procedures performed in private hospitals. These costs were determined for lumbar and cervical procedures separately and weighted by the proportion of procedures performed in public and private hospitals, the number of spinal levels involved and the level of usage of different fusion methods. The base case analysis used prostheses cost information provided by the Applicant while the sensitivity analysis used prostheses cost information provided by other industry sources.

The incremental cost of lumbar AIDR was estimated to be $1,054 per separation when all methods of fusion were included. The incremental cost was sensitive to the cost of prostheses and could increase to $7,570 if cost information provided by other industry sources was the true cost. However, when only interbody fusion was considered, lumbar AIDR was projected to result in either a cost saving of $3,458 (base case) or an extra cost of $262 (sensitivity analysis) per separation.

Cervical AIDR was found to be more costly than cervical spinal fusion, irrespective of the fusion method used. The incremental cost of $9,438 (range $8,413 to $13,346) per separation was almost entirely due to the higher cost of the prostheses.

The results presented here are based on the best estimates available and are indicative of the likely costs and benefits of AIDR compared to spinal fusion. The results should be interpreted with caution in view of the lack of long-term clinical data and the exclusion of downstream costs of future associated procedures or treatment for adverse events.

Recommendations

On the basis of currently available evidence regarding safety, effectiveness and cost effectiveness, MSAC recommends 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 conservative therapy.

MSAC will review this recommendation in three years.

In the absence of adequate evidence of effectiveness, MSAC recommends that public funding for AIDR in the cervical spine should not be supported.

- The Minister for Health and Ageing accepted this recommendation on 6 June 2006. -

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of artificial intervertebral disc replacement (AIDR), also known as total disc arthroplasty, which is a therapeutic technology to replace intervertebral discs in the spine.

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 AIDR in the cervical and lumbar regions of the spine for individuals who have failed non-operative treatment and have the following morbidities:

For cervical AIDR,

- radiculopathy and/or myelopathy with changes secondary to degeneration of the disc or disc prolapse.

For lumbar AIDR,

- significant axial back pain with changes secondary to degeneration of the disc or disc prolapse with or without radiculopathy or myelopathy; and/or
- significant axial back pain due to a major disc prolapse.

Background

Artificial intervertebral disc replacement

Intervertebral discs reside between the vertebral bones and are composed of water, collagen and proteoglycans (Ann & Juarez 2004). The function of the intervertebral disc is to promote ventral movement through the combined effort of several discs and also to act as a shock absorber to prevent compression of the spine (Bridwell 2004). Artificial intervertebral discs have been developed to replace endogenous intervertebral discs and act as a functional prosthetic replacement similar to hip or knee prostheses (National Institute for Clinical Excellence [NICE] 2003). AIDR is performed on the cervical or lumbar spine.

Anatomy of the spine

The main function of the spine is to protect and support the nerve fibres which make up the spinal cord. The spine is composed of joints, ligaments, muscles, bones and intervertebral discs. The joints are composed of two opposing bone ends that are surrounded by cartilage and have a vital role in providing stability when an individual moves. Ligaments provide postural support for the muscles and are essential for the co-ordination and implementation of movement. The bones (vertebrae) are essential for providing the anterior structure of the spine (Ann & Juarez 2004, Subach 2004).

The spine is subdivided into 31 segments according to their location. These segments are further organized into the cervical, thoracic, lumbar and sacral regions, as shown in Figure 1. The cervical region is located in the highest region of the spine and consists of the C1–C7 segments. The cervical region is important for the processing of information in the upper region of the body, that is, the back of the head, neck, shoulders, arms and hands. The lumbar region consists of the lower region of the spine (L1-L5) and is essential in carrying the weight of the torso (Spine-health.com 2005, Eidelson 1999).

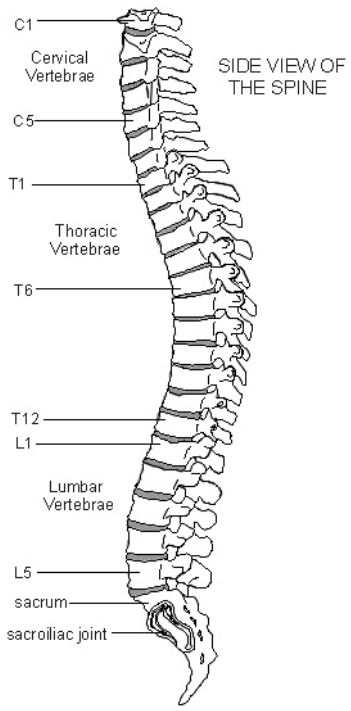

Figure 1 Spine anatomy
(Patient UK 2005)

The intervertebral discs lie between the vertebral bones and are composed of water, collagen and proteoglycans. The intervertebral disc is subdivided into the annulus fibrosus, which is predominantly composed of collagen fibres, and the nucleus pulposus, which has a larger proportion of water and proteoglycans than the annulus fibrosus and consists of a jelly-like substance that assists in preventing compression of the spine. The annulus fibrosus is situated in the outer region of the intervertebral disc and envelops the nucleus pulposus. The annulus fibrosus comes into close contact with the nociceptors (pain receptors).

Artificial intervertebral discs

AIDR is designed to theoretically simulate the decompressive and supportive properties of the natural intervertebral discs by restoring the natural distance between the two vertebrae, thus maintaining or restoring motion and relieving pain (Huang & Sandhu 2004). There are two types of artificial intervertebral discs; one type replaces the nucleus pulposus, and the other replaces the entire intervertebral disc (Anderson & Rouleau 2004).

Prosthetic discs for total disc arthroplasty are 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), see Figure 2. The overall design and material composition however can vary between commercially available prosthetic discs. Current prosthetic discs use materials used for many years in other well-established medical devices eg: hip and knee replacements (Davies MA 2005, personal communication, 19 June 2005).

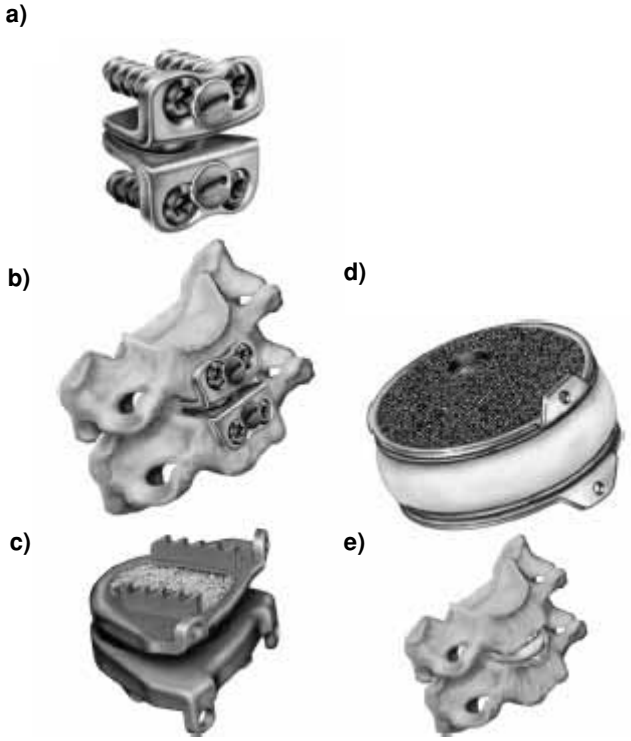

Figure 2 Types of cervical discs

(Mummaneni and Haid 2004)

a) Metal-on-metal designs – disc alone; b) Metal-on-metal designs implanted in the spine; c) Metal-on-metal designs – disc alone; d) Metal-on-polymer designs – disc alone; e) Metal-on-polymer design implanted in the spine.

The procedure

All surgery is performed under general anaesthetic. Patient positioning and intraoperative real time fluoroscopy depending on the device used, is critical to the exposure and successful insertion of the arthroplasty device. Whilst an anterior exposure is required in all procedures, a key difference between cervical and lumbar disc arthroplasty relates to the surgical approach. The approach and exposure for cervical disc arthroplasty is identical to that used for anterior fusion procedures and one that is familiar to all spinal surgeons. For lumbar disc arthroplasty a transperitoneal or retroperitoneal approach is required. Because most lumbar fusion procedures are performed posteriorly, most spinal surgeons require the assistance of an "access surgeon" to minimise rare but serious approach related complications. Important structures that need to be mobilised include the aorta, iliac vessels, sympathetic plexus, and intraperitoneal structures including 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).

Once the anterior lumbar or cervical spine is exposed then disc arthroplasty proceeds in much the same way. A complete discectomy is required prior to removing and shaping variable amounts of vertebral endplate. In the cervical spine in particular the most important step occurs next, a neural decompression. 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 to achieve this result. 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). Insertion and positioning of the endplate are shown in Figures 3 to 5.

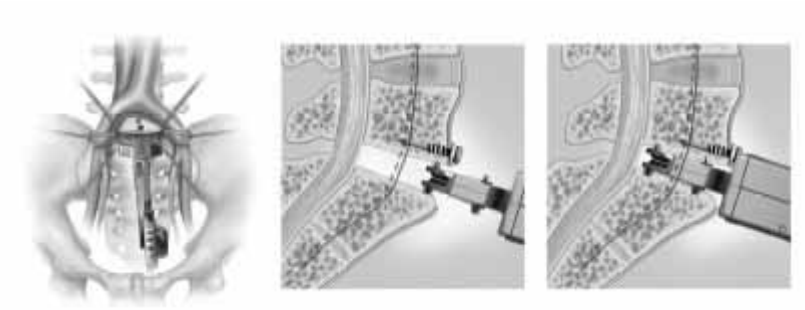

Figure 3 Prothesis endplate insertion

(Geisler 2005)

The endplates are loaded into the spreading and insertion forceps and lined up to a midline marker. The endplates are inserted into the disc space until proper placement is verified by live fluoroscopy.

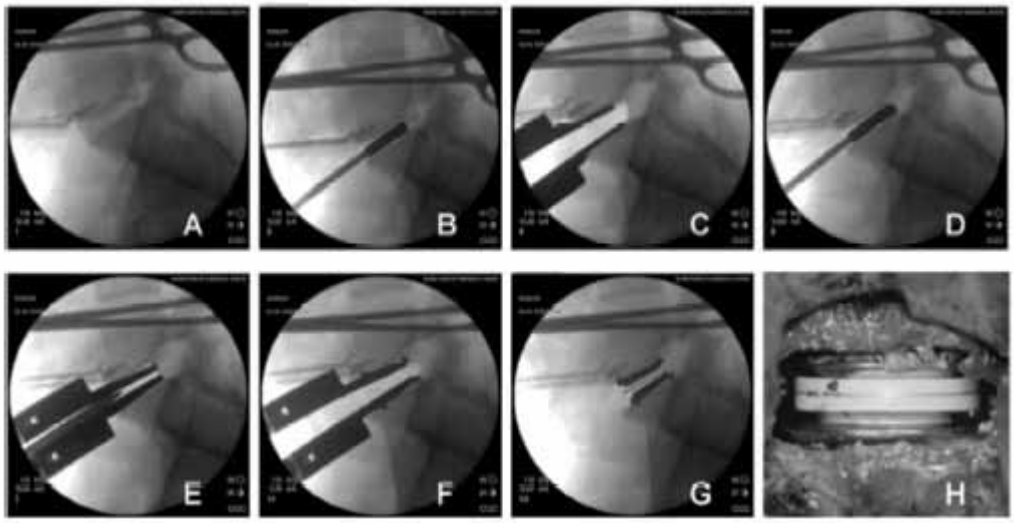

Figure 4 Final positioning of the prothesis

(Geisler 2005)

A. Initial lateral fluoroscopy; B. Following initial discectomy without bony resection; C. Disc space is distracted after the remaining disc is removed with a chisel; D. Trial spacer inserted into the disc space; E. 5˚ endplate trials with partially distracted disc space to aid in selecting endplate angles; F. Endplate angles in final position and distracted; G. Final artificial disc placement shown in lateral fluoroscopy; H. Final artificial disc placement shown in photographic views.

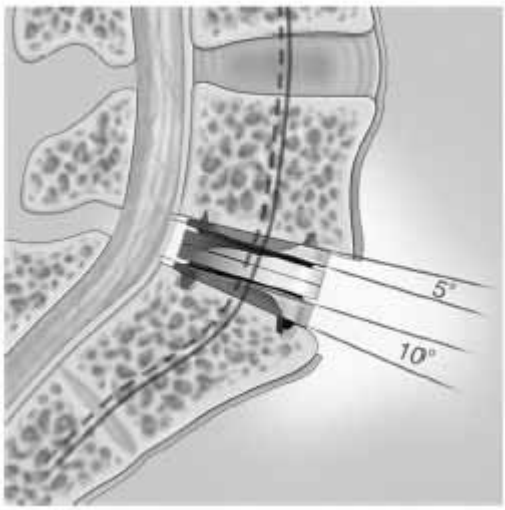

Figure 5 Final positioning of the prosthesis
(Geisler 2005)

Intended purpose

The primary indications for AIDR considered in this review include individuals who have failed non-operative treatment (eg muscle strengthening, weight control, aerobic training, normal activities, the passage of time and analgesic medications including anti-inflammatory medications and epidural) with the following morbidities:

Cervical region

- radiculopathy and/or myelopathy with changes secondary to degeneration of the disc or disc prolapse.

Lumbar region

- significant axial back pain with changes secondary to degeneration of the disc or disc prolapse with or without radiculopathy; or
- significant axial back pain due to major disc prolapse.

Myelopathy refers to compression of the spinal cord resulting in neurological deficit, for example a decrease in an individual's motor and sensory abilities.

The term radiculopathy is defined as compression of a radicular nerve (nerve root) from a prolapsed (displaced) disc that may cause a very sharp pain that radiates from the spine to the limb (ie, the neck, arm, lower back or leg). A prolapsed disc occurs when the disc is displaced, herniated or bulging from its normal position within the bone column. The disc may place pressure on the nerve root and cause symptoms such as radiating pain, numbness, tingling and weakness (CancerWeb 1997, Kasper et al 2005).

Axial back pain represents the most common type of low back pain and is characterised by the pain worsening with activity or change in position and relief by rest (Spine-health.com 2005).

A list of indications and contraindications suggested by the manufacturers for cervical and lumbar AIDR is presented in Appendix C.

Clinical need/burden of disease

There is considerable uncertainty regarding the prevalence and incidence of:

- cervical radiculopathy and/or myelopathy with changes secondary to degeneration of the disc or disc prolapse;
- axial lumbar back pain with changes secondary to degeneration of the disc or disc prolapse;
- axial lumbar back pain due to disc prolapse.

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) and The National Health Survey of Australia conducted in 1995. The definition of back problems used in this survey included cases where episodes of back pain resulted in at least moderate pain, and moderate or greater limitations in walking and/or undertaking usual activities (Mathers 1999).

Self-reported data from the AIHW (2004) suggested that back problems affected 5.4 per cent of the total population of Australia in 1998, making it the most frequent musculoskeletal condition after arthritis.

Another measure of the burden of disease is years lived with disability or YLD. Years lived with disability is a measure of the number of healthy life years lost as a result of developing a non-fatal disease that are calculated by multiplying the incidence of the condition by the average duration by an explicit disability weight (Victorian Department of Human Services 2004). The disability weight is derived from a Person Trade Off method in which a small group of health experts are asked to determine weights for a set of health conditions (Victorian Department of Human Services 2004).

The 1995 National Health Survey of the Australian population covered a range of health-related issues during a 12-month period from February 1995 to January 1996. The National Health Survey of Australia estimated the burden of disease arising from back problems in Australia to be 2,065 YLD for males and 1,903 YLD for females (Mathers 1999). The incidence of back problems in Australia was estimated to be 65,938 per 100,000 from the same survey (Mathers 1999). For comparison, the estimated burden of disease arising from osteoarthritis was 23,603 YLD for males and 34,764 YLD for females and the incidence of osteoarthritis was 465 per 100,000 (Mathers 1999). The relatively low values for YLD indicate that, whilst numerous individuals experience back problems, many cases resolve quickly and only a small proportion of individuals develop chronic back problems. In contrast, the relatively small incidence yet relatively high YLD of the chronic condition osteoarthritis indicate that individuals with osteoarthritis experience a significant burden of disease.

There is uncertainty in the prevalence of cervical or lumbar back pain in the Australian setting. A study in Switzerland found that approximately 14 per cent of the population had chronic (defined as pain for greater than six months) back pain (Dvorak et al 2003).

In the 1995 National Health Survey, 2.2 per cent of the population self-reported disorders of the intervertebral disc, including displacement and degeneration of the disc (Mathers 1999). There is some uncertainty in these estimates as they were derived from self-report and it is unknown how many individuals who reported disorders of the intervertebral disc had been properly diagnosed. Powell et al (1986) reported that approximately one-third of women who have been diagnosed with disc degeneration pathology have experienced no symptoms of pain. Therefore there is a degree of uncertainty regarding the prevalence and incidence of degenerative disc disease (DDD).

The true incidence and prevalence in the Australian setting of cervical and lumbar radiculopathy and/or myelopathy and lumbar disc prolapse are not known.

An alternative method for estimating the number of individuals who may be eligible to undergo AIDR is to consider the number of individuals who are currently eligible for, and undertaking, spinal fusion. Cervical and lumbar spinal fusion is currently performed for a number of indications, including some that would not be eligible for AIDR, for example, fracture, tumours or infection. All MBS item numbers for spinal fusion map to Diagnosis Related Groups (DRGs) I09A and I09B. Combining public and private hospital contributions, the total number of DRGs I09A and I09B for the 2002/2003 financial year was 4,992 (Australian Government Department of Health and Ageing [DoAH] 2004a).

AIDR is currently funded on an interim basis under MBS item numbers applicable for spinal fusion. Hence the 4,992 individuals reported to have undergone spinal fusion in the 2002/2003 financial year may also include some individuals who underwent AIDR rather than spinal fusion.

The numbers of individuals who may be eligible for cervical or lumbar AIDR is not known.

Existing procedures

Cervical spinal fusion is the current treatment option for cervical radiculopathy and/or myelopathy with secondary changes to the degeneration of the disc or disc prolapse.

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; and
- non-surgical treatments including:
  - muscle strengthening;
  - weight control;
  - aerobic training;

- normal activities;
- the passage of time; and
- analgesic medications including anti-inflammatory medications and epidural injections.

Comparator

Cervical

Cervical spinal fusion.

Lumbar

Lumbar spinal fusion.

Marketing status of the device/technology

Table 1 presents the TGA listing or registration numbers of cervical and lumbar artificial intervertebral discs available in Australia.

Table 1 TGA listing or registration numbers of cervical and lumbar artificial intervertebral discs

Disc	TGA listing or registration number
Cervical	
Bryan, manufactured and marketed by Medtronic Sofamor Danek	L 78918
Prestige, manufactured and marketed by Medtronic Sofamor Danek	L 78918
ProDisc C, manufactured by Spine Solutions/Synthes marketed by Taylor Bryant in Australia	R 99693
Lumbar	
SB Charité™ III, manufactured and marketed by DePuy Spine	L 96121
ProDisc, manufactured by Spine Solutions/Synthes and marketed by Taylor Bryant in Australia	R 99693

The following discs are not registered or listed by the TGA:

Cervical

PCM, manufactured by LINK

Lumbar

Maverick, manufactured and marketed by Medtronic Sofamor Danek

Current reimbursement arrangement

The AIDR procedure is currently reimbursed on an interim basis under MBS items 48684 and 48660 (Table 2).

Table 2 MBS Item numbers used for current reimbursement for AIDR

MBS Item Number	Description	Fee	Benefit
48684	SPINE, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any of one of items 48642–48675 applies – 1 or 2 levels (Anaes) (Assist)	$798.85	75% of half of the fee = $298.45
48660	SPINAL FUSION (anterior interbody) to cervical, thoracic or lumbar regions – 1 level (Anaes) (Assist)	$918.65	75% = $689.00

Source: Australian Government, DoHA (2004a)

Approach to assessment

Review of literature

The medical literature was searched via a number of electronic databases to identify relevant studies and reviews for the period covered by each of the databases (Table 3). The search was completed on 11 February 2005. Reference lists of the identified articles were also scanned to locate studies not identified in the electronic search.

Table 3 Electronic databases used in this review

Database	Period covered
Cochrane Library	2005, Issue 1
Medline	From 1966 to search date
Medline in-process & other non-indexed citations	11/02/2005
EMBASE	From 1968 to search date
Australasian Medical Index	From 1968 to search date
CINAHL	From 1982 to search date

In order to identify all of the relevant information published in journal articles, a comprehensive search of the literature was performed. The search strategy for OVID databases is presented at Appendix D. The search was modified for other databases and HTA and clinical trial register websites.

All of the terms that can be used to describe AIDR were identified. These included the trade names by which the products are known, text words and thesaurus terms of the databases. This set of words (the core terms) formed the basis of our searching (Appendix D).

Other search strategies

Relevant health technology assessment websites (listed in Appendix E) were searched to identify completed reviews or economic evaluations of AIDR. Relevant clinical trial register websites (listed in Appendix E) were also searched to identify clinical trials currently under way.

Selection Criteria

Criteria were developed *a priori* to determine eligibility of relevant studies assessing patient outcomes following placement of AIDR (Table 4), based on those agreed upon by MSAC and the Members of the Advisory Panel.

Table 4 Inclusion and exclusion criteria for health outcomes following AIDR

In patients with cervical radiculopathy and/or myelopathy with changes secondary to degeneration of the disc or disc prolapse, who have failed non-operative treatment, is AIDR safe, effective and cost-effective compared with spinal fusion? **In patients with significant lumbar axial back pain with changes secondary to degeneration of the disc or disc prolapse with or without radiculopathy or myelopathy, or due to major disc prolapse, who have failed non-operative treatment, is AIDR safe, effective and cost-effective compared with spinal fusion?**		
Characteristics	**Inclusion**	**Exclusion**
Participants	Cervical • Patients with radiculopathy and/or myelopathy with changes secondary to degeneration of the disc or disc prolapse who have failed non-operative treatment Lumbar • 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 • Patients with significant axial back pain due to major disc prolapse who have failed non-operative treatment	• Patients contraindicated to AIDR including those with spondylolisthesis > grade 1 • Patients treated in the thoracic region of the spine • Chronic pain conditions ie fibromyalgia • Patients who have not failed non-operative treatment • Back or neck pain not emanating from the disc
Intervention	AIDR	Disc nucleus replacement
Comparator	Cervical • Cervical spinal fusion Lumbar • Lumbar spinal fusion	• Discectomy • Microdiscectomy • Disc nucleus replacement
Outcomes	Efficacy • Reduction in pain (e.g. use of pain medication, rating scales) • Adjacent segment degeneration • Quality of life • Ability to perform activities of daily living (work and/or recreation) • 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	None defined

Table 4 (cont'd) Inclusion and exclusion criteria for health outcomes following AIDR

Characteristics	Inclusion	Exclusion
Study design	HTAs, systematic reviews, meta-analyses and RCTs were sought initially. If these were unavailable, other controlled trials, comparative studies and cohort studies may have been assessed. In the event that these too were unavailable, case series of consecutively selected patients may have been considered for inclusion	Narrative reviews, editorials, letters, articles identified as preliminary reports when results are published in later versions, articles in abstract form only, case reports and collections of case reports in which results are only presented by individual study patient and not summarised, case series enrolling <10 patients
Publication	All relevant articles, irrespective of language used	Abstracts

Assessment of validity

Critical appraisal refers to the process of evaluating the study design of included articles. The most rigorous study design for assessing the validity of therapeutic interventions is considered to be an RCT (Guyatt et al 1993, Sackett et al 2000).

Assessment of primary 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 5) 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 5 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[a]
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

[a] See Table 6

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. The designations of the levels of evidence are shown in Table 6.

Table 6 Designations of levels of evidence

Level of evidence[a]	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly-designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test/post-test

[a] Modified from NHMRC 1999

The NHS Centre for Reviews and Dissemination (2001) assembled a list of criteria used to evaluate the validity of evidence from various study designs. The relevant validity criteria used in this review for assessing the quality of evidence are listed in Table 7.

Table 7 Validity criteria according to study design

Study design[a]	Validity criteria
Randomised controlled trial	Randomised method; allocation concealment; blinding of patients, investigators and outcome assessors; proportion lost to follow-up; intention to treat analysis
Cohort	Prospective/ retrospective; comparable groups at inception; identification and adjustment for confounding factors; blind outcome assessment; sufficient duration of follow-up; proportion lost to follow-up
Case-control	Explicit definition of cases; adequate details of selection of controls; comparable groups with respect to confounding factors; interventions and other exposures assessed in same way for cases and controls; appropriate statistical analysis
Case series	Indication was comparable across patients; disease severity was comparable across patients; explicit entry criteria; outcome assessed in all patients; follow-up time uniform; outcomes assessed objectively; outcomes assessed in a blinded manner; outcome measures quantified

[a] Modified from NHS Centre for Reviews and Dissemination (2001)

Data extraction

Data were extracted using standardised instruments created for the assessment. Two reviewers examined each article and any discrepancies in evaluation were discussed and resolved through consensus.

Data analysis

Statistical analysis of data provided in the original publications was performed using Review Manager 4.2.2 (© 2003 The Cochrane Collaboration).

Expert advice

An Advisory Panel with expertise in neurosurgery, orthopaedic surgery, surgery, rheumatology, management of spinal pain and consumer health 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

Search results

A single search strategy for both cervical and lumbar AIRD identified 1,881 articles. After review of the abstracts, 85 articles were ordered for full text assessment. Three additional articles were identified from reference lists of articles identified in the search.

Cervical

AIDR versus spinal fusion

One RCT and one HTA report met the inclusion criteria.

Lumbar

AIDR versus spinal fusion

Three articles reporting on two RCTs, two systematic reviews and three HTAs met the inclusion criteria.

Case series

Fourteen case series that met the selection criteria were included for critical appraisal. Data extracted from these case series can be found at Appendix F.

An additional 11 non-English case series identified have not been included in this report.

Figure 6 below presents the flowchart demonstrating the selection of articles assessing the effectiveness of AIDR for cervical and lumbar myelopathy and/or radiculopathy and lumbar major disc prolapse.

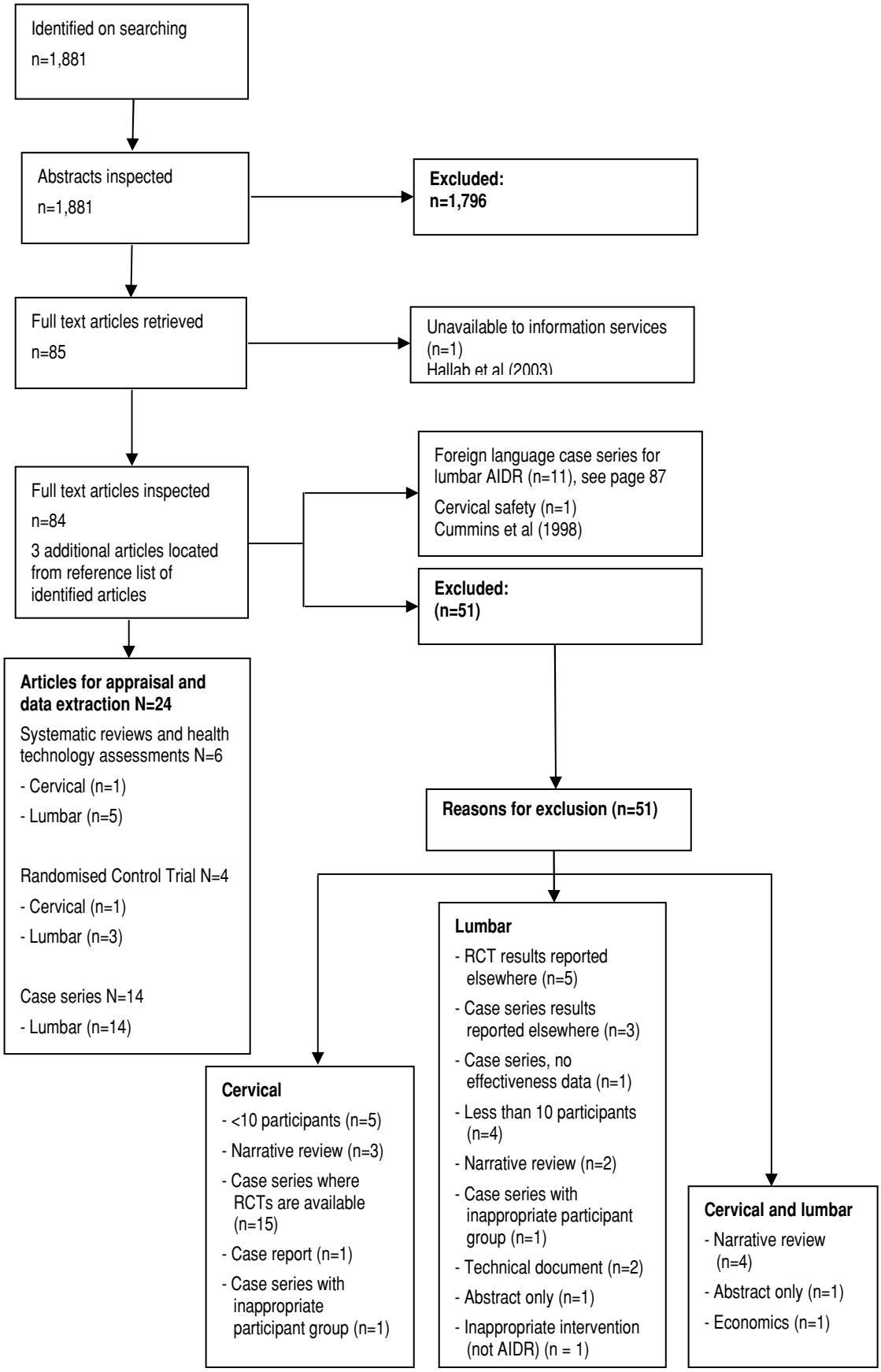

Figure 6 Flowchart demonstrating the selection of articles assessing the effectiveness of AIDR for myelopathy, radiculopathy or disc prolapse

Is it safe?

The systematic search strategy was designed to identify all publications relating to the safety and effectiveness of AIDR (refer to Appendix D).

Cervical

Safety results from the RCT

Porchet & Metcalf (2004) presented the results of a prospective, RCT comparing the Prestige II cervical disc with anterior decompression and fusion in individuals with single level cervical symptomatic DDD. Twenty-seven participants were randomised to receive the Prestige II disc and 28 received anterior decompression and fusion. The severity of adverse events in this trial was assessed according to the following World Health Organisation recommendations:

- grade 1 – noticeable to the patient but does not interfere with routine activity;
- grade 2 – interferes with routine activity but responds to symptomatic therapy or rest; and
- grade 3 – events significantly limit the patient's ability to perform routine activities despite symptomatic therapy.

Table 8 presents the adverse events reported in the RCT. The trial reported adverse events related to the surgical procedure and events irrespective of their relationship to treatment. The latter category refers to any adverse event occurring in either of the groups, whether as a direct result of the surgical procedure or independently of the procedure, such as pancreatitis.

In the cervical AIDR group, 17 adverse events were recorded (adverse event rate of 63.0%). Nineteen adverse events were observed in the cervical spinal fusion treatment group, an adverse event rate of 67.9 per cent. The number of participants in each of the treatment arms experiencing these adverse events was not reported. A comparison of the adverse event rates between the two treatment groups showed that there were no significant differences in the total number of adverse events reported for cervical AIDR and cervical spinal fusion (RR, 0.93, 95% CI: 0.63, 1.36) (Porchet & Metcalf 2004).

Of the 17 adverse events experienced by participants in the cervical AIDR group, three (17.6%) were grade 1, 13 (76.5%) were grade 2 and one (5.9%) was grade 3. Of the 19 adverse events experienced by participants in the cervical spinal fusion group, 16 (84.2%) were grade 2 and three (15.8%) were grade 3 (two of which involved secondary myelopathy and required adjacent level surgery).

Of the 17 adverse events reported in the cervical AIDR group, 14 (82.4%) resolved after three months. Of the three permanent events (17.6%), one was grade 3 (pancreatitis) and was not considered related to the procedure and the remaining two involved one incident of continuous neck pain and one of shoulder pain with no evidence of neurocompression. In addition, there was one case of malposition of the artificial intervertebral disc, which was resolved by removal of the disc and a subsequent cervical spinal fusion procedure.

Of the 19 adverse events reported in the cervical spinal fusion group, 15 (78.9%) resolved after a mean period of three months and the remaining four (21.1%) were considered to lead to permanent disability. These involved neck and arm pain for three participants and one case of secondary myelopathy requiring adjacent level surgery.

Table 8 Adverse events occurring in participants randomised to cervical AIDR or cervical spinal fusion

Adverse event	AIDR (n=27) Frequency (%)	Spinal fusion (n=28) Frequency (%)	Relative risk (95%CI)
Adverse events[a]	17 (63.0)	19 (67.9)	0.93 (0.63, 1.36)
Events related to surgical procedure	0 (0.0)	3 (10.7)	0.15 (0.01, 2.74)
Events irrespective of relationship to treatment:			
Neck and/or arm pain	6 (22.2)	11[b] (39.3)	0.57 (0.24, 1.31)
Secondary myelopathy requiring adjacent level surgery	0 (0.0)	2[c] (7.1)	0.21 (0.01, 4.13)
Graft had to be replaced	NA	2 (7.1)	NA
Malposition of the disc	1[d] (3.7)	NA	NA
Haematoma at graft harvest site	NA	1 (3.6)	NA
Transient recurrent palsy	1[e] (3.7)	0 (0.0)	3.11 (0.13, 73.11)
Dysphagia	1[e] (3.7)	0 (0.0)	3.11 (0.13, 73.11)
Pancreatitis	1[f] (3.7)	0 (0.0)	3.11 (0.13, 73.11)

Source: Porchet & Metcalf (2004). Abbreviations: NA, not applicable
[a] Porchet & Metcalf (2004) state that these values refer to registered adverse events
[b] Three patients were considered to be permanently affected
[c] One patient was considered to be permanently affected
[d] The disc was removed and the patient underwent a fusion procedure
[e] Patient recovered after three months
[f] Considered to be unrelated to the surgical procedure

The long-term (>5 years) comparative safety of cervical AIDR and cervical spinal fusion is unknown.

Safety results from the case series

Table 9 presents complications from case series of cervical AIDR. Case series are included irrespective of the specific indication - it was considered sufficient that participants had been treated for cervical AIDR. Overall complications were not consistently reported in the literature. Follow-up was up to 65 months.

Safety outcomes for 578 participants (701 discs) over 11 studies were reported in case series of cervical AIDR. The frequencies of the adverse events reported below are expressed as the percentage of participants experiencing the adverse event. New or worsening pain was observed in four participants in three of the case series (Bryan 2002, Duggal et al 2004, Sekhon 2004), ranging from 2.1 per cent (Bryan 2002) to 9.1 per cent (Sekhon 2004) of participants. Haematomas were also frequently observed and reported in a total of 10 participants over four studies (Anderson et al 2004b, Bryan 2002, Goffin et al 2003, Jöllenbeck et al 2004), ranging from one per cent (Bryan 2002) to four per cent (Jöllenbeck et al 2004) of participants. Haematomas generally required evacuation.

Temporary dysphonia or other transient vocal cord problems were reported in six participants across four studies (Bryan 2002, Duggal et al 2004, Pickett et al 2004, Wigfield et al 2002b), ranging from one per cent (Bryan 2002) to 13.3 per cent (Wigfield

et al 2002b) of participants. Temporary dysphagia was reported in one of 26 participants (3.8%) in Duggal et al (2004) and all of the participants (n=50, 100%) in the study by Jöllenbeck et al (2004) experienced difficulty swallowing after surgery.

Three participants (2.2%) in the study by Anderson et al (2004b) and two participants (1.4%) in the study by Goffin et al (2003) required revision decompression surgery. Migration or suspected migration of the artificial intervertebral disc was observed in six participants across four studies (Anderson et al 2004b, Duggal et al 2004, Goffin et al 2003, Pimenta et al 2004) but appeared not to be associated with any major clinical outcomes. The proportion of participants experiencing migration or suspected migration of the prosthesis ranged from 1.4 per cent (Goffin et al 2003) to 3.8 per cent (Duggal et al 2004).

Adjacent level surgery was performed in two participants: one of 146 (0.7%) in the study by Goffin et al (2003) and one of 15 (6.7%) in the study by Wigfield et al (2002b). Removal of the artificial intervertebral disc and subsequent cervical spinal fusion were performed in three participants: one of 10 (10.0%) in Pontillart (2001), one of 15 (6.7%) in Wigfield et al (2002b) and one of 20 (5.0%) in the study by Cummins et al (1998). One participant of 50 (2.0%) required removal of the disc alone (Jöllenbeck et al 2004). Infections were not reported in the included cases series.

Table 9 Adverse events associated with cervical AIDR – case series

Study	Study size	Length of follow-up	Types of adverse events	Outcome of adverse events
Bryan cervical disc				
Anderson et al (2004b)	N=136 175 discs	Up to 24 months	• Cerebrospinal fluid leak while decompressing posteriorly in the disc space (n=1)	• Not reported
			• Oesophageal injury (n=1)	• Not reported
			• Haematoma (n=4)	• Required evacuation
			• Incomplete removal of neural compression (n=3)	• Revision decompression
			• Device migration (<3 mm) associated with a partially milled cavity (n=2)	• Not reported
Bryan (2002)	N=97 97 discs	Up to 24 months	• Dysphonia (n=1)	• Temporary
			• Pain experienced after the 3-month follow-up due to failure to remove an osteophyte (n=1)	• Foraminotomy
			• Pain in shoulder, arm and sternum approximately 6 months following surgery (n=1)	• Neural compression ruled out on MRI
			• Non-specific shoulder pain and axial pain	• Not reported
			• Pain and shortness of breath due to a loosened drainage catheter	• Re-operation revealed a haematoma which was evacuated 26 hours post-operatively
Duggal et al (2004)[a]	N=26 30 discs	Up to 27 months (Mean: 12.3 months, Range: 1.5–27 months)	• Increased radicular pain directly following surgery (n=1)	• Improved over several weeks
			• Transient unilateral vocal cord paralysis (n=1)	• Resolved within 6 weeks
			• Dysphagia (n=1)	• Persisted for 6 weeks post-operatively
			• Possible device migration (2 mm) at 2 years post surgery (n=1)	• Not reported

Table 9 (cont'd) Adverse events associated with cervical AIDR – case series

Study	Study size	Length of follow-up	Types of adverse events	Outcome of adverse events
Bryan cervical disc (cont)				
Goffin et al (2003)	N=146 189 discs	Up to 24 months	• Device migration seen in one participant and suspected in a second • Prevertebral haematoma (n=2) • Epidural haematoma (n=1) • Residual symptoms (n=1) • Residual myelopathic symptoms (n=1) • Incorrect level operated on, resulting in unresolved pain (n=1) • Pain in shoulder, arm and sternum (n=1) • Unresolved non-specific shoulder pain (n=1) • Radiculopathy caused by disc herniation (n=1) • Cerebrospinal fluid leak while decompressing posteriorly (n=1) • Pharyngeal tear/oesophageal wound incurred during intubation and an anterior decompression caused by ongoing nerve root compression (n=1)	• Temporary • Required evacuation (re-intervention) • Required evacuation (re-intervention) • Posterior foraminotomy without device involvement (re-intervention) • Posterior decompression (re-intervention) • Follow up surgery at the correct level. Temporary dysphonia occurred after this surgery • Neural compression ruled out • Not reported • Device implant at adjacent level. Severe dysphonia occurred after this surgery • Not reported • Required surgical repair – an anterior decompression
Pickett et al (2004)	N=14 15 discs	Up to 24 months (Mean: 12 months, Range: 6–24 months)	• Transient unilateral vocal cord paralysis (n=1)	• Resolved by 6 weeks
Sekhon (2004)	N=11 15 discs	Up to 32 months (Mean: 18.4 months)	• Worsening of pre-operative symptoms approximately 10 days post surgery (n=1) • Persistent neck and arm pain, despite anti-inflammatory medication	• Resolved after 72 hours with dexamethasone therapy • Evidence of spondylotic bridging creating an interbody fusion 17 months following surgery

Table 9 (cont'd) Adverse events associated with cervical AIDR – case series

Study	Study size	Length of follow-up	Types of adverse events	Outcome of adverse events
Prestige I (Frenchay disc)				
Wigfield et al (2002b)[b,c]	N=15	Up to 24 months	• Persistent radicular pain during the first 12 months following surgery (n=2)	• Investigated with plain radiographs and CT myelograms (no foraminal or cord compromise detected)
			• Neck pain (n=4)	• One participant had a CT myelogram (no foraminal or cord compromise detected). One participant required removal of the artificial disc and a subsequent fusion. One participant developed the pain after a car accident and one participant had two broken screws in the device
			• Recurrent arm pain (n=2)	• One case resolved spontaneously. The second required foraminotomy at an adjacent level
			• Progression of myelopathy (n=2)	• One participant underwent decompression laminectomy, two levels below the artificial disc. The participant then developed a progressive kyphotic deformity at the intervening level and underwent fusion at this level
			• Transient dysphonia (n=2)	• Resolved within 3 to 6 months
Porous coated motion disc				
Pimenta et al (2004)	N=53 82 discs	Up to 12 months	• Device migration (4 mm), 3 months post surgery	• No clinical symptoms
			• Grade 1 heterotopic ossification in the nine-month follow-up	• Not reported
Disc not specified				
Jöllenbeck et al (2004)	N=50 51 discs	Up to 14 months	• Haemorrhage causing breathing difficulties (n=2)	• Surgical removal of haematoma within 6 hours of surgery
			• All participants reported minor difficulty with swallowing	• Resolved after three days
Pointillart (2001)	N=10 10 discs	Up to 24 months	• Intense neck pain (n=2)	• In one instance, removal of the disc and spinal fusion resolved the pain
Bristol/Cummins				
Cummins et al (1998)	N=20 22 discs	Up to 65 months	• Persistent or increased pain (n=3)	• Not reported
			• Transient hemiparesis as a result of a drill injury to the spinal cord at the time of screw placement	• Recovered completely except for a deltoid muscle paresis that appeared 3 months post-operatively
			• In 5 participants receiving a single stainless steal screw in the anterior joint: partial screw pull-out (n=3), broken screw (n=1), joint subluxation (n=1)	• Not reported
			• In 15 participants receiving A-O screws in the anterior joint: partial screw pull-out (n=2), broken screw (n=1), persistent mild dysphagia (n=3), loose joint and persistent pain (n=1)	• Participant with loose joint and persistent pain had prosthesis removed because of an improper ball and socket interface (manufacturing error) and underwent interbody fusion. Outcomes not reported for other events

N = number of participants

[a] May be further results from Pickett et al (2004)

[b] Selected patients considered most at risk of adjacent-level disease

[c] Robertson & Metcalf (2004) reported 4-year results from this study, however no further complications were observed

Anderson et al (2004a) analysed Bryan and Prestige discs that had been explanted from the cervical spine in order to assess wear of the device and any host inflammatory response. Overall, of the 5,500 Bryan discs known to have been implanted at the time of publication, 11 (0.2%) had been explanted. Of these 11 explants, seven (63.6%) were removed due to persistent neurological symptoms and four (36.4%) due to infection. Three of the 300 implanted Prestige discs (1.0%) were explanted. Of these three explants, one (33.3%) was removed due to incorrect placement, one (33.3%) due to infection and one (33.3%) to treat adjacent level degeneration. Comparison of simulator-generated data of wear-related characteristics to data obtained from explanted devices indicated that actual wear was five- to 10- fold less than that predicted. In addition, inflammatory responses observed from the explanted devices were reported to be minimal and not typical of that seen in failed joint arthroplasties.

Tsuji et al (1990) implanted artificial ceramic intervertebral discs into the cervical spine of two patients. In both cases the discs appeared to migrate into the lower vertebra at six to 12 months after surgery. This migration progressed with time. No subsequent publications using ceramic discs were identified in the literature search.

Safety results from the systematic reviews and HTA reports

In addition to the case series reported above, the ASERNIP-S Procedure Brief (2001b) reported the results from Cummins et al (1998), a case series of 20 patients with the Bristol/Cummins disc who were followed for an average of 2.4 years. The safety results from this study are included in Table 9. The following adverse events were reported:

- Five partial screw pullouts.
- Two broken screws.
- One partial dislocation resulting in moderate, persistent dysphagia.
- One transient hemiparesis due to spinal cord injury whilst drilling.
- One loose joint.
- Persistent pain.

In addition, the ASERNIP-S Procedure Brief (2001b) presented results of an ongoing European multi-centre trial. Whilst this trial is not adequately referenced in the ASERNIP-S Procedure Brief (2001b) as the results may not have been published at the time of writing, they appear to have been reported subsequently in Goffin et al (2002). A later publication by Goffin et al in 2003, which has been included in the evaluation of the safety of cervical AIDR (Table 9), includes results of the participants in Goffin et al (2002) and additional participants. The ASERNIP-S Procedure Brief (2001b) reported the following adverse events from this European study:

- One incidence of minor intraoperative bleeding.
- One incidence of unresolved pain following initial surgery.
- One incident of dysphonia.

Lumbar

Safety results from the RCTs

Two multicentre RCTs comparing lumbar AIDR and lumbar spinal fusion have been conducted. These include the DePuy Spine Charité™ Artificial Disc Trial (Geisler et al 2004, Guyer et al 2004, McAfee et al 2003a, McAfee et al 2003b) and the FDA ProDisc II Trial (Delamarter et al 2003, Zigler 2004). Participants enrolled in the former had single level disease at L4-L5 or L5-S1, and those participating in the latter had DDD at no more than two adjacent vertebral levels between L3 and S1.

Table 10 presents the adverse events reported in the DePuy Spine Charité™ Artificial Disc Trial Report P040006 and the associated publications (Geisler et al 2004, Guyer et al 2004, McAfee et al 2003a, McAfee et al 2003b). No significant differences in the rates of any of the adverse events were observed between the 205 participants treated with lumbar AIDR with SB Charité™ and the 99 participants treated with the BAK Interbody Fusion Device (BAK Cage) (RR=0.98, 95% CI: 0.86, 1.11). In addition, no significant differences in adverse events that were considered to be device related were observed between the two treatment groups (Trial Report P040006) (RR=1.81, 95% CI: 0.62, 5.31). Infections were reported in 12.2 and 6.1 per cent of participants randomised to lumbar AIDR and lumbar fusion, respectively. Severe or life-threatening infections were reported in 1.5 and 2.0 per cent of participants randomised to lumbar AIDR and lumbar spinal fusion, respectively. No statistically significant differences were observed between the rates of infection for the treatment groups (Table 10).

Table 10 Adverse events from the DePuy Spine Charité™ Artificial Disc Trial – Lumbar AIDR compared with lumbar spinal fusion

Adverse event[a]	AIDR (n=205) Frequency (%)	Spinal fusion (n =99) Frequency (%)	Relative Risk (95% CI)
Adverse events irrespective of relationship to treatment			
Any	156 (76.1)	77 (77.8)	0.98 (0.86, 1.11)
Severe or life-threatening	30 (14.6)	9 (9.1)	1.61 (0.80, 3.26)
Adverse events related to treatment			
Device-related	15 (7.3)	4 (4.0)	1.81 (0.62, 5.31)
Device failures	10 (4.9)	8 (8.1)	0.60 (0.25, 1.48)
Adverse events irrespective of relationship to treatment:			
Pain (back or lower extremity)	107 (52.2)	52 (52.5)	0.99 (0.79, 1.25)
Pain (other)	27 (13.2)	9 (9.1)	1.45 (0.71, 2.96)
Neurological	34 (16.6)	17 (17.2)	0.97 (0.57, 1.64)
Infection	25 (12.2)	6 (6.1)	2.01 (0.85, 4.75)
Approach problems (abdominal)	18 (8.8)	8 (8.1)	1.09 (0.49, 2.41)
DDD progression, natural history	6 (2.9)	4 (4.0)	0.72 (0.21, 2.51)
Additional surgery, index level	10 (4.9)	8 (8.1)	0.60 (0.25, 1.48)
Intraoperative complications	2 (1.0)	3 (3.0)	0.32 (0.05, 1.90)
Abnormal bone formation	2 (1.0)	0 (0.0)	2.43 (0.12, 50.08)
Severe or life-threatening adverse events irrespective of relationship to treatment:			
Pain (back or lower extremity)	10 (4.9)	5 (5.1)	0.97 (0.34, 2.75)
Other	11 (5.4)	3 (3.0)	1.77 (0.51, 6.20)
Other, cardiovascular	0 (0.0)	1 (1.0)	0.16 (0.01, 3.94)
Infection	3 (1.5)	2 (2.0)	0.72 (0.12, 4.27)
Additional surgery, index level, removal	4 (2.0)	0 (0.0)	4.37 (0.24, 80.36)
Additional surgery, index level, delayed fusion	1 (0.5)	0 (0.0)	1.46 (0.06, 35.43)
Additional surgery, index level, re-operation	1 (0.5)	0 (0.0)	1.46 (0.06, 35.43)
Approach problems (abdominal)	2 (2.0)	1 (1.0)	0.97 (0.09, 10.52)
Approach problems (hernia)	1 (0.5)	0 (0.0)	1.46 (0.06, 35.43)
Approach problems (retrograde ejaculation)	1 (0.5)	1 (1.0)	0.48 (0.03, 7.64)
Additional surgery, unrelated to index level	1 (0.5)	1 (1.0)	0.48 (0.03, 7.64)
Neurological (nerve root injury)	1 (0.5)	0 (0.0)	1.46 (0.06, 35.43)
Device failures			
Re-operation	0 (0.0)	1 (1.0)	0.16 (0.01, 3.94)
Revision	0 (0.0)	1 (1.0)	0.16 (0.01, 3.94)
Removal	2 (1.0)	0 (0.0)	2.43 (0.12, 50.08)
Supplemental fixation	8 (3.9)	6 (6.1)	0.64 (0.23, 1.81)

Source: Report P040006 and associated publications: Geisler et al 2004, Guyer et al 2004, McAfee et al 2003a, McAfee et al 2003b)
[a] Occurring in participants randomised to lumbar AIDR or spinal fusion

Adverse events reported in an RCT comparing lumbar AIDR with ProDisc II prostheses and circumferential lumbar spinal fusion reported that there were no instances of implant migration, breakage or mechanical failure, and that no revision surgery was required (Delamarter et al 2003).

Adverse events reported in an RCT comparing lumbar AIDR with ProDisc II (55 participants) and circumferential lumbar spinal fusion (23 participants) are summarised in Table 11 (Zigler 2004). No significant differences in rates of adverse event were observed between the treatment groups. Adverse events included one participant (1.8%) randomised to lumbar AIDR requiring re-intervention the day after surgery due to dislodgement of the polyethylene spacer, which had been improperly inserted. The spacer was replaced without further complication. One participant (1.8%) experienced laceration of an iliac vein that was repaired during the index procedure without further complications or need for a transfusion. Following the procedure, one participant (4.3%) randomised to the lumbar fusion treatment group complained of bilateral leg pain, which had spontaneously resolved by the three-month follow-up visit. One participant (4.3%) randomised to lumbar fusion experienced a deep wound infection that required operative irrigation and debridement. Among participants randomised to lumbar AIDR, one (1.8%) presented with a superficial wound infection that resolved following antibiotic treatment, one (1.8%) complained of sacroiliac joint pain that was managed with steroid injection and chiropractic management with partial relief, and two (3.6%) experienced leg pain that was managed with Neurontin and epidural injections.

Table 11 Adverse events reported from one centre of the ProDisc II Trial – Lumbar AIDR compared with lumbar spinal fusion

Adverse event[a]	AIDR (n=55) Frequency (%)	Spinal fusion (n =23) Frequency (%)	Relative Risk (95% CI)
Dislodgement of polyethylene spacer	1 (1.8)	NA	NA
Iliac vein laceration	1 1.8)	0 (0.0)	1.29 (0.05, 30.45)
Sacroiliac joint pain	1 (1.8)	0 (0.0)	1.29 (0.05, 30.45
Bilateral leg pain	0 (0.0)	1 (4.3)	0.14 (0.01, 3.38)
Leg pain	2 (3.6)	0 (0.0)	2.14 (0.11, 42.97)
Deep wound infection	0 (0.0)	1 (4.3)	0.14 (0.01, 3.38)
Superficial wound infection	1 (1.8)	0 (0.0)	1.29 (0.05, 30.45

Source: Zigler 2004
[a] Occurring in participants randomised to lumbar AIDR or spinal fusion

The long-term (>5 years) comparative safety of lumbar AIDR and lumbar spinal fusion is unknown.

Safety results from the case series

Safety outcomes for 553 participants (706 discs) over 15 studies were reported in case series of lumbar AIDR (Table 12). Case series are included irrespective of the specific indication as it was considered sufficient that participants had been treated for lumbar AIDR.

The adverse events reported in Mayer et al (2002) appear also to have been reported in Mayer & Wiechert (2002). The safety of lumbar AIDR as reported in the identified case series is presented in Table 12. The frequencies of the adverse events reported below are expressed as the percentage of participants experiencing the adverse event. Revision surgery was required in 30 participants in nine studies (Aunoble et al 2004, Caspi et al 2003, Cinotti et al 1996, David 1993, Enker et al 1993, Fraser et al 2004, Lemaire et al 1997, Mayer et al 2002, Tropiano et al 2003). The proportion of participants in each of the studies undergoing revision surgery ranged from 2.9 per cent (Lemaire et al 1997,

Mayer et al 2002) to 28.6 per cent (Fraser et al 2004). In four participants, the artificial disc was replaced and in the remaining participants, lumbar spinal fusion was required The artificial disc was removed before fusion in five cases.

Revision was required as a result of disc migration, persistent symptoms of pain or bone complications such as vertebral fractures and periprosthetic ossifications. Some cases of pain were managed with medication and analgesics. Infections were rarely reported in the included cases series, however Zeegers et al (1999) reported that one of 50 participants (2.0%) had experienced infection of the urinary tract.

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Table 12 Adverse events associated with lumbar AIDR – case series

Study	Study size	Length of follow-up	Type of adverse event	Outcome
SB Charité™ III				
Caspi et al (2003)	N=20 23 discs	48 months	• Migration of the prosthesis (n=2) – one 2 days after surgery due to incomplete severing of the post-longitudinal ligament and the other 2 weeks post-surgery due to a small fracture in the lower endplate	• Revision surgery was performed and a larger prosthesis was inserted in both cases
			• Intraoperative laceration of the ureter and thrombosis of the iliac artery (n=1)	• Complications immediately treated
			• Spontaneous ossification of the intervertebral anterior ligament (n=2)	• Intensive physiotherapy halted progression
			• Different stages of ligation (n=4). (All 4 rated their postoperative results as poor, despite good radiographic results)	• Not reported
Cinotti et al (1996)	N=46 56 discs	Mean: 3.2 years Range: 2–5 years	• Back pain or leg symptoms (n=16)	• Required medication: analgesics taken continuously (n=12) or occasionally (n=4)
			• Bilateral radicular pain soon after surgery (n=1)	• Participant underwent removal of prosthesis and circumferential fusion
			• Persistent back pain (n=7)	• Participants underwent posterolateral fusion without removal of the artificial discs 2–4 years after surgery
			• Anterior dislocation of the implant (n=1) – experienced 6 days post-surgery. The participant had a large prosthesis placed anteriorly	• Revision surgery where a smaller artificial prosthesis was implanted
			• Perianular ossifications (n=7, including 3 of 18 who wore a corset after surgery). Shown by radiographs. Of the remaining 4, 3 showed a malposition of the prostheses in the sagittal plane. 4/7 experiencing perianular ossifications developed spontaneous interbody fusions at the operated levels	• No effect on clinical outcome
			• Undersized prostheses and collapse of the implants into the vertebral bodies (n=4)	• No effect on clinical outcome

Table 12 (cont'd) **Adverse events associated with lumbar AIDR – case series**

Study	Study size	Length of follow-up	Type of adverse event	Outcome
SB Charité™ III (cont)				
David (1993)	N=22 29 discs	Minimum of 12 months	• Sexual problems 6 months after the procedure, thought due to psychological factors (n=1) • Severe L5 sciatica after insertion of an L5-S1 prosthesis on a very narrow disc • Secondary dislocated prosthesis at L5-S1	• Not reported • Prosthesis removed 10 days after surgery and anterior fusion with less distraction was achieved with complete recovery of the participant • Repeated surgery 10 days after index surgery
Lemaire et al (1997)	N=105 154 discs	Mean: 51 months	• Vascular (n=5) – 2 phlebitis, 2 pulmonary embolism and 1 acute leg ischaemia subsequent to atheromatous plaque mobilisation • Temporary neurologic deficits (n=2) – 1 total regressive sexual disorder at 1 year and 1 paralysis at L5 when getting out of bed because of posterior joint instability with radicular stretching • Bone complications (n=4) – 1 L5 endplate posttraumatic fracture, 1 L5 lower end plate sinking of osteoporotic origin, 2 periprosthetic ossifications. 3/4 attributable to the technique	• Participant with acute leg ischaemia required endarterectomy. Outcome not reported for other participants • Recovery achieved 3 months after revision and fixation • Participant with endplate posttraumatic fracture required revision with arthrodesis. Outcome for other participants not reported
Sott & Harrison (2000)	N=14 15 discs	Mean: 48 months Range: 18–68 months	• Warmer left foot than right due to interference with the left paravertebral sympathetic nerves (n=5) • Implant migration (n=1) – the lower prosthetic endplate sank by 3 mm into the inferior vertebral endplate	• Participants had been warned of this during informed consent, as a result of which there were no complaints • No deterioration had occurred at last follow-up visit (30 months) and clinical outcome was reported as good
Su et al (2003)	N=31 37 discs	Mean: 26 months Range: 17–41 months	• Slight displacement of the gliding core, with no clinical symptoms (n=1) • Slight displacement of the core due to a technical problem, with no clinical symptoms) (n=1)	• Not reported • Not reported

Table 12 (cont'd) **Adverse events associated with lumbar artificial intervertebral disc replacement – case series**

Study	Study size	Length of follow-up	Type of adverse event	Outcome
SB Charité™ III (cont)				
Xu et al (2004)	N=34 41 discs	Mean: 18.6 months Range: 3–38 months	• Anterior subluxation of the inferior endplate on S1 (n=1, L4-L5 combined with L5-S1 disc replacement). Found at 3-month follow-up • Mild laceration in iliac vein during operation (n=1) • Mild lower back pain after the operation (n=2). 1/2 had mild depression and felt heat and pain in the waist	• Not managed due to lack of symptoms • No adverse result after repair • No abnormalities found during examination at hospitalisation
Zeegers et al (1999)	N=50 75 discs	24 months	• Neurological, including dysaesthesia of legs, paresis/muscle weakness and cramps in legs (n=10) • Wound, haematoma including painful/numb scar and haematoma (n=17) • Abdominal problems including retroperitoneal haematoma, visceral dysfunction and abdominal pain (n=3) • New, or progression of old, pain including low back or leg pain (n=5) • Vegetative dysfunctions including sympathectomy effect and disturbance of miction (n=8) • Aortal lesion at removal of prosthesis (n=1) • General complications including infection of urinary tract, impotence or retrograde ejaculation and deep vein thrombosis (n=5) • Malposition of prosthesis (n=2)	• Most complications were temporary.with the exception of 3 cases of dysaesthesia of legs, 4 cases of sympathectomy effect and 1 case of malposition of the prosthesis which were permanent
ProDisc				
Aunoble et al (2004)	N=2	Not reported	• Severe acute low-back pain (n=2), in both cases, radiographs revealed dislocation of the polyethylene inlay of the prosthesis: – At 4 months after implantation of the prosthesis (n=1) – At 1 month after implantation of the prosthesis (n=1)	• The prosthesis was removed using a transperitoneal approach. The individual underwent anterior lumbar interbody fusion • The pain was initially managed with analgesics. However, at 19 months after surgery, the pain worsened and the individual required posterior fixation with pedicular screws and posterolateral graft fusion

Table 12 (cont'd) **Adverse events associated with lumbar AIDR – case series**

Study	Study size	Length of follow-up	Type of adverse event	Outcome
ProDisc (cont'd)				
Bertagnoli & Kumar (2002)	N=108 134 discs	Not reported	• Postoperative systemic septicaemia, not related to surgery • Residual leg pain or back pain including facet joint pain (n=9)	• Resolved with a course of antibiotics • Treated with analgesics
Mayer et al (2002)	N=34	Mean (SD): 5.8 (3.0) months	• L5 nerve root irritation (n=1) – several days after surgery, due to extra-foraminal protrusion of nucleus material compromising the L5 nerve root on the left side • Pain with no notable trauma (n=1). Radiographs revealed an inlay dislocation anteriorly	• A 3-week outpatient course of conservative treatment and perineural infiltrations led to complete and permanent pain reduction • Revision surgery with replacement of the artificial disc
Mayer & Wiechert (2002)[a]	N=26	Mean: 6 months Range: 3–18 months	• L5 root irritation (n=1) – due to intraforaminal disc protrusion • Extrusion of the polyethylene inlay (n=1)	• Treated with conservative therapy, resolved in 30 days • Revision surgery with explantation of the implant and insertion of a new one
Tropiano et al (2003)	N=53 68 discs	Mean: 1.4 years Range: 1–2 years	• Postoperative vertebral body fracture (n=1) • Implant malposition (n=2). Following revision, one participant experienced retrograde ejaculation • Persistent radicular pain (n=2) – without radiographically evident neural compression	• Anterior fusion with prosthesis removal was required • Revision surgery 6–8 weeks after index surgery. Retrograde ejaculation resolved 8 months after second surgery • Treated with medication

Table 12 (cont'd) **Adverse events associated with lumbar artificial intervertebral disc replacement – case series**

Study	Study size	Length of follow-up	Type of adverse event	Outcome
Acroflex				
Enker et al (1993)	N=6	Not reported	• Upper back and leg pain (n=1) – 1 year after disc replacement at L2-L3 for disc degeneration. At revision, the rubber core of the artificial disc was found to be fractured	• Successful revision by anterior interbody fusion using an autologous strut graft with anterior plate stabilisation
			• No relief from pre-operative pain despite satisfactory radiographic appearance at 3-year follow-up. Disc replacement at L5-S1	• Not reported
Fraser et al (2004)	N=28 32 discs	24 months	• Partial forward displacement of implant (at L5-S1) (n=1)	• No revision surgery required. Participant had satisfactory subjective outcome
			• Serial thin section CT demonstrated rubber tears (n=10)	• Majority of lesions were minor anteroinferior tears. One participant had evidence of autofusion. Most had a moderate amount of annular and periannular ossification
			• Unremitting severe pain – no cause determined	• Revision surgery (interbody fusion supplemented by pedicle screw fixation and posterolateral grafting) after 12 months of follow-up. The participant's condition did not improve despite CT evidence of graft consolidation
			• Extensive anterior disruption of rubber with associated osteolysis and deterioration in clinical condition (n=3)	• Revision surgery (implant removed and interbody fusion supplemented by pedicle screw fixation and posterolateral grafting) 3 years after index surgery
			• Rubber failure (n=4)	• Revision surgery (posterolateral fusion with pedicle screw and rod fixation with removal of the artificial disc)
			• Nerve root irritation (n=2)	• Not reported
			• Partial anterior disc expulsion (n=1)	• Not reported
			• Minor anterior polyolefin tear (n=7)	• Not reported
			• Pulmonary embolus (n=1)	• Not reported
			• Retrograde ejaculation (n=1)	• Not reported

[a] Mayer & Wiechert (2002) may have reported the same adverse events as Mayer et al (2002)

Griffith et al (1994) reported on adverse events occurring in 93 participants (139 discs) receiving the SB Charité™ III artificial disc and adverse events occurring in 49 participants (58 discs) receiving earlier designs (Models I and II) of the artificial disc (Table 13).

Griffith et al (1994) reported that one of the three surgeons had been involved in the early development of the prosthesis and had submitted data from Models I and II as early as September 1984. No further demographic data regarding the surgeons were reported. The rates of the complications for Models I and II could not be quantified as the number of participants receiving these individual designs was not reported. Inappropriate choice of prosthesis size resulting in disc migration/subsidence or dislocation occurred in 6.5 per cent of participants receiving Model III, corresponding to 4.3 per cent of the number of discs implanted (Griffith et al 1994).

Table 13 Adverse events reported with the use of lumbar AIDR (SB Charité™ Models I, II and III)

Complication	SB™ Charité™ Model I	SB Charité™ Model II	SB Charité™ Model III n/N (%)
Device failure:			
• plate break	2	13	0/93 (0.0)
• plate fissure	0	24	0/93 (0.0)
• core	0	1	1/93 (1.1)
Related to prosthetic choice (ie size):			
• implant migration	8	12	5/93 (5.4)
• dislocation	0	0	1/93 (1.1)
Other procedural complications	2	7	30/93 (32.3)
Equivocal	0	0	16/93 (17.2)

Griffith et al (1994) also reported complications related to the procedure rather than to the device itself. It is unclear if the reported adverse events are for the three models combined or for Model III only. Adverse events included phlebitis/leg thrombosis (n=2), injured vein (n=6), wound bleeding/dehiscence (n=2), superficial wound infection (n=1), muscle atrophy (n=1), urinary tract infection (n=4), incontinence (n=3), constipation/defecation difficulty (n=4), nausea (n=1), skin paresthesia (n=1), haematoma (n=11), hypotension by blood loss (n=1), retroejaculation (n=1) and sympathetic sign in left leg (n=1).

Complications considered equivocal included allergy (n=1), a feeling of instability (n=2), new paresthesia (n=1), unspecified neurologic (n=2), abdominal, leg, thigh or lumbar pain (n=10). Griffith et al (1994) stated that the majority of these complications occurred due to the necessity of an anterior surgical approach for implantation of the artificial disc.

Re-operations were reported for a total of five of 49 participants (10.2%) receiving SB Charité™ Models I and II: nucleotomy for cauda equina (n=1), anterior-posterior fusion for instability and/or migration causing pain (n=2) and anterior-posterior fusion for dislocation (n=2) (Griffith et al 1994). Three of 93 participants (3.2%) receiving SB Charité™ Model III required re-operation: percutaneous nucleotomy (n=1), foraminotomy to relieve pain (n=1) and subsequent anterior-posterior fusion (n=1) (Griffith et al 1994).

van Ooij et al (2003) reported on a series of 27 individuals selected on the basis of unsatisfactory results or complications following lumbar AIDR with the SB Charité™ artificial disc. The 27 individuals were drawn from a larger group of patients, however the number of individuals in that population is unknown. Early complications included one case of anterior dislocation of the prosthesis within one week of surgery. The participant subsequently had the disc replaced with a carbon cage filled with bone. A further individual experienced dislocation of the prosthesis three months after surgery and removal of the artificial disc at 12 months. Other early complications included abdominal wall or retroperitoneal haematomas (n=4), retrograde ejaculation, loss of libido and erectile dysfunction (n=1) and erectile dysfunction without retrograde ejaculation (n=1).

van Ooij et al (2003) also reported on late complications experienced by 26 of the 27 selected participants who maintained the artificial disc for a mean of 91 months (range, 15–157 months). Many individuals were reported to experience incapacitating back and leg pain. Twelve of the 26 participants had evidence of DDD at another level. Seven of these had evidence of DDD at the time of index surgery, but symptoms were not considered to be related to those levels.

Facet joint arthrosis was observed in 11 participants and subsidence of the prothesis was observed in 18. Two participants experienced slow anterior migration of the disc which resulted in compression of the great vessels in one case. A further two participants had breakage of the metal wire around the polyethylene core and required revision surgery. Hyperlordosis of the operated segment was observed in three participants, resulting in opening of the facet joints in the superior part and a compression of the inferior part.

Safety results from the systematic reviews and HTA reports

Two rapid reviews (ASERNIP-S 2001a, ASERNIP-S 2003), a NICE report (NICE 2003) and two systematic reviews (de Kleuver et al 2003, Gamradt & Wang 2005) were included in the assessment of the safety of lumbar AIDR. All of the studies assessing the SB Charité™ III artificial disc included in the ASERNIP-S Rapid Review (2001a) are also included in the ASERNIP-S Rapid Review (2003). In addition, the NICE (2003) review appears to be based on the ASERNIP-S Rapid Review (2003).

Many of the studies included in the assessment of the safety of lumbar AIDR in these systematic reviews and HTA reports have been included herein (pages 24–34, and Tables 10–13). Exceptions to this include four non-English case series and data from an abstract only reported in ASERNIP-S (2003), NICE (2003), de Kleuver et al (2003) and Gamradt & Wang (2005). These publications included Buttner-Janz et al (1988), Buttner-Janz et al (2002), Hopf et al (2002), Ross & Tandon (1997) and Wittig et al (1989).

Overall, complication rates of between three and 50 per cent were reported (ASERNIP-S Rapid Review 2001a, ASERNIP-S Rapid Review 2003, NICE 2003, de Kleuver et al 2003). In addition, two studies reported complication rates of 13 and 17 per cent which were claimed to be attributable to the anterior approach to surgery used (ASERNIP-S Rapid Review 2003). Furthermore, Gamradt & Wang (2005) concluded that the majority of complications related to the surgical approach used rather than the implant itself.

Device migration was reported at rates of 4.3 to 43.6 per cent (ASERNIP-S Rapid Review 2003), device failure at rates of one to 17 per cent (ASERNIP-S Rapid Review 2003) and re-operation rates three to 24 per cent (ASERNIP-S Rapid Review 2003,

NICE 2003). de Kleuver et al (2003) reported that the overall rate of vascular complications appeared low, with six venous injuries, two arterial injuries and six thrombotic complications from 411 participants.

Gamradt & Wang (2005) reported that a review of the biomechanical testing of the SB Charité™ III device indicated no polyethylene failures in 10 million cycles *in vitro*.

The NICE (2003) review contained data regarding an RCT of the Charité™ artificial disc compared to BAK spinal fusion, submitted for FDA approval. After two years, the trial found that complication rates were equivalent between the two procedures.

Safety of the anterior approach for surgery

Polly (2003) performed a literature-based review of morbidity relating to an anterior approach to spinal surgery and to a conjectural analysis of potential complications of AIDR based on current experience with total joint arthroplasty. The complications of anterior spinal surgery were vessel injury, thrombosis with possible embolic phenomenon with the potential for death, long-term venous insufficiency, retrograde ejaculation and ureteral injury. These complications may also be relevant to patients undergoing AIDR. Polly (2003) also concluded that there may be a potential for dislodgement of the prosthesis in addition to potential infections, which would result in the removal of the implant. Concerns were also raised regarding a learning curve within the medical community performing the procedure, that is, that higher rates of patient morbidity may occur when the procedure is performed by less experienced clinicians.

Is it effective?

Cervical AIDR versus cervical fusion

Critical appraisal of RCTs

One multi-centre, prospective RCT has been reported for cervical AIDR – the Artificial Cervical Disc Primary Indication Study (ACDPI). This trial compared cervical AIDR using the Prestige cervical disc to anterior cervical fusion using iliac crest autograft, for the treatment of single level cervical symptomatic DDD (Porchet & Metcalf 2004). The Application to the MSAC includes additional details of the trial protocol and case studies of the individual adverse events (Appendix 7 of the Application). Data included in this assessment report were taken from Porchet & Metcalf (2004) unless otherwise stated. Table 14 presents the descriptive characteristics of the RCT.

Table 14 Descriptive characteristics of the RCT: Cervical AIDR versus cervical fusion

Study	Location	Enrolment period	Indication	Artificial disc used	Type of spinal fusion	Follow-up	Study population		
							N	Number of males (%)	Age (years)
Porchet & Metcalf (2004) ACDPI trial	4 centres: 3 European 1 Australian	Not reported	Single level cervical symptomatic DDD	Prestige II	Anterior cervical fusion using iliac crest autograft	6 weeks, 3, 6, 12 (n=37) and 24 (n=24) months post surgery	All: 55 AIDR: 27 Fusion: 28	All: 29 (53) AIDR: 17 (63) Fusion: 12 (43)	Mean ±SD (Range) AIDR: 44.3±8.9 (32–64) Fusion: 43.2±6.9 (28–58)

Patient selection criteria for the RCT

Eligibility criteria for Porchet & Metcalf (2004) are presented in Table 15. Participants were required to have cervical DDD defined as intractable radiculopathy or myelopathy and were required to have been unresponsive to non-operative treatment for approximately six weeks.

Table 15 Patient selection criteria for the RCT: Cervical AIDR versus cervical fusion

Study	Inclusion	Exclusion
Porchet & Metcalf (2004) ACDPI trial	• Cervical DDD, defined as an intractable radiculopathy or myelopathy[a] caused by neuroradiologically documented disc herniation or osteophyte formation • Single level disease in C4-5 to C6-7 • Unresponsiveness to non-operative treatment for approximately 6 weeks or the presence of progressive symptoms or signs of nerve root compression • Older than 18 years of age • Pre-operative NDI >30 • Provision of informed consent	• Previous surgical treatment of the cervical spine • Cervical spine condition other than symptomatic cervical disc disease requiring surgical treatment • Osteopaenia, osteoporosis, osteomalacia • Cancer • Active bacterial infection, local or systemic[b] • Diabetes[b] • Fever (temperature >101°F) at the time of surgery[b] • Stainless steel allergy or intolerance[b] • Mentally incompetent participant[b] • Alcohol or drug abuser[b] • Participant has received drugs which may interfere with bone metabolism within two weeks of surgery[b] • A history of endocrine or metabolic disorder known to affect osteogenesis[b] • A condition requiring post-operative medications that may interfere with stability of the implant[b] • <18 years of age at the time of surgery

Abbreviations: NDI, neck disability index

[a] This inclusion criterion is derived from Porchet & Metcalf (2004), however Appendix 7 (p4) of the Application states that myelopathy is an exclusion criterion for the trial

[b] From Appendix 7 of the Application

Validity of RCT

The results of the validity assessment for Porchet & Metcalf (2004) are presented in Table 16 and discussed below.

Table 16 Validity of the RCT: Cervical AIDR versus cervical fusion

Study	Validity					Outcome measures
	Method of randomisation	Concealment of allocation	Inclusion of randomised participants	Blinding	Losses to follow-up	
Porchet & Metcalf (2004) ACDPI trial	Schedule generated using the Statistical Analysis System at each site	No The investigator and participant were blinded to randomisation until after eligibility for the trial was determined, at which point the investigator, surgeon and participant were unblinded[a]	Yes 1:1 AIDR:fusion	Radiographs had site-independent review by two radiologists, however it is uncertain if they were blinded. Follow-up evaluations assessed by one clinician directly involved in the surgery	Trial not completed at time of publication	Primary[a]: Pain/disability status as measured by the NDI Secondary[a]: • Range of motion • Neurological status, based on motor, sensory and reflex measurements and the foraminal compression test • Medical outcomes study 36-item short form health survey (SF-36) • Neck pain status measured using a VAS • Arm pain status, measured using a VAS • Participant satisfaction • Participant global perceived effect • Disc height measurement • Neck function index

Abbreviations: NDI, neck disability index; VAS, visual analogue scale
[a] Appendix 7 of the Application

Randomisation and allocation concealment

Participants meeting the inclusion criteria were initially assigned a sequential clinical investigation number then randomised according to a schedule generated using the Statistical Analysis System. Randomisation was 1:1 at each site. Porchet & Metcalf (2004) do not state if allocation was concealed from participants, investigators and/or outcome assessors. However the additional data provided in Appendix 7 of the Application states that the investigator and participants were blinded to randomisation until after eligibility for the trial had been determined, at which point the investigator, surgeon and participants were unblinded. They were therefore not blinded to group allocation.

Blinding

Radiographs submitted for site-independent radiological review were pooled and assessed by two independent radiologists, however outcome assessment of clinical measures was not blinded.

Follow-up and intention-to-treat

The ACDPI trial was designed to continue until each participant had completed 24 months of post-surgical follow-up. Participants were to be assessed at six weeks, three, six, 12 and 24 months after surgery. At the time of publication, 37 (67.3%) and 9 (16.4%)

participants had been assessed at the 12- and 24-month follow-up, respectively, however the number from each of the treatment arms was not reported.

Sample size and power

The trial was designed to demonstrate equivalence between cervical AIDR and cervical spinal fusion ie, that cervical AIDR is no worse than cervical spinal fusion. Using a significance level of 0.05, a power of 0.80 and a minimum clinically significant difference in neck disability index (NDI) of 15 per cent, it was estimated that approximately 60 individuals would participate in the trial.

Results of the RCT

Porchet & Metcalf (2004) reported the mean range of motion (ROM) without standard deviations at the treated level in each of the treatment groups (Table 17). Participants undergoing cervical AIDR maintained a similar ROM of 5.9˚ at 12 months follow-up compared with baseline (5.9˚), however participants undergoing cervical spinal fusion showed no significant preservation of motion at the 12-month follow-up (1.1˚, which is considered to be no movement). Porchet & Metcalf (2004) reported that no statistically significant differences in adjacent-level motions were observed at 12 months.

Table 17 Range of motion reported in the RCT: Cervical AIDR versus cervical fusion

Follow-up at: (months)	Mean of range of motion	
	AIDR	Spinal fusion
Baseline	5.9°	6.3°
1.5	7.2°	2.5°
3	6.5°	1.6°
6	7.0°	2.1°
12	5.9° (n=22)	1.1° (n=14)

Table 18 presents the clinical outcomes from Porchet & Metcalf (2004) and whilst not explicitly reported, it appears that the values reported are means for the treatment groups Standard deviations and the number of participants in each treatment group contributing to the data were not reported. The improvement in NDI in the treatment group was statistically equivalent ($p<0.05$, non-inferiority margin = 10) up to the 24-month follow-up. With respect to neck pain, the statistical significance of improvement from the pre-operative score within each treatment group could not be shown between the two treatment arms. With respect to arm pain, statistical equivalence was demonstrated between the two treatment arms ($p<0.05$, non-inferiority margin = 10) up to the 24-month follow-up. Neurological status was assessed using a scale based on four measurements: motor, sensory, reflexes and the foraminal compression tests. No details were provided regarding the scoring of this scale, ie maximum score and whether higher or lower scores delineate a better clinical outcome.

Table 18 Clinical outcomes of the RCT: Cervical AIDR versus cervical fusion

Study	Follow up (months)	Clinical outcome[a]							
		NDI[b,c]		Neck pain (VAS)[c,d]		Arm pain (VAS)[c,d]		Neurological status[e]	
		AIDR	Fusion	AIDR	Fusion	AIDR	Fusion	AIDR	Fusion
Porchet & Metcalf (2004) ACDPI trial	Baseline	53	60	13.3	14.9	13.9	14.2	92	84
	1.5	19	25	5.9	5.3	3.6	4.9	96	91
	3	16	22	5.7	5.4	4.1	5.3	96	95
	6	19	21	7.0	5.5	4.9	5.6	98	95
	12	17	19	5.5	5.5	4.9	6.1	98	97
	24	10	22	4.7	5.9	4.4	7.7	99	94

Abbreviations: NDI, neck disability index; VAS, visual analogue scale

[a] Mean NDI, VAS (neck and arm pain) and neurological scores of participants undergoing cervical disc replacement or spinal fusion. Measures assumed to be means. No SD reported

[b] The NDI is a questionnaire containing 10 questions used to measure cervical pain and disability associated with activities of daily living. Lower scores represent less pain and disability

[c] Results read off Figure 6 of Porchet & Metcalf (2004) therefore results are approximate

[d] 20-point composite score. Lower scores represent a better outcome

[e] Results taken from a graph in Appendix 7 of the Application and are therefore approximate

Further clinical outcomes of adjacent level surgery and the number of participants requiring re-operation in the cervical AIDR and fusion groups in the ACDPI trial (Porchet & Metcalf 2004) are presented in Table 19.

Table 19 Adjacent level surgery and re-operation in the RCT: Cervical AIDR versus cervical fusion

Study	Adjacent level surgery (%)		Re-operation (%)	
	AIDR n/N (%)	Fusion n/N (%)	AIDR n/N (%)	Fusion n/N (%)
Porchet & Metcalf (2004) ACDPI Trial	0/27 (0.0)	2/28 (7.1)	1[a]/27 (3.7)	0/28 (0.0)

[a] The initial Prestige disc was malpositioned, therefore it was removed and spinal fusion performed. This participant was only identified in Porchet & Metcalf (2004)

Tables 20 and 21 present the operative and general health outcome results reported in Porchet & Metcalf (2004). It was not reported whether there were any significant differences in the amount of blood loss or days in hospital between the two treatment groups. Statistically significantly fewer participants treated with cervical AIDR required bracing than those treated with cervical fusion (RR=0.12, 95% CI 0.04, 0.34; Table 20). With respect to SF-36 scores (Table 21), the differences between the two treatment arms were reported as not statistically significant at all time points.

Table 20 Operative and general health outcomes of the RCT: Cervical AIDR versus cervical fusion

Study	Mean blood loss[a,b] (mL)		Bracing[a] (%)		Mean hospital stay[a] (days)	
	AIDR[b]	Fusion[b]	AIDR n/N (%)	Fusion n/N (%)	AIDR[b]	Fusion[b]
Porchet & Metcalf (2004) ACDPI trial	86	153.7	3/27 (11.5)	27/28 (96.2)	2.8	2.9

[a] Appendix 7 of the Application
[b] Number not reported

Table 21 SF-36 physical component scores in the RCT: Cervical AIDR versus cervical fusion

Study	Mean SF-36 Physical Component Score[a]	
	AIDR[b]	Fusion[b]
Porchet & Metcalf (2004) ACDPI trial	Baseline: 36 6 months: 46 12 months: 50 24 months: 53	Baseline: 34 6 months: 43 12 months: 47 24 months: 45

[a] Results read off Figure 7 of Porchet & Metcalf (2004). therefore results are approximate
[b] Number not reported

Discussion of RCT

The RCT was designed to demonstrate equivalence, which may account for the majority of outcomes not being reported as statistically significantly different between the treatment groups. Porchet & Metcalf (2004) concluded that the Prestige II disc is a viable alternative to cervical spinal fusion. However, the trial enrolled a limited number of participants, did not report full data and measures of variance at all time points and included relatively short-term follow-up. In addition, participants, investigators and outcome assessors were not blinded to treatment. Non-blinding combined with the relatively subjective nature of many of the outcomes assessed may have led to bias in the results obtained. Equivalence trials generally require large samples and hence the RCT described by Porchet &Metcalf (2004) may have been underpowered for the conclusions drawn.

Critical appraisal of systematic reviews and HTA reports

The one procedure brief identified (ASERNIP-S 2001b) may not have been a systematic review as the search strategy was not reported. It included a multicentre, prospective European trial of 86 participants who were required to have cervical disc herniation accompanied by either radiculopathy or myelopathy and to be unresponsive to conventional treatment. The results of this reported trial appear to have been subsequently reported in Goffin et al (2002) and Goffin et al (2003). Goffin et al (2003) was not included in the evaluation of the effectiveness of cervical AIDR in the current review as this reports results of a case series.

In addition, data from a British trial of two cohorts, one receiving cervical AIDR and the other cervical fusion were included in the procedure brief. These data came from an abstract from the Congress of Neurosurgeons meeting in San Antonio, Texas and were subsequently published in Wigfield et al (2002a). They were excluded from the current

report as the study was not randomised and constituted an inappropriate patient group because enrolled participants were not required to have failed non-operative treatment.

Validity of systematic reviews and HTA reports

The validity of the identified systematic reviews and HTA reports assessing the effectiveness of cervical AIDR is summarised in Table 22.

Table 22 Validity of systematic reviews and HTA reports of cervical AIDR

Indicator of validity	ASERNIP-S 2001b Procedure Brief
Focused question	No
Inclusion and exclusion criteria	• Artificial discs included: – Bristol (Cummins) disc – Bryan cervical disc system • Patients: Not reported • Studies: Not reported
Explicit comprehensive search strategy	Search strategy: Not reported
Assessed validity of included studies	No

Results from the systematic reviews and HTA reports

The primary studies included in the current review and the published procedure brief (ASERNIP-S 2001b) are listed in Table 23.

Table 23 Studies included in the current review and HTA report for cervical AIDR

Study design	Current assessment report	ASERNIP-S 2001b procedure brief
RCTs	Porchet & Metcalf (2004)	None
Case series	None for assessment of effectiveness	Reports an unreferenced multicentre, prospective randomised European trial[a] Cummins et al (1998)[b] Wigfield (2000)[c]

[a] Results later published in Goffin et al (2002, 2003). These publications were not included in the current assessment report as they described a case series

[b] Reports adverse event data only

[c] Data from an abstract presented at the Congress of Neurosurgeons meeting in San Antonio, Texas. Results subsequently published in Wigfield et al (2002a), which was not included in the current assessment report as the study was not randomised and constituted an inappropriate patient group because participants were not required to have failed non-operative treatment

The ASERNIP-S procedure brief (2001b) reports effectiveness outcomes for participants receiving the Bryan cervical artificial disc. These results were later published in case series (Goffin et al 2002, 2003). Using Odom's classification system of 'excellent', 'good' or 'fair' to perform a neurological assessment, 79 per cent (34/43) of participants had an excellent result at six months that increased to 91 per cent (21/23) at 12 months. Radiographic measurement of post-operative ROM was made at 6 and 12 months. Ninety-one per cent of participants (40/44) had flexion/extension ROM equal to or greater than 2° at six months compared to 88 per cent (15/17) at 12 months. No anterior-posterior device migration greater than three millimetres was observed in any participant, however one case of a cephalic shell migration of a three millimetres displacement in an anterior direction was observed.

The ASERNIP-S procedure brief also contains effectiveness data from a British trial of two cohorts of patients (Wigfield 2000) who received either an artificial Bristol joint/disc (n=12) or an autologous bone graft fusion (n=13). The data included in the procedure brief was extracted from an abstract presented at the Congress of Neurosurgeons meeting in San Antonio, Texas and were subsequently published in Wigfield et al (2002a). This study was, however, excluded from the current report as it was non-randomised and constituted an inappropriate patient group because enrolled participants were not required to have failed non-operative treatment. The cervical fusion group showed a significant increase in adjacent level movement at one-year follow-up compared to the Bristol artificial joint group ($p<0.001$). The main increase in movement occurred at discs that were considered normal pre-operatively.

Discussion of systematic reviews and HTA reports

The ASERNIP-S procedure brief (ASERNIP-S 2001b) concluded that the current research evidence suggested that the Bryan cervical disc had an excellent outcome based on neurological assessment and that the Bristol (Cummins) disc was protective against undesirable motion seen with cervical fusion, in addition to maintaining motion at the site of prosthesis. This conclusion should be treated with caution due to the following limitations of the report:

- It lacks a focussed question or patient group, therefore it is not possible to assess whether the included participants are representative of those assessed in the current review, specifically with respect to the requirement to have failed non-operative therapy.
- The search strategy is not reported, therefore it is not possible to ascertain whether the report is systematic. Lack of a systematic search of multiple databases could potentially lead to publication bias.
- It includes only data from non-randomised studies, however it does not include all of the non-randomised studies identified in the current report.

Lumbar AIDR versus lumbar fusion

Two trials comparing lumbar AIDR and lumbar spinal fusion were identified – the DePuy Spine Charité™ Artificial Disc Trial and the Food and Drug Administration (FDA) ProDisc II Trial.

A systematic search of the literature identified four publications relating to the DePuy Spine Charité™ Artificial Disc P040006 Trial Report provided by the Applicant. Only one of the four (Geisler et al 2004) reported the results of the entire trial population and was therefore the source of data for this review. The remaining three (Guyer et al 2004, McAfee et al 2003a, McAfee et al 2003b) only reported results from individual centres involved in the trial.

Two RCTs comparing ProDisc II with spinal fusion (Delamarter et al 2003, Zigler 2004) were also identified. Delamarter et al (2003) and Zigler (2004) reported results from two of 19 centres participating in the Food and Drug Administration (FDA) ProDisc II Trial. Neither the results of the entire ProDisc II trial nor results from the other 17 centres involved in the trial were published at the time of writing. Publication of single centre

results within a larger multi-centre RCT is generally considered very poor research practice. In addition, there may be reporting bias if only centres with large populations or those with positive results reported their data. Two additional publications (Zigler 2003, Zigler et al 2003) relating to Zigler (2004) were also identified. The two reported interim results on a subset of the participants covered in Zigler (2004) and are therefore not reported in this review as separate populations.

The descriptive characteristics of the identified RCTs are presented in Table 24. All of the trials were performed in the United States of America and the length of follow-up was six to 24 months. The trial populations varied in size from 53 to 267 participants. Each enrolled about 50% males and participants of a similar age.

Critical appraisal of the RCTs

Table 24 Descriptive characteristics of RCTs: Lumbar AIDR versus lumbar fusion

Study	Location	Enrolment period	Indication	Type of artificial disc used	Type of spinal fusion	Length of follow-up (months)	Study population		
							N	Number of males (%)	Mean age (range) (years)
SB Charité™ III									
Trial Report P040006 Geisler et al (2004)	USA	Training: 21 Mar 2000 to 22 May 2001 Randomised: 16 May 2000 – 24 Apr 2002	Spinal arthroplasty with single level lumbar DDD, L4-L5 or L5-S1	SB Charité™ III (Charité artificial disc)	Anterior interbody fusion with BAK cage	24	Total: 267 AIDR[a]: 182 Fusion[b]: 85	130/267 (48.7) AIDR: 83 (45.6) Fusion: 47 (55.3)	AIDR: 39.5 (19–60) Fusion: 40.1 (20–60)
ProDisc II									
Delamarter (2003)	USA	Not reported	Patients with one or two levels of lumbar DDD with predominate back pain	ProDisc II	Circumferential fusion	6	53	30/53 (56.6)	AIDR: 40.3 (19–59) Fusion: 42.2 (26–59)
Zigler (2004)	USA	2003	DDD at one or two adjacent vertebral levels, L3–S1	ProDisc II	Standard circumferential spinal fusion	6 (n=78) 12 (n=54))	78 (initial cohort)	20/39 (51.3)[c]	AIDR: 37.7 for n=28 Fusion: 41.6 for n=11

[a] 205 participants randomised
[b] 99 participants randomised
[c] Not reported for the remaining 39 subjects

The inclusion and exclusion criteria for enrolment into each of the trials are presented in Table 25. Eligibility for enrolment required that participants were aged between 18 and 60 years and had failed conservative treatment for at least six months. Participants enrolled in the DePuy Spine Charité™ Artificial Disc Trial were required to have an Oswestry Disability Index (ODI) score of 30 points or greater, whereas those enrolled in the FDA ProDisc II Trial (Delamarter et al 2003, Zigler 2004) required a minimum score of 40 out of 100. Participants enrolled in the DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006, Geisler et al 2004) were to have single level disease at L4-L5 or L5-S1, and those participating in the FDA ProDisc II trial were to have DDD at no

more than two adjacent vertebral levels between L3 and S1. Individuals were excluded from both trials if they had multiple level (>2) degeneration or previous lumbar fusion, were morbidly obese (body mass index >40), had a metal allergy or autoimmune disease or were pregnant or considering becoming pregnant. The inclusion and exclusion criteria reported in Delamarter et al (2003) and Zigler et al (2004) appear to differ, with Zigler et al (2004) providing significantly more detail than Delamarter et al (2003).

Table 25 Patient selection criteria for the RCTs: Lumbar AIDR versus lumbar fusion

Study	Inclusion	Exclusion
SB Charité™ III		
Trial Report P040006 Geisler et al (2004)	• Male or female • 18–60 years • Symptomatic DDD with objective evidence of lumbar DDD (by CT or MR scan followed by discogram). DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. DDD patients may also have up to 3 mm of spondylolisthesis at the involved level. • Single level disease at L4-L5 or L5-S1 • At least 6 months of unsuccessful conservative therapy • ODI score ≥30 points • Patient a surgical candidate for an anterior approach to the lumbar spine (<3 abdominal surgeries) • Back pain at the operative level only by discogram • Leg pain and/ or back pain in the absence of nerve root compression, per MRI or CT scan, without prolapse or narrowing of the lateral recess • VAS = 40 mm • Able to comply with protocol • Informed consent	• Previous or other spinal surgery at any level, except prior discectomy, laminotomy, laminectomy, or nucleolysis at the same level • Multiple level degeneration • Previous trauma to the L4, L5, or S1 levels in compression or burst • Non-contained or extruded herniated nucleus pulposus • Mid-sagittal stenosis of <8 mm (by MR or CT) • Spondylolisthesis >3 mm • Lumbar scoliosis (>11° sagittal plane deformity) • Spinal tumour • Active systematic or surgical site infection • Facet joint arthrosis • Arachnoiditis • Isthmic spondylolisthesis • Chronic steroid use • Metal allergy • Pregnancy • Autoimmune disorders • Psychosocial disorders • Morbid obesity (BMI >40) • Bone growth stimulator use in spine • Investigational drug or device use within 30 days • Osteoporosis or osteopaenia or metabolic bone disease • Positive single or bilateral straight leg raising test
ProDisc II		
Delamarter et al (2003)	• Patients aged 18–60 years • Failed conservative treatment for at least 6 months • Minimum ODI score of 40 out of 100 • No more than one- or two-level DDD from L3 to S1	• Patients with metal allergies • Previous lumbar fusions • Compromised vertebral bodies • Severe facet degeneration

Table 25 (cont'd) Patient selection criteria for the RCTs: Lumbar AIDR versus lumbar fusion

Study	Inclusion	Exclusion
ProDisc II (cont'd)		
Zigler (2004)	• Age 18–60 years • At least 6 months of failed non-operative therapy • DDD at one or two adjacent vertebral levels between L3 and S1, where a diagnosis of DDD requires: – Primarily back and/or radicular pain – Radiographic confirmation of any one of the following by CT, MRI, discography, plain film, myelography and/or flexion/extension films: I. Lack of instability (defined as >3 mm of translation or >5° of angulation) II. Decreased disc height >2 mm III. Scarring/thickening of the annulus fibrosus IV. Herniated nucleus pulposus V. Vacuum phenomenon • ODI score of ≥20/50 (40%) • Psychosocially, mentally or physically able to fully comply with this protocol, including adhering to the follow-up schedule and requirements and the filling out of forms	• >2 degenerative levels • End plate dimensions <34.5 mm in the coronal plane and/or <27 mm in the sagittal plane • Known allergy to titanium, polyethylene, cobalt, chromium or molybdenum • Prior lumbar fusion • Post traumatic vertebral body compromise/deformity • Facet joint degeneration • Lytic spondylolisthesis or spinal stenosis • Degenerative spondylolisthesis of grade >1 • Back or leg pain of unknown aetiology • Osteoporosis • Metabolic bone disease (excluding osteoporosis, eg Paget disease) • Morbid obesity (BMI >40 or weight >100 pounds over ideal body weight) • Pregnant or interested in becoming pregnant in the next 3 years • Active systemic/local infection • Medications or drugs known to potentially interfere with bone/soft tissue healing excluding smoking (eg, steroids) • Rheumatoid arthritis or other autoimmune spondylarthopathies • Systemic disease including, but not limited to, AIDS, HIV, hepatitis • Active malignancy: a patient with a history of any invasive malignancy (except non-melanoma skin cancer), unless treated with curative intent and no clinical signs or symptoms of the malignancy for at least 5 years

The validity of the RCTs are presented in Table 26. Whilst the outcomes measured in Delamarter et al (2003) and Zigler et al (2004) appear to be different, the main outcomes measured in the two publications are the same (ODI, pain on the Visual Analogue Scale [VAS] and patient satisfaction). Differences exist in the minor outcomes reported in the two publications that may have arisen from the particular interests of the centres involved.

Validity of RCTs

Table 26 Validity of RCTs: Lumbar AIDR versus lumbar fusion

Study	Validity					Outcome measures
	Method of randomisation	Concealment of allocation	Inclusion of randomised participants	Blinding	Losses to follow-up	
SB Charité™ III						
Trial Report P040006 Geisler et al (2004)	Block randomisation in all 15 sites Ratio of AIDR:Fusion = 2:1 The first 5 patients in all 15 sites were not randomised but received the intervention	Not reported	No	Not reported	Overall, 12 subjects (5 from treatment group, 7 from control group)	Primary[a]: 'Overall Success' defined as a participant with all of the following conditions: • improvement >25% in ODI score at 24 months compared with baseline • no device failures requiring revision, re-operation or removal • no pseudoarthritis (control group) • absence of major complications, defined as vessel injury, neurological damage, or nerve root injury • maintenance or improvement in neurological status at 24 months, with no permanent neurological deficits compared to baseline • ODI Score at 24 months or later Secondary: • Pain VAS improvement of = 20 mm • SF-36 improvement = 15% • Disc height (lateral X-ray) • Displacement or migration of the device • Radiolucency around the implant for Charité patients at 24 months

Table 26 (cont'd) Validity of RCTs: Lumbar AIDR versus lumbar fusion

Study	Validity					Outcome measures
	Method of randomisation	Concealment of allocation	Inclusion of randomised participants	Blinding	Losses to follow-up	
ProDisc II						
Delamarter et al (2003)	Not reported	Not reported	Unclear	All patients were blinded to treatment until after the surgical procedure	Not reported	• ODI • Pain on the VAS before surgery and at each follow-up • Patient satisfaction • Investigator initiated structured queries on types of recreational activity, ambulatory status, and medications taken for pain • Fusion patients rated their pain at graft harvest site as none, mild, moderate or severe
Zigler 2004	Not reported	Not reported	Unclear	Not reported	Not reported	• ODI • VAS assessing pain • Patient satisfaction rates (0 totally dissatisfied to 10 completely satisfied) • ROM, motor strength, tension signs, reflexes, sensations and standing X-rays (neutral, flexion extension and coronal plane bending films)

[a] Not clearly defined in Trial Report P040006

Randomisation and allocation concealment

The method of randomisation was reported for the DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006, Geisler et al 2004) but not for the FDA ProDisc II trial (Delamarter et al 2003, Zigler 2004). Concealment of allocation was reported for neither trial.

Blinding

It is unclear from the DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006, Geisler et al 2004) if participants were blinded or whether any methods of blinding were used. Delamarter et al (2003) reported that participants were blinded to allocation of treatment until the surgical procedure was performed. Zigler (2004) did not explicitly report that patients were blinded until surgery was performed, however as Delamarter et al (2003) and Zigler (2004) relate to the same FDA ProDisc II Trial, it is likely that the participants reported in Zigler (2004) were informed of which procedure they had undergone after surgery.

Follow-up and intention-to-treat

Participant follow-up in the RCTs is presented in Table 27. In the DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006, Geisler et al 2004), 83.9 per cent of the participants were followed-up for 24 months. Zigler (2004) reported no losses to follow-up at six months and that 69.2 per cent of participants were followed-up for 12 months. Between-group losses to follow-up were not reported. Delamarter et al (2003) did not report losses to follow-up.

Table 27 Patient follow-up: Lumbar AIDR compared with lumbar fusion

Study	Follow up period (months)	AIDR n/N (%)	Spinal fusion n/N (%)	All n/N (%)
SB Charité™ III				
Trial Report P040006 Geisler et al 2004	24	177/205 (86.3)	78/99 (78.8)	255/304 (83.9)
ProDisc II				
Delamarter et al 2003	6–15	35	18	53
Zigler 2004	6 12	55/55 (100.0) Not reported	23/23 (100.0) Not reported	78/78 (100.0) 54/78 (69.2)

Sample size and power

The DePuy Spine Charité™ Artificial Disc Trial was designed to demonstrate equivalence between lumbar AIDR and lumbar spinal fusion, ie that lumbar AIDR is no worse than lumbar spinal fusion. The sponsor justified the sample size used in the DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006, Geisler et al 2004) on the assumption of a 70 per cent success rate for both treatment groups. The estimated sample size was 174 participants for lumbar AIDR and 87 participants for lumbar fusion. Assuming a 10 per cent dropout rate, 194 participants would be randomised to lumbar AIDR and 97 to lumbar fusion. The trial reported that the first five participants enrolled at each of the 15 centres involved in the trial would undergo lumbar AIDR for training purposes, so that a total of 366 participants would need to be enrolled (269 for lumbar AIDR and 97 for lumbar fusion).

The rationale for the sample size in the FDA ProDisc II trial was not reported (Delamarter et al 2003, Zigler 2004).

Results of RCTs

The primary outcome measures for the DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006) were 'overall success' (defined in Table 26) and the ODI score. Table 28 presents the proportion of participants achieving 'overall success' and the success rates for each of the variables included in the overall success composite score in each treatment group at 24 months. Compared to the lumbar fusion group, participants in the lumbar AIDR group achieved a statistically significantly greater proportion of overall success at 24 months ($p<0.0001$) despite there being no significant differences between the individual variables included in the overall success composite score (Table 28). The statistical methods used to compare these results were not reported.

Table 28 'Overall success' and success rates for each of the variables included in the overall success composite score: Lumbar AIDR versus lumbar fusion

Outcome variable	AIDR (n=182)	Fusion (n=85)	p-value
Overall success			
ODI score success (>25% improvement), device failure success (none), major complication success (none) and neurological deterioration success (none)	114 (62.2%)	45 (52.9%)	<0.0001
Individual success rates			
ODI score success (>25% improvement)	127 (69.7%)	49 (57.6%)	0.0540
Device failure success (none)	174 (95.6%)	77 (90.6%)	0.1632
Major complication success (none)	180 (98.9%)	84 (98.8%)	1.000
Neurological deterioration success (none)	160 (87.9%)	74 (87.1%)	0.8437

Table 29 presents the results for the ODI. Trial Report P040006 and Geisler et al (2004) reported that there was a statistically significant difference ($p<0.0001$) in mean ODI scores at all follow-up visits for participants randomised to lumbar AIDR and lumbar fusion compared with baseline. No standard deviations in ODI scores were reported. Comparison of ODI scores between the lumbar AIDR and lumbar fusion groups showed that participants randomised to AIDR had statistically significantly lower ODI scores at six weeks ($p=0.0485$), three months ($p=0.0087$) and six months ($p=0.0126$), but not at 12 months (0.1197) or 24 months ($p=0.3407$). The statistical methods used to compare these results were not reported.

Delamarter et al (2003) also reported ODI scores achieved for participants randomised to lumbar AIDR and lumbar fusion at six weeks, three and six months after surgery. Delamarter et al (2003) did not report standard deviations. A statistically significant difference between the lumbar AIDR and fusion groups was observed at three months post-operatively, but not at six weeks or six months after surgery (Table 29).

Zigler (2004) reported that there was a progressive decrease in ODI scores in the participants randomised to lumbar AIDR during six months of follow-up. A smaller decrease in ODI scores was observed for the lumbar fusion group and a statistically significant difference between the two groups was observed only at three months ($p=0.02$).

Table 29 Mean ODI score: Lumbar AIDR versus lumbar fusion

Follow-up (months)	SB Charité™ III			ProDisc II					
	Trial Report P040006, Geisler et al (2004)			Delamarter et al (2003)			Zigler et al (2004)		
	AIDR (N, mean)	Fusion (N, mean)	p-value	AIDR	Fusion	p-value	AIDR	Fusion	p-value
Baseline	N=182, 49.8	N=85, 51.7	NR	31.26	30.67	NS	NR	NR	NS
1.5	N=174, 37.4	N=78, 43.7	0.0485	20.65	25.00	NS	NR	NR	NS
3	N=168, 29.6	N=81, 36.7	0.0087	17.93	25.00	<0.05	NR	NR	0.02
6	N=170, 27.1	N=76, 34.8	0.0126	15.07	14.57	NS	NR	NR	NS
12	N=169, 25.9	N=72, 30.9	0.1197	NR	NR	NA	NA	NA	NA
24	N=177, 25.8[a]	N=79, 30.1[a]	0.3407	NR	NR	NA	NA	NA	NA

Abbreviations: NS, not statistically significant; NR, not reported; NA, not applicable
Negative change indicates improvement in ODI
[a] Results reported in both Trial Report P040006 and Geisler et al (2004), all other results presented only in Trial Report P040006

The proportion of participants in the DePuy Spine Charité™ Artificial Disc Trial experiencing at least 25 per cent improvement in ODI scores from baseline was also reported (Table 30). There was a statistically significant difference in the proportion of participants achieving a 25 per cent improvement in ODI scores between the lumbar AIDR and lumbar fusion groups at six weeks, three and six months, but not at 12 or 24 months (Table 30). However, Geisler et al (2004) reported that 62 and 49 per cent of participants randomised to lumbar AIDR and lumbar fusion, respectively, had a 25 per cent improvement in ODI scores at 24 months and also reported a statistically significant difference between the two groups at this time point (p=0.0354).

Table 30 Proportion of participants achieving at least 25 per cent improvement in ODI scores: Lumbar AIDR versus lumbar fusion

Follow-up (months)	SB Charité™ III Trial Report P040006		
	AIDR n/N (%)	Fusion n/N (%)	p-value
1.5	80/174 (46.0)	24/78 (30.8)	0.0269
3	107/168 (63.7)	37/81 (45.7)	0.0091
6	121/170 (71.2)	41/76 (53.9)	0.0130
12	120/169 (71.0)	47/72 (65.3)	0.3637
24	128/177 (72.3)	49/79 (62.0)	0.1860

The ROM of participants during follow-up is presented in Table 31. The vertebral ROM was measured on the lateral flexion and extension views using the Cobb method at the operated level and was measured at three, six, 12 and 24 months (Trial Report P040006, Geisler et al 2004). Trial Report P040006 stated that the ROM for participants randomised to lumbar AIDR was near physiologic levels.

Delamarter et al (2003) also reported results of ROM for the treated vertebral segments L4-L5 and L5-S1 separately. Estimated motion was measured from radiographs by

measuring the flexion-extension angle difference. Participants randomised to lumbar AIDR had an increase in motion at the six-month follow-up for the L4-L5 vertebral segment compared with baseline, however participants randomised to lumbar fusion had a significant decrease in motion. A significant difference in ROM was observed between participants randomised to lumbar AIDR and lumbar fusion ($p<0.04$) at six months (Delamarter et al 2003). A similar trend was reported for the L5-S1 vertebral segments, with an increase in ROM in participants receiving lumbar AIDR compared with lumbar fusion, however the difference was not statistically different at six-months follow-up.

Table 31 Range of motion: Lumbar AIDR versus lumbar fusion

Study	Range of motion		
	AIDR	Fusion	p-value
SB Charité™ III			
Trial Report P040006 Geisler et al (2004)	**N, Mean (SD)**	**N, Mean (SD)**	
	3 months: N=133, 4.9° (3.89°) [a]	NR	NR
	6 months: N=163, 6.0° (4.56°) [a]	NR	NR
	12 months: N=161, 7.0° (4.92°) [a]	NR	NR
	24 months: N=175, 7.4° (5.24°)[b]	N=NR, 1.1° (0.87°)[c]	NR[d]
ProDisc II			
Delamarter et al (2003)	**Mean (SD) [Range]**	**Mean (SD) [Range]**	
	L4-L5	L4-L5	
	Baseline: 7.04° (5.60°) [–5.00° to +18.00°]	Baseline: 11.46° (7.86°) [0.00° to +27.00°]	NR[d]
	1.5 months: 7.62° (4.21°) [–5.00° to +15.00°]	1.5 months: Not measured	NA
	3 months: 7.55° (4.15°) [–1.00° to 17.00°]	3 months: Not measured	NA
	6 months: 10.11° (3.33°) [+5.00° to +17.00°]	6 months: 0.00° (4.24°) [–3.00° to +3.00°]	<0.04
	L5-S1	L5-S1	
	Baseline: 6.17° (8.19°) [–25.50° to +16.00°]	Baseline: 3.33° (8.23°) [–10.00° to +21.00°]	NR[d]
	1.5 months: 5.42° (5.80°) [–10.00° to +13.00°]	1.5 months: Not measured	NA
	3 months: 8.67° (6.46°) [+1.00° to +24.00°]	3 months: Not measured	NA
	6 months: 7.62° (4.43°) [+2.00° to +17.00°]	6 months: 4.75° (4.19°) [+2.00° to +11.00°]	NS
Zigler (2004)[e]	Forward bending	Forward bending	
	Baseline: 13.18	Baseline: 10.91	0.37
	6 months: 7.32	6 months: 13.43	0.02
	Left lateral bending	Left lateral bending	
	Baseline: 2.89	Baseline: 2.64	0.75
	6 months: 1.10	6 months: 2.86	0.02
	Right lateral bending	Right lateral bending	
	Baseline: 2.84	Baseline: 2.64	0.19
	6 months: 1.30	6 months: 3.00	0.01

Abbreviations: N, number; NA, not applicable; NR, not reported; NS, not statistically significant
Negative change indicates improvement in ODI
[a] Results reported in Trial Report P040006
[b] Results reported in both Trial Report P040006 and Geisler et al (2004)
[c] Results reported in Geisler et al (2004), but not in Trial Report P040006
[d] Unable to calculate as the number of participants was not reported
[e] Reported ROM in distance in inches (the greater the value, the more restricted the motion)

Zigler (2004) reported that participants randomised to lumbar AIDR showed statistically significantly improved ROM at three and six months following surgery compared with baseline values. As shown in Table 31, participants randomised to lumbar AIDR (n=55) had significantly improved ROM compared with participants randomised to fusion (n=23) six months post-operatively.

Other outcomes reported in the RCTs were pain as measured by the VAS and neurological status (Table 32). The DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006) reported that a significant improvement in pain was observed in 74 and 62 per cent of participants randomised to lumbar AIDR and lumbar fusion, respectively. Worsening of pain was observed in 12 per cent of participants randomised to lumbar AIDR and 16 per cent of those allocated to lumbar fusion. Geisler et al (2004) reported that the mean VAS scores were 72 and 30.6 at baseline and 24 months, respectively, for the lumbar AIDR group and 71.8 and 36.3 at baseline and 24 months, respectively, for the lumbar fusion group.

Delamarter et al (2003) reported statistically significant differences in VAS scores for the lumbar AIDR and lumbar fusion groups at three and six months post-operatively, with the AIDR group having significantly less pain. No significant differences in VAS scores were observed between the treatment groups at six months (Delamarter et al 2003). Zigler (2004) stated that no significant differences in VAS scores were observed between participants randomised to lumbar AIDR or lumbar spinal fusion, although there was a trend toward an increasing improvement over time in participants receiving ProDisc II.

The neurological status of participants randomised to lumbar AIDR and lumbar fusion was also reported for individuals in the DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006). The proportions of participants in both treatment groups experiencing no change in their neurological status were 77 and 76 per cent of participants in the lumbar AIDR and lumbar fusion groups, respectively. Delamarter et al (2003) and Zigler (2004) did not report on the neurological status of participants in the FDA ProDisc II trial.

Table 32 Pain as measured by the VAS and neurological status of participants in the RCTs: Lumbar AIDR versus lumbar fusion

Study	Pain (VAS)			Neurological status	
	AIDR	Fusion	p-value	AIDR	Fusion
SB Charité™ III					
Trial Report P040006	n/N (%)	n/N (%)		n/N (%)	n/N (%)
	Significant improvement: 128/174 (73.6) Some improvement: 22/174 (12.6) No change: 3/174 (1.7) Deterioration: 21/174 (12.1)	Significant improvement: 49/79 (62.0) Some improvement: 11/79 (13.9) No change: 6/79 (7.6) Deterioration: 13/79 (16.5)	0.0759 NR NR NR	No change: 131/171 (76.6) Significantly improved: 5/171 (2.9) Slightly improved: 27/171(15.8) Slightly deteriorated: 7/171 (4.1) Significantly deteriorated: 1/171 (0.6)	No change: 58/76 (76.3) Significantly improved: 5/76 (6.6) Slightly improved: 7/76 (9.2) Slightly deteriorated: 3/76 (3.9) Significantly deteriorated: 3/76 (3.9)
ProDisc II					
Delamarter (2003)	Baseline: 7.44 1.5 months: 2.89 3 months: 3.65 6 months: 4.38	Baseline: 6.84 1.5 months: 4.74 3 months: 4.78 6 months: 3.96	NS <0.01 <0.001 NS	NR	NR
Zigler et al (2004)	Baseline: NR 1.5 months: NR 3 months: NR 6 months: NR 12 months: NR	Baseline: NR 1.5 months: NR 3 months: NR 6 months: NR 12 months: NR	NS NS NS NS NS	NR	NR

Abbreviations: NS, not statistically significant; NR, not reported

Geisler et al (2004) and Zigler (2004) reported the blood loss experienced by participants receiving either lumbar AIDR or lumbar fusion. Participants randomised to lumbar AIDR lost 207 mL (Geisler et al 2004) and 68.9 mL (Zigler 2004) and participants randomised to lumbar fusion lost 224 mL (Geisler et al 2004) and 175.0 mL (Zigler 2004) of blood. Zigler (2004) also reported the mean time of hospital stay for the two treatment groups as an average of 2.1 and 3.5 days for those randomised to lumbar AIDR and lumbar fusion, respectively.

Table 33 presents results of the SF-36 Physical Component Score and Mental Composite Score of participants randomised to lumbar AIDR and lumbar fusion in the DePuy Spine Charité™ Artificial Disc Trial (Trial Report P040006). A similar proportion of participants in each treatment group achieved at least a 15 per cent improvement in both the Physical Component Score and Mental Composite Score.

Table 33 General health outcomes reported in RCT of SB Charité™ III: Lumbar AIDR versus lumbar fusion

SF-36 Physical Component Score and Mental Composite Score[a]	
AIDR	**Fusion**
N=136	N=62
At 24 months: 99 (73%) had 15% or more improvement in PCS 68 (50%) had 15% improvement for MCS	At 24 months: 41 (66%) had 15% or more improvement in PCS 34 (55%) had 15% improvement for MCS

Abbreviations: PCS, physical component score; MCS, mental composite score
[a] Reported in Trial Report P040006, Giesler et al (2004)

Discussion of RCTs

The search strategy identified a number of publications associated with two RCTs comparing lumbar AIDR and lumbar spinal fusion. The two RCTs and their relevant publications include the DePuy Spine Charité™ Artificial Disc Trial (Geisler et al 2004, Guyer et al 2004, McAfee et al 2003a, McAfee et al 2003b) and the ProDisc II trial (Delamarter et al 2003, Zigler 2004). These publications reported results of the RCTs differently, precluding the performance of any meta-analyses. Enrolment criteria for participants in each of the trials varied slightly.

Data reported from the trials included relatively short-term follow-up with a maximum of 24 months. In addition, participants and investigators were not blinded to treatment, which, when combined with the relatively subjective nature of many of the outcomes assessed, may have led to bias in the results obtained. The results from the ProDisc II trial should be interpreted with caution as both Delamarter et al (2003) and Zigler (2004) reported results from only two of 19 centres involved in the multicentre trial. This may have led to reporting bias if only centres with large populations or those with positive results reported their data.

Case series

Although excluded from the effectiveness section of this review, 25 case series reporting on the use of lumbar AIDR were identified – 14 published in English and 11 published in other languages (Appendix F). Of the 14 case series reported in the English language, eight explicitly stated that enrolled participants were required to have failed at least six months of non-operative treatment, whereas five did not state this criterion for participant inclusion. These five case series were included in the Appendix F however, as the participants were reported to have symptoms for many years and were thus assumed to have undergone non-operative treatment for their symptoms. The remaining case series reported neither the requirement that participants had failed non-operative treatment nor the duration of symptoms before entry to the study.

None of the 14 case series met all of the validity criteria. It is uncertain how many of the studies reported outcomes—which varied across the studies—that were subjective or from non-validated measures.

Critical appraisal of systematic reviews and HTA reports

Two rapid reviews (ASERNIPS-2001a, ASERNIPS-2003), a NICE report and two systematic reviews (de Kleuver et al 2003, Gamradt & Wang 2005) were included in the assessment of the effectiveness of lumbar AIDR. All of the studies assessing the SB Charité™ III artificial disc included in the ASERNIP-S Rapid Review (2001a) were also included in the ASERNIP-S Rapid Review (2003). In addition, the NICE review (2003) appears to be based on the ASERNIP-S Rapid Review (2003). Although the ASERNIP-S Rapid Review (2001a) did not state whether it pertains to lumbar or cervical AIDR, all of the discs named in the review are used for the former.

Many of the studies included in the assessment of the safety of lumbar AIDR in these systematic reviews and HTA reports have been reported in the results from the RCTs and case series above (pages 48–54, Tables 28-33 and Appendix F of this Assessment Report). Three of the identified reviews included no data from RCTs comparing lumbar AIDR and lumbar fusion (ASERNIP-S 2001a, ASERNIP-S 2003, de Kleuver et al 2003).

The NICE (2003) report included results of Geisler et al (2004), but no results from the ProDisc II trial (Delamarter et al 2003, Zigler 2004). Gamradt & Wang (2005) included data from both the DePuy Spine Charité™ Artificial Disc Trial and the ProDisc II trial, however data for the latter were derived from Zigler et al (2003) and not the later publication, Zigler (2004). Further exceptions to this include four non-English case series and data reported in an abstract only reported in ASERNIP-S (2003), NICE (2003), de Kleuver et al (2003) and Gamradt & Wang (2005). These publications included Butter-Janz et al (1988), Butter-Janz et al (2002), Hopf et al (2002), Ross et al (1997) and Wittig et al (1989).

Validity of systematic reviews and HTA reports

The validity of the identified systematic reviews and HTA reports assessing the effectiveness of AIDR in the lumbar spine is summarised in Table 34.

Table 34 Validity of systematic reviews and HTA reports: Lumbar AIDR versus lumbar fusion

Indicator of validity	Study				
	ASERNIP-S Rapid Review (2001a)	**ASERNIP-S Rapid Review (2003)**	**NICE (2003)**	**de Kleuver et al (2003)**	**Gamradt & Wang (2005)**
Focused question	No	No	No	How do the clinical results compare to arthrodesis, the only surgical gold standard available?[a.]	Purpose of the review: • To examine the anatomy and biomechanics of the lumbar motion segment to determine the features that successful AIDR prostheses must possess • To review early clinical results of three prostheses in use in humans
Inclusion and exclusion criteria	**Artificial discs**				
	Inclusion Acroflex SB Charité™ III	Inclusion Currently commercially available artificial discs ie SB Charité™ III	Inclusion Currently commercially available artificial discs ie SB Charité™ III Exclusion Prostheses that only replace the nucleus	Inclusion • Acroflex (1 study) • SB Charité™ III (8 studies)	Inclusion • SB Charité™ III • ProDisc
	Participants				
	Not reported	Inclusion • Herniated lumbar intervertebral disc • DDD in the lumbar region • Post-laminectomy syndrome • Low back pain refractory to conservative treatment for >6 months • Participants currently considered suitable for spinal fusion surgery Exclusion • Not reported	Inclusion • Herniated lumbar intervertebral disc • DDD in the lumbar region • Post-laminectomy syndrome • Low back pain refractory to conservative treatment for >6 months • Participants currently considered suitable for spinal fusion surgery Exclusion • Not reported	Exclusion The indication for participants was not DDD at the lumbar level	Not reported

Table 34 (cont'd) Validity of systematic reviews and HTA reports: lumbar AIDR versus lumbar fusion

Indicator of validity	Study				
	ASERNIP-S Rapid Review (2001a)	ASERNIP-S Rapid Review (2003)	NICE (2003)	de Kleuver et al (2003)	Gamradt & Wang (2005)
Inclusion and exclusion criteria (cont'd)	**Studies**				
	Not reported	Inclusion Articles were obtained based on the abstract containing safety and efficacy data from RCTs, other controlled or comparative studies, case series and case reports	Inclusion Articles were obtained based on the abstract containing safety and efficacy data from RCTs, other controlled or comparative studies, case series and case reports	Inclusion Category 1, 2 (non-randomised) and 3 (non-experimental) studies Exclusion Outcome parameter was not a clinical measure Non-peer reviewed journal	Not reported
Explicit comprehensive search strategy	Search strategy not reported	Multiple databases searched, including the Internet. Search strategy not reported	Multiple databases searched, including the Internet. Search strategy not reported	Comprehensive search strategy and multiple databases searched. References of the selected articles were included in the search Two independent reviewers selected the articles. A third reviewer was consulted when consensus could not be reached	Medline and conference abstracts searched
Assessed validity of included studies	No	Yes	Yes	Yes, based on a checklist presented in the article	No

Only the systematic review by de Kleuver et al (2003) had a focused research question (Table 34). In addition to this primary question, the following secondary questions were included:

- What are radiological results in terms of:
  - loosening (in total hip arthroplasty radiologic loosening is recognised as a precursor of clinical loosening)
  - subsidence of the implant into the vertebral bodies
  - polyethylene wear?
- Does the motion segment retain its mobility? And if it does, do these motions resemble a normal motion segment?
- Can the arthroplasty reduce the incidence of adjacent segment degeneration compared to arthrodesis? What is the incidence of facet joint degeneration at the operated level?
- How does the perioperative complication rate compare to fusion operations?
- Is there an acceptable and safe salvage procedure in case of failure? Can the device, if necessary, be removed without major complications?
- What would be considered the indication for arthroplasty of a vertebral motion segment?

Although Gamradt & Wang (2005) did not include a focused research question *per se*, the authors outlined a purpose of their review. Overall, none of the systematic reviews or HTAs exclusively included participants representative of those of interest in the current review, that is individuals with significant axial back pain from the disc with or without myelopathy or suffering a major disc prolapse, who have failed non-operative treatment. Only the review by de Kleuver et al (2003) reported the search strategy used, however all of the reports except ASERNIP-S Rapid Review (2001a) recorded the databases searched. The validity of the included studies was assessed in three of the five reviews (ASERNIP-S Rapid Review 2003, the NICE report 2003, de Kleuver et al 2003).

Results from the systematic reviews and HTA reports

The primary studies included in the current review and the published systematic reviews and HTAs are listed in Table 35.

Table 35 Studies included in the systematic reviews and HTA reports: Lumbar disc replacement

Study design	Current Review	ASERNIP-S Rapid Review (2001a)	ASERNIP-S Rapid Review (2003)	NICE (2003)[a]	de Kleuver et al (2003)	Gamradt & Wang (2005)
RCTs	Charité™ III disc: Geisler et al (2004) P040006 Trial Report ProDisc: Delamarter et al (2003) Zigler (2004)	None included	None included	Geisler et al (2004)	None included	Charité™ III disc: Hochschuler et al (2002)[b] Mayer et al (2002) McAfee et al (2003a, b)[c] Charité™ III prosthesis FDA trial (www.fda.gov)[d] ProDisc: Zigler et al (2003)[e]
Non-randomised comparative studies	None included	None included	Buttner-Janz et al (2002)[f]	Buttner-Janz et al (2002)[f]	None included	None included
Case series	Charité™ III disc: Caspi et al (2003) Cinotti et al (1996) David (2000) Griffith et al (1994) Lemaire et al (2000) Sott & Harrison (2000) Su et al (2003) Xu et al (2004) Zeegers et al (1999) ProDisc: Bertagnoli & Kumar (2002) Huang et al (2003) Mayer et al (2002) Tropiano et al (2003) Acroflex: Fraser et al (2004)	Cinotti et al (1996) Enker et al (1993)[g] Griffith et al (1994) Lemaire et al (1997)	Cinotti et al (1996) David et al (1993) Enker et al (1993) Griffith et al (1994) Hopf et al (2002)[f] Ross et al (1997)[h] Sott and Harrison (2000) Zeegers et al (1999)	Cinotti et al (1996) Griffith et al (1994) Lemaire et al (1997) Zeegers et al (1999)	Buttner-Janz et al (1988)[f] Cinotti et al (1996) David (1993) Enker et al (1993) Griffith et al (1994) Lemaire et al (1997) Sott and Harrison (2000) Wittig et al (1989)[f] Zeegers et al (1999)	Charité™ III disc: Caspi et al (2003) Cinotti et al (1996) David (2000) Griffith et al (1994) Lemaire et al (2000) van Ooij et al (2003)[i] Zeegers et al (1999) ProDisc: Bertagnoli & Kumar (2002) Huang et al (2003) Mayer et al (2002) Tropiano et al (2003)

Reasons why publications not included in the current review:

[a] NICE has not amended the date of posting the HTA on website, does include results of Geisler et al (2004)

[b] Hochschuler reports on the AIDR arm in a single centre participating in the DePuy Spine Charité™ Artificial Disc Trial; results of these participants included in Geisler et al (2004) and Trial Report (P040006)

[c] McAfee et al (2003a, b) report on results from a single centre participating in the DePuy Spine Charité™ Artificial Disc Trial; results of these participants included in Geisler et al (2004) and P040006

[d] Refers to Trial Report (P040006)

[e] Updated results reported in Zigler (2004)

[f] Non-English case series

[g] Fewer than 10 participants enrolled

[h] Abstract only

[i] Reports unsatisfactory results and complications only

All of the studies using the SB Charité™ III artificial disc included in the ASERNIP-S Rapid Review (2001a) were included in the ASERNIP-S Rapid Review (2003). The ASERNIP-S Rapid Review (2003), based entirely on non-randomised studies, found that several studies reported significant reduction in leg and/or back pain. Good or excellent clinical outcomes were reported in 24 to 79 per cent of participants.

The ASERNIP-S Rapid Review (2001a) reported that with the Acroflex disc, four of the six participants (66.7%) had a satisfactory result based on analgesia use and symptoms. With regards to the SB Charité™ III disc involving 93 participants, Griffith et al (1994) reported significant reduction in back and leg pain ($p<0.05$), improvement in neurological weakness ($p<0.01$) and increase in walking distance ($p<0.01$) between pre- and post-operative results. Lemaire et al (1997) studied 105 participants and reported an average relative gain of 82 per cent using a modified Stauffer-Coventry score. Cinotti et al (1996) reported that 69 per cent of participants with single level disc replacement had a satisfactory clinical result compared to 40 per cent undergoing multiple-level replacements. In this study, eight of the 43 participants underwent subsequent lumbar spinal fusion due to unsatisfactory results with lumbar AIDR.

The NICE review (2003; which appears to be based on the ASERNIP-S Rapid Review 2003) reported re-operation rates of three to 24 per cent (three studies) and implant related problems for one to four per cent (three studies). Overall clinical results were reported as satisfactory, good or excellent in at least 60 per cent of participants in the three studies that included this outcome. Two of the four studies that reported pain relief found a statistically significant reduction in low back and/or leg pain in the majority of participants. Four studies reported return to work as an outcome and found that 67 to 87 per cent of participants were able to return to work after surgery. In addition, results from an RCT (304 participants) of the Charité™ artificial disc compared to BAK spinal fusion found an improvement in ODI score of 62 per cent in the Charité™ treatment arm after 24 months compared to 49 per cent for the patients undergoing lumbar spinal fusion.

The systematic review by de Kleuver et al (2003) identified no controlled trials and nine case series. Overall, 564 lumbar AIDRs were analysed in 411 participants. Results were classified as good or excellent in 50 to 81 per cent of participants in the studies.

Gamradt & Wang (2005) concluded that the short-term results as measured by pain relief and disability were good in several studies; however questions still remain regarding the long-term efficacy with regards to relief of pain and maintenance of motion. Gamradt & Wang (2005) also concluded that recovery times with lumbar AIDR appeared to be shorter than those observed with spinal fusion.

With respect to the SB Charité™ III disc, Gamradt & Wang (2005) presented data sourced from a variety of publications from several case series and preliminary results from an FDA RCT. Participants in the RCT were randomised to receive either the SB Charité™ III disc or to anterior lumbar interbody arthrodesis with a BAK cage. Gamradt & Wang (2005) reported 24-month follow-up data in which 63 per cent of the participants receiving the SB Charité™ III disc and 53 per cent of those undergoing interbody fusion were considered a clinical success. They also reported that the SB Charité™ III participants showed significantly greater improvement in ODI at the six-week and six-month follow-up. Gamradt & Wang (2005) concluded that on the basis of this FDA trial, lumbar AIDR with the SB Charité™ III disc is at least as effective as BAK interbody lumbar fusion after 24 months follow-up.

With respect to the ProDisc artificial intervertebral disc, Gamradt & Wang (2005) presented details of several case series. They also reported an FDA-regulated multicentre investigational device exemption trial, currently under way, in which participants have been randomly assigned to receive either lumbar AIDR (28 participants) or 360-degree lumbar fusion with iliac crest bone graft (11 participants). Early results at six months have shown operative time to be shorter in the ProDisc treatment arm compared to the lumbar spinal fusion arm (75 minutes and 218 minutes, respectively) and hospital stay to be shorter in the ProDisc arm (2.1 versus 3.5 days). A trend towards earlier recovery and increased satisfaction with the ProDisc device were also reported at the six-month follow-up.

Discussion of systematic reviews and HTA reports

Both ASERNIP-S Rapid Reviews (2001a, 2003) noted that both satisfactory results and complications have been reported in the literature. The reviews concluded that further studies are required to define the clinical indications and contraindications for lumbar AIDR. The ASERNIP-S Rapid Review (2003) was based on only one comparative study and case series, therefore the quality of the available evidence was low and lacked direct comparison with lumbar spinal fusion.

de Kleuver et al (2003) concluded that insufficient data were available to assess the performance of lumbar AIDR adequately. They concluded that there was no evidence to support that lumbar AIDR reliably, reproducibly and over longer periods of time fulfils the three primary aims of clinical efficacy, continued motion and few adjacent segment problems. de Kleuver et al (2003) also concluded that although the short-term results of lumbar AIDR appear comparable to those of lumbar spinal fusion, the available studies are of a limited quality as a basis for drawing definitive conclusions. With respect to the seven questions asked, de Kleuver et al (2003) concluded that:

- The short-term clinical results appeared to be comparable to those of lumbar spinal fusion.
- Radiologic loosening was not addressed in any of the studies.
- Subsidence of the artificial intervertebral discs was only incidentally reported.
- Polyethylene wear has not been reported or accurately measured to date.
- The mobility of the motion segment is frequently lost as fusion often occurs between the two vertebrae, as a result of which one of the primary aims of the procedure is not achieved.
- There is no direct comparative evidence to support or refute the efficacy of lumbar AIDR to reduce adjacent segment degeneration compared with lumbar spinal fusion.
- The complication rate is highly variable.
- Removal of the artificial disc may be problematic but subsequent lumbar spinal fusion may be performed in the case of failure.

Gamradt & Wang (2005) noted that the majority of studies reporting on the SB Charité™ III disc are small, non-randomised and retrospective with incomplete reporting of complications and short duration of follow-up. The report concluded that according to most published series, artificial intervertebral discs are implanted in participants of average age 40 years and that *in vivo* failure rates, long-term pain relief and revision options remain unanswered. With respect to the ProDisc studies, Gamradt & Wang (2005) concluded that the lack of long-term follow-up indicates that the prosthesis has been incompletely evaluated. They also concluded that the literature leaves several questions incompletely answered. These are:

- Will these devices and techniques show an improvement over post-lateral fusion in the long term?
- Is pain relieved in the long term?
- What are the life span and wear characteristics of these prostheses *in vivo*?
- What future problems will these devices create when revision is necessary?
- Does lumbar disc prosthesis really halt the cascade of posterior facet arthropathy and adjacent segment degeneration, as hypothesised?
- Are the current devices cost-effective?

Expert opinion

Training

Very few surgeons in Australia have the necessary skills or training to perform AIDR. Only a small number of the neurosurgeons and orthopaedic surgeons trained in spinal surgery deal with complicated cases such as fusions that require spinal instrumentation, and only a small subset of those have the necessary training and desire to perform AIDR.

Surgeons currently performing AIDR in Australia have undergone additional training in the devices used that includes theoretical instruction, simulated surgery with models, cadaver surgery, live surgical instruction by a recognised expert with that device, assisting in live surgery and surgical mentoring.

FDA efficacy trials for lumbar disc arthroplasty have been carried out in specialist institutions where extremely high numbers of patients are seen and procedures are undertaken by only experienced surgeons who have been implanting these types of devices for long periods of time (prior to the commencement of the FDA trials), that is, 'they are off the learning curve'. This is an artificial situation. In Australia, it will take the majority of spinal surgeons a very long time to gain adequate experience (if they adhere to a reasonable patient selection procedure) the possible result being a high complication rate. The issues associated with surgical salvage for complications arising from arthroplasty are currently poorly understood.

The concerns regarding complications with lumbar AIDR are less applicable to cervical AIDR as the procedure is a variation of the standard approach for routine anterior

surgery. Complications with cervical AIDR are more likely to arise from poor patient selection and device-related problems.

The number of trained neurosurgeons and orthopaedic surgeons interested in performing AIDR is likely to increase as access to the device increases. In NSW, there are about seven qualified neurosurgeons and six qualified orthopaedic surgeons. There are fewer in the other states.

The number of surgeons performing AIDR has been relatively constant in the medium term because of limitations of interim funding. It is expected that some orthopaedic surgeons and neurosurgeons will pursue the additional training to perform complex spinal surgery and pursue this as part of their subspecialty practice.

In the opinion of the Advisory Panel, the training of surgeons in the use of these devices should be the responsibility of, and be overseen by, the Royal Australasian College of Surgeons and not the manufacturers, as is currently the case.

Clinical need

It is difficult to derive accurate current and anticipated AIDR usage from raw data on fusion. By the very nature of its indications and contraindications, AIDR will replace only a percentage of cases now considered for fusion procedures. For example, the two most common degenerative conditions that currently lead to fusion surgery (degenerative spondylolisthesis, and isthmic spondylolisthesis) are contraindications to lumbar AIDR. A broad estimate of five per cent of lumbar and 40 per cent of cervical fusion cases being replaced by AIDR is probably reasonable. Huang et al (2005) also estimated that approximately five per cent of lumbar fusion cases may be replaced by AIDR.

Estimating the number of AIDR procedures from the sale of the devices in Australia is an alternative to estimating usage from fusion data.

Cervical AIDR sales in Australia

The following devices for cervical AIDR are used in Australia: Bryan Disc, Prestige LP, ProDisc C, and PCM.

NSW statistics may reflect a steady state picture of usage as surgeon numbers are highest, take-up of the procedure was earliest, the number of AIDR surgeons is static, and minimal artificial restrictions on access to AIDR in public and private hospitals exist. From sales figures for all devices in 2005, a reasonable estimate of cervical disc arthroplasty usage is 400 per year and are likely to remain at that level in the near future. Industry sources estimate that 310, 360 and 410 cervical procedures were or will be performed in 2004, 2005 and 2006, respectively.

Lumbar AIDR sales in Australia

The following devices for lumbar AIDR are used in Australia: Maverick, ProDisc and Charitè™.

Industry sources indicate total sales for the three devices available in Australia of 400 per year and estimate the number of lumbar procedures at 400, 520 and 630 in 2004, 2005 and 2006, respectively. Sales numbers have been fairly static over the last few years or

possibly declining in some states as surgeons tighten indications in their own practice and the number of new adopters of the procedure remains low or non-existent.

Complications

Procedural and device complications in both the cervical and lumbar regions are probably currently under-reported and there are significant potential complications associated with AIDR. Most procedural and device complications in the lumbar region will require re-operation as many patients will require a fusion for salvage. The percentage of arthroplasty implants in the cervical spine that will fuse spontaneously is unknown. Complications of fusion and AIDR may include:

- death (rarely), paralysis, spinal cord injury, stroke, bowel and bladder problems;
- infection, deep venous thrombosis, pulmonary emboli, wound problems etc (ie complications relevant to all surgery);
- a small chance of worsened pain, weakness or numbness and nerve damage;
- a chance of pseudarthrosis (fusion failure) or instrumentation failure with fusion cases, requiring more surgery;
- pain at bone graft donor sites;
- accelerated degenerative change at adjacent segmental levels (although this is controversial); and
- short-term device failure (rarely) in AIDR.

As long-term durability of the devices is unknown, a percentage of patients may require revision in 10–20 years, although the incidence is likely to be low with cervical procedures.

Perceived benefits and research in Australia

Whilst Australian doctors have the privilege of having access to new technology years in advance of our North American colleagues, as a group, spinal surgeons have been very conservative and responsible with its use. Australian surgeons presented numerous papers at the recent international Spine Arthroplasty Society meeting in the US, and their views and experience were widely valued. Australian surgeons interested in spine arthroplasty have met three times in the last year to discuss techniques, results and research relating to one of the first disc arthroplasty devices. Whilst almost all surgeons are collecting prospective outcome data on their patients, it was agreed at the last company sponsored meeting "Bryan User Group Meeting", that a multicentre study, pooling similar data will be commenced in an attempt to answer in a more rigorous way, questions raised by surgeons and the community. This data needs to be independently obtained and assessed. Apart from efficacy and complications, perceived benefits such as earlier return to function and work will need to be examined.

What are the economic considerations?

Summary of key issues in the clinical effectiveness of AIDR for an economic analysis

The framework for the economic evaluation of any medical technology considered by MSAC is the comparison of the costs and benefits of that technology compared with the current alternative treatment for patients. The approach taken is to calculate an incremental cost-effectiveness ratio $(C_I–C_C)/(O_I–O_C)$ where C_I is the total cost of resources used associated with the intervention, C_c is the total cost of resources used by the comparator, O_I is the output associated with the intervention, and O_C is the outcome associated with the comparator. The perspective taken is a broad one that includes not only the financial implications to the government health budget, but also the value of all socially relevant health-related resource use. Where there is no difference in outcomes or complications, or it seems clear that there will be unmeasurable gains, only a comparative cost analysis of the treatment pathway is required. The available evidence suggests there is no difference in measured outcomes of pain and disability six to 24 months after either AIDR or spinal fusion in the lumbar or cervical spine. Any evidence for differences in adverse events and surgical procedure rates is equivocal. On the assumption that procedures are equivalent in terms of outcomes, the economic analysis considers only the comparative costs of AIDR and spinal fusion.

Review of the literature on the cost-effectiveness of AIDR

A systematic review of the literature was performed by the evaluators to identify publications on the cost-effectiveness of cervical AIDR and cervical fusion, lumbar AIDR and lumbar fusion, and lumbar AIDR and non-surgical treatment.

Both medical and economic databases were searched, including EMBASE, EconLit, HEED, NHS EED, HTA and DARE. The cut-off date for the search was 1 March 2005. In addition, HTA websites were searched to identify potentially relevant publications. The approach used to undertake this review is described in 'Approach to Assessment'.

The literature search failed to identify any publications reporting cost-effectiveness results of head-to-head RCTs or studies, or sets of trials or studies involving a common reference. The identified publications report on trials or studies that address the comparison of different surgical fusion techniques, the differences between lumbar fusion and non-surgical treatment in terms of clinical outcomes and costs, and the potential impact of AIDR on health care resources. Publications comparing different surgical fusion techniques were considered to be outside the scope of this assessment. The remaining identified publications were regarded as containing potentially useful information and are summarised in Appendix G.

Comparative cost of AIDR and spinal fusion

Definition and measurement of costs

Direct health care costs covering hospital care, prostheses and medical fees for procedures performed in private hospitals were included in the comparison. These costs were determined separately for lumbar and cervical procedures and weighted to take into account the proportion of procedures performed in public and private hospitals, the number of spinal levels involved, the proportion of fusion procedures using the screw and rod (or plate) fusion method and the proportion of procedures using the interbody fusion method.

The cost of hospital care is based on resources required for:

- DRG I09A (spinal fusion with catastrophic or severe complications or comorbidities); and
- DRG I09B (spinal fusion with no catastrophic or severe complications or comorbidities).

Cost data and the number of separations came from the National Hospital Cost Data Collection (NHCDC) 2002–2003 (Australian Government DoHA 2004a) and are adjusted for increases in the price of health care services (totalling 12.2% to March 2005). Medical fees for Medicare Benefits Schedule (MBS) items are taken from the MBS Book November 2004 edition (DoHA 2004b) and include fees for the surgeon, surgical assistance and anaesthesia management.

The DoHA provided the evaluators with the relevant MBS items (Appendices I and J). The sponsors of the Application provided the average price of prostheses used in spinal interbody fusion and AIDR. The Application gives itemised costing of prostheses used in one- and two-level cervical interbody fusion and the total price of a one-level lumbar interbody fusion system. It is assumed that the cost given in the Application is the price for 2004. It should be noted that the sponsors are the suppliers or distributors of both spinal fusion implants and AIDR prostheses. Various independent sources were contacted, including major Australian health funds, the Australian Health Insurance Council and the Prostheses Section at DoHA, to verify the price given by the sponsors, but were unable to assist in this matter, citing commercial sensitivity or lack of information. At the time of writing, the benefits payable for TGA-approved prostheses were not available in Schedule 5.

Other sources of information on the costs of prostheses included researchers in the United Kingdom Spine Stabilisation Trial (UKSST) and members of the Advisory Panel. Cost information obtained from the UKSST indicated that the price of prostheses used in lumbar fusion is about three to 14 times higher in Australia than in the UK. It appears that there is also significant price variability between hospitals in Australia (Table 36). For this reason, the price of prostheses is varied in the sensitivity analysis to test the robustness of the results.

In summary, the true cost of spinal fusion and AIDR prostheses is difficult to determine. It should be noted that although the NHCDC 2002–2003 provides an average cost of spinal prostheses per DRG I10A and I10B, this estimate is unreliable due to the method of costing used by the majority of hospitals contributing to the data. For the period

2002–2003, 204 public hospitals and 113 private hospitals provided costing data. Of these, 98 per cent of hospitals in the private sector and 57 per cent of hospitals in the public sector allocated estimates of costs using cost modelling software instead of patient costing (Australian Government DoHA 2004a).

Table 36 Price comparison of prostheses

Prosthesis	Cost provided by Applicant ($)	Cost from other industry sources ($)
Lumbar disc arthroplasty (one-level)	9,833[a]	8,000–15,882[b]
Cervical disc arthroplasty (one-level)	11,439[a]	10,800–14,000[b]
Cervical interbody cage	3,000[a]	1,500–3,145[b]
Lumbar interbody fusion cage, screws and rods (one-level)	13,861[a]	9,600–16,694[b]

[a] Average price
[b] Range of costs

Rehabilitation costs after discharge from hospital were not taken into account in the cost analysis. They might include the costs of physiotherapy, pain relief medications, nursing care and GP consultation. The omission of rehabilitation costs would affect the total cost of the procedure if the use of these health care services differs between patients undergoing spinal fusion and AIDR. However, there is no evidence for differences in the use of health care services following these procedures.

The measurement of costs associated with AIDR and spinal fusion was impeded by the lack of data on the number of separations for each technology, the level of the spine involved, the part of the spine involved, and the various spinal fusion approaches and implant systems. The current spinal fusion DRGs do not capture these details, therefore results of the cost comparison should be interpreted with caution.

It should be noted that the cost of bone morphogenic protein (BMP) has not been included in the costing of spinal fusion. According to members of the Advisory Panel, one to 11 per cent of spinal fusion procedures will incorporate the use of BMP and thereby affect the cost of spinal fusion. However, the use of BMP in spinal fusion may also have an impact on the effectiveness of the procedure, which was not considered in the current evaluation.

Assumptions used in the cost analysis

Key assumptions used in the cost analysis are tabulated in Tables 37 and 38. Details of the cost calculations using these assumptions are contained in Appendices I–M.

Table 37 Key assumptions used in the cost analysis

№	Variable	Finding	Source/comment
1	Reduction in the number of patients requiring re-operation for ASD as a result of having cervical or lumbar AIDR	No difference	Evidence is lacking
2	Reduction in the number of patients suffering chronic pain following AIDR	No difference	Clinical trial evidence suggests no difference between 6 and 24 months
3	Number of cages required for a single level cervical interbody fusion	1 cage	Advisory Panel expert opinion
4	Number of cages required for a two-level cervical interbody fusion	2 cages	Advisory Panel expert opinion
5	Hospitalisation cost	Same for all procedures regardless of anatomical site and type of prostheses	NHCDC data do not differentiate between lumbar and cervical fusion. Data on the hospitalisation cost of AIDR in Australia are not available
6	Proportion of spinal procedures (spinal fusion and AIDR) performed in private hospitals	70.6%	NHCDC data 2002–2003
7	Amount of autogenous bone harvested for interbody fusion for both cervical and lumbar procedures	• Small quantity for single level fusion • Large quantity for multiple-level fusion	• Item 47726 is applicable • Item 47729 is applicable
8	Surgical assistance at spinal operations	Required for all procedures	Advisory Panel expert opinion. Item 51303 is applicable
9	Anaesthesia perfusion time for single-level procedures	2.46–3.00 hours	The literature is inconclusive on the time differential between spinal fusion and AIDR and data on the difference between cervical and lumbar procedures are not available. Item 23120 is applicable for all procedures
10	Anaesthesia perfusion time for multiple-level procedures	3.16–3.30 hours	Data are lacking. This time period is equivalent to 14 basic anaesthesia units. A similar number of units is allocated to the management of anaesthesia for multiple level procedures. Item 23140 is applicable
11	Proportion of interbody fusion performed	22.8% of spinal fusion procedures	NHCDC data and Medicare claimed data for items 48654, 48675 for 2001–2002 and 2002–2003
12	Proportion of spinal procedures involving multiple levels	17.1% of spinal procedures	Medicare claimed data for items 20600, 20620, 20630 and 20670 for 2001–2002 and 2002–2003
13	Proportion of one-level spinal fusion procedures involving the cervical spine	16.9% of one-level spinal fusion procedures	Medicare claimed data for items 20600, 20620 and 20630 for 2001–2002 and 2002–2003.
14	Proportion of two-level procedures involving the cervical spine	16.9% of two-level spinal fusion procedures	Data not available
15	Type of pedicle screws used in spinal fusion	Polyaxial screws	Advisory Panel expert opinion

Unit cost used in the cost analysis

The base case analysis used information on prosthesis cost provided by the sponsors. The unit cost according to resource type is tabulated in Table 38. The cost for units 1–8 is provided as a weighted average and is computed as follows (see also Appendices I–L):

Cost of hospitalisation per separation = $(C_{pub} \times W_{pub}) + (C_{pri} \times W_{priv})$ where C_{pub} is the average cost of hospitalisation for DRG I10A and I10B in public hospitals, W_{pub} is the proportion of DRG I10A and I10B separations in the public sector, C_{pri} is the average cost of hospitalisation for DRG I10A and I10B in private hospitals and W_{pri} is the proportion of DRG I10A and I10B separations in the private sector.

The average cost of hospitalisation for each DRG in public hospitals is determined by subtracting the estimated average cost of prostheses per DRG from the total average cost for that DRG. The average cost of hospitalisation in private hospitals is calculated using the same method. Using the latest NHCDC data available (2002–2003) the weighted average cost of hospitalisation for DRGs I09A and I09B (adjusted for inflation) in the public and private sector is estimated to be $11,184 excluding prosthesis costs.

Medical fees per separation = $Total\ MBS\ fees\ claimable \times W_{pri}$. The total MBS fees claimable are determined by applying the multiple operation formula to the Medicare fees for the relevant MBS items to obtain the sum of fees, and weighting the sum by the proportion of procedures involving one and more than one level of the spine. The average medical cost is estimated at $2,296 to $2,621, excluding possible out-of-pocket expenses incurred by patients. It should be noted that for spinal fusion this cost has been calculated on the basis of two different fusion methods: (i) posterolateral fusion with bone grafts using patient's own bone, pedicle screws and rods or plates, and (ii) interbody fusion.

Cost of prostheses per separation = $(CP_1 \times W_1) + (CP_2 \times W_2)$ where CP_1 is the cost of prostheses used in procedures involving one level of the spine, W_1 is the proportion of procedures involving one level, CP_2 is the cost of prostheses used in procedures involving two levels of the spine and W_2 is the proportion of procedures involving two levels. For spinal fusion this cost has been calculated on the basis of two different fusion methods: (i) posterolateral fusion with bone grafts using patient's own bone, pedicle screws and rods or plates, and (ii) interbody fusion.

Table 38 Unit cost by resource item

№	Resource item	Unit cost[a] ($)
1	Cost of hospitalisation for lumbar AIDR excluding prosthesis	11,184[b]
2	Cost of hospitalisation for lumbar fusion excluding prosthesis	11,184[b]
3	Cost of hospitalisation for cervical AIDR excluding prosthesis	11,184[b]
4	Cost of hospitalisation for cervical fusion excluding prosthesis	11,184[b]
5	Medical fees for lumbar fusion	2,275[b]
6	Medical fees for cervical fusion	2,192[b]
7	Medical fees for lumbar AIDR	2,041[b]
8	Medical fees for cervical AIDR	2,069[b]
9	Cost of prostheses for a one-level lumbar AIDR	9,833
10	Cost of prostheses for a two-level lumbar AIDR	19,666
11	Cost of prostheses for a one-level lumbar fusion using screws and rods	8,916
12	Cost of prostheses for a two-level lumbar fusion using screws and rods	10,314
13	Cost of prostheses for a one-level lumbar interbody fusion	13,861
14	Cost of prostheses for a two-level lumbar interbody fusion	20,202
15	Cost of prostheses for a one-level cervical AIDR	11,439
16	Cost of prostheses for a two-level cervical AIDR	22,878
17	Cost of prostheses for a one-level cervical fusion using screws and plates	3,750
18	Cost of prostheses for a two-level cervical fusion using screws and plates	3,750
19	Cost of prostheses for a one-level cervical interbody fusion	3,000
20	Cost of prostheses for a two-level cervical interbody fusion	6,000

Source: prostheses cost (base case): sponsors, hospitalisation cost: NHCDC 2002–2003 (DoHA 2004 a), medical fees: MBS Book November 2004 edition (DoHA 2004b).
[a] Refer to Appendices I–L for calculation details.
[b] Weighted average.

Sensitivity analyses

Due to uncertainties regarding the true cost of prostheses, one-way sensitivity analyses were conducted to provide an indication of the likely changes in the cost comparison. Cost information provided by industry sources was used in these analyses rather than that provided by the sponsors and two scenarios were explored:

- Scenario 1: assumed that where there is a range of prices for a prosthesis, the lower price (see Appendix N) is the true cost.
- Scenario 2: assumed that where there is a range of prices for a prosthesis, the higher price (see Appendix N) is the true cost.

Results of the cost analysis

Lumbar AIDR versus lumbar fusion

Table 39 presents the base case comparison of the cost of lumbar AIDR compared to lumbar fusion. It was assumed that the cost of hospitalisation is identical and there is no difference in downstream costs of associated procedures in the future (for adjacent segment disease, for example) or treatment for adverse events. The results suggest that when both methods of fusion are taken into account, lumbar AIDR is more expensive on average than lumbar fusion. The incremental cost of lumbar AIDR was estimated to be approximately $1,054. However, when only interbody fusion is considered, a cost

saving of $3,458 per separation was estimated for lumbar AIDR (see Appendix M). This saving is less than the savings of $4,028 (public sector) and $4,954 (private sector) estimated by the sponsors.

The difference in the saving amount can be attributed to different methods of estimating the cost of prostheses. The sponsors estimated the cost of prostheses used in a one-level interbody lumbar procedure, whereas this assessment calculated the weighted average cost of prostheses used in both one- and two-level interbody lumbar procedures. It should be noted that the prosthesis cost differential accounts for most of the predicted incremental cost or saving and there is some uncertainty surrounding the true cost of lumbar prostheses.

Table 39 Cost comparison of lumbar AIDR versus lumbar fusion, base case

Base case	Cost with spinal fusion ($)	Cost with AIDR ($)
Weighted average cost of hospitalisation	11,184	11,184
Weighted average cost of medical fees	1,606	1,621
Weighted average cost of prostheses	10,475	11,514
Total cost/separation	23,265	24,319
Incremental cost/separation		1,054

Note: The base case analysis used prostheses cost information provided by the sponsors.

In the sensitivity analysis, when all methods of fusion are considered, the incremental cost of lumbar AIDR is predicted to be $1,054–$7,570 per separation (Table 40). However, if only the interbody fusion method is included in the comparison, the incremental cost is estimated to lie between –$3,458 (base case) and $262 (Scenario 2).

Table 40 Incremental cost of lumbar AIDR, by scenario and fusion method

Scenario	Incremental cost considering all fusion methods ($)	Incremental costs considering interbody fusion only ($)
Base case	1,054	–3,458
Scenario 1	1,816	–1,843
Scenario 2	7,570	262

Note: The base case analysis used prostheses cost information provided by the sponsors. Scenario 1 and 2 drew on cost information from other industry sources. Where there was a range of prices for a prosthesis, Scenario 1 assumed the lower price to be the true cost and Scenario 2 assumed the higher price to be the true cost.

Cervical AIDR versus cervical fusion

Table 41 presents the comparison of the cost of cervical AIDR and cervical fusion. Given that the hospitalisation cost is assumed to be the same for both procedures, the incremental cost of $9,438 is almost entirely due to the higher cost of the cervical AIDR prostheses. The incremental cost is slightly less ($8,413) when cervical AIDR is compared with cervical interbody fusion alone. This incremental cost differs from the estimates of $7,148 for the public sector and $6,872 for the private sector provided by the sponsors for the interbody fusion versus AIDR comparison. As discussed, different methods of estimating the cost of prostheses account for the discrepancy.

Table 41 Cost comparison of cervical AIDR versus cervical fusion, base case

Base case	Cost with spinal fusion ($)	Cost with AIDR ($)
Weighted average cost of hospitalisation	11,184	11,184
Weighted average cost of medical fees	1,548	1,641
Weighted average cost of prostheses	4,050	13,395
Total cost/separation	16,782	26,220
Incremental cost/separation		9,438

Note: The base case analysis used prostheses cost information provided by the sponsors.

The incremental cost of cervical AIDR remains above $8,000 per separation regardless of the method of fusion considered and the source of prostheses cost information used (Table 42). As in the case for lumbar AIDR, the prosthesis cost differential accounts for most of the predicted incremental cost and there is some uncertainty regarding the true cost of cervical implants. Additionally, the analysis assumes no difference in downstream costs of future associated procedures or treatment for adverse events.

Table 42 Incremental cost of cervical AIDR, by scenario and fusion method

Scenario	Incremental cost considering all fusion methods ($)	Incremental cost considering interbody fusion only ($)
Base case	9,438	8,413
Scenario 1	10,314	10,797
Scenario 2	13,346	11,696

Note: The base case analysis used prostheses cost information provided by the sponsors. Scenarios 1 and 2 used cost information from other industry sources. Where there was a range of prices for a prosthesis, Scenario 1 assumed the lower price to be the true cost and Scenario 2 assumed the higher price to be the true cost.

Estimated extent of use and financial implications for the health sector

Experts from the Advisory Panel have estimated that about 5 per cent of lumbar fusion patients would qualify for lumbar AIDR and approximately 40 per cent of cervical fusion cases would meet indications for cervical AIDR. Based on these estimates, the number of spinal fusion separations for 2002–2003 and assumptions 13 and 14 (Table 37), it is projected that the substitution of spinal fusion with AIDR would cost the health sector $3.4–6.1 million per annum (Table 43). If the substitution reaches 50 per cent for lumbar procedures and 100 per cent for cervical procedures, the net cost of substitution is predicted to be $10.1–27.0 million per annum (Table 43). The projections should be interpreted with caution because the long-term clinical effectiveness and safety of AIDR are unknown.

Table 43 Incremental cost incurred by the health sector for substitution of fusion procedures with AIDR

Scenario	Incremental cost for lumbar procedures ($)	Incremental cost for cervical procedures ($)	Total incremental cost ($)
Assuming 5% and 40% substitution of lumbar and cervical fusion procedures, respectively, with AIDR			
Base case	218,618	3,184,940	3,403,558
Scenario 1	376,670	3,480,554	3,857,225
Scenario 2	1,570,151	4,503,730	6,073,882
Assuming 50% and 100% substitution of lumbar and cervical fusion procedures, respectively, with AIDR			
Base case	2,186,182	7,962,350	10,148,531
Scenario 1	3,766,704	8,701,385	12,468,089
Scenario 2	15,701,512	11,259,326	26,960,839

Note: The base case analysis used prostheses cost information provided by the sponsors. Scenarios 1 and 2 used cost information from other industry sources. Where there was a range of prices for a prosthesis, Scenario 1 assumed the lower price to be the true cost and Scenario 2 assumed the higher price to be the true cost.

Conclusions

Safety

Cervical AIDR

The safety of cervical AIDR was assessed from one RCT comparing cervical AIDR and cervical spinal fusion, 11 case series and one HTA report. The trial reported no statistically significant differences in the total number of adverse events experienced by participants allocated to cervical AIDR and those randomised to cervical spinal fusion (RR=0.93, 95% CI: 0.63, 1.36). The long-term (>5 years) comparative safety of cervical AIDR and cervical spinal fusion is unknown.

Safety results for a total of 578 participants (701 discs) who underwent cervical AIDR were reported in 11 case series. Adverse events reported included new or worsening pain, revision decompression surgery, migration or suspected migration of the prosthesis, adjacent level surgery and removal of the prosthesis with or without cervical spinal fusion. With the exception of one study in which all participants were reported to experience transient dysphagia, each of these adverse events occurred at a rate of less than 14 per cent in the individual case series. Follow-up in the case series was for a maximum of 65 months.

Lumbar AIDR

Two multicentre RCTs comparing lumbar AIDR and lumbar spinal fusion have been conducted. No significant differences in the rates of any of the adverse events were observed between the 205 participants treated with lumbar AIDR using the SB Charité™ and the 99 participants treated with the BAK Interbody Fusion Device (BAK Cage) (RR=0.98; 95% CI: 0.86, 1.11). No significant differences were observed in the proportion of participants experiencing any or severe or life-threatening infections who were randomised to lumbar AIDR or lumbar spinal fusion. Another publication reporting adverse events occurring in an RCT comparing lumbar AIDR with ProDisc II (55 participants) and circumferential lumbar spinal fusion (23 participants) reported disc-related problems, minor intraoperative complications, episodes of pain and mild infections which cleared with minimal intervention. The long-term (>5 years) comparative safety of lumbar AIDR and lumbar spinal fusion is unknown.

Adverse event data from the 15 case series (a total of 553 participants who underwent lumbar AIDR and 706 discs) reported that revision surgery was required in 30 participants (range, 2.9–28.6 per cent of participants for the studies in which this adverse event was reported). Revision was required as a result of disc migration, persistent symptoms of pain or bone complications such as vertebral fractures and periprosthetic ossifications. Some cases of pain were managed with medication and analgesics. Follow-up was for a maximum of 157 months.

Effectiveness

Cervical AIDR versus cervical spinal fusion

Evidence for the effectiveness of cervical AIDR versus cervical spinal fusion was derived from one RCT. The trial was designed to demonstrate equivalence between cervical AIDR and cervical spinal fusion ie, that cervical AIDR is no worse than cervical spinal fusion. At the level of the treated disc, participants undergoing cervical AIDR maintained a similar ROM at 12 months follow-up as at baseline, however those undergoing cervical spinal fusion showed no significant preservation of motion. There were no significant differences between the treatment groups at the 24-month follow-up for NDI, neck pain, arm pain and neurological status.

The conclusion from the RCT was that the Prestige II disc is a viable alternative to cervical spinal fusion, however the trial was subject to the following limitations:

- A limited number of participants were enrolled.
- The trial did not report full data and measures of variance at all time points.
- The trial included relatively short-term follow-up.
- The participants, investigators and outcome assessors were not blinded to treatment, which, combined with the relatively subjective nature of many of the outcomes assessed, may have led to bias in the results obtained.

Lumbar AIDR versus lumbar spinal fusion

Evidence for the effectiveness of lumbar AIDR versus lumbar spinal fusion was derived from two RCTs. One trial was designed to demonstrate equivalence between lumbar AIDR and lumbar spinal fusion ie, that lumbar AIDR is no worse than lumbar spinal fusion. Data in the trials were reported inconsistently and the variance around the mean values for various outcomes was not reported, precluding meta-analyses.

The trial assessing the Charité™ disc reported that a statistically significantly greater number of participants undergoing lumbar AIDR achieved 'overall success' at the 24-month follow-up compared with participants undergoing lumbar spinal fusion. Participants undergoing lumbar AIDR also showed statistically significantly reduced ODI scores at six weeks, three and six months, but not at 12 or 24 months, of follow-up in this trial.

The publications reporting limited results from the ProDisc II trial reported a statistically significantly reduced ODI scores at three months of follow-up in participants undergoing lumbar AIDR compared with those undergoing lumbar spinal fusion, however no significant differences in this outcome was observed between the treatment groups at the six-week or six-month follow-up. One publication reported that participants undergoing lumbar AIDR showed statistically significantly greater ROM when the treated level was L4-L5 at six months follow-up, however no differences were observed between the treatment groups when the treated level was L5-S1.

The second publication reported that participants undergoing lumbar AIDR had statistically significantly greater motion for forward, left lateral and right lateral bending at the six-month follow-up.

The data presented have the following limitations:

- The follow-up was relatively short term, with a maximum 24 months.
- Participants and investigators were not blinded to treatment.
- Many of the outcomes were of a relatively subjective nature.

Lack of blinding and the subjective nature of the outcomes assessed may have led to bias in the results obtained. In addition, the results from the ProDisc II trial should be interpreted with caution as the two publications identified reporting results of this trial included the results from only two of 19 centres involved in the multicentre trial. This may have led to reporting bias if only centres with large populations or those with positive results reported their data.

Cost-effectiveness

The results presented in this assessment report are based on the best estimates available and are indicative of the likely costs and benefits of AIDR compared to spinal fusion. Nevertheless, in the absence of high quality evidence on the use of both procedures in clinical practice, a number of uncertainties remain that may impact on the cost comparisons presented.

In particular:

- The long-term clinical effectiveness and safety of AIDR, including any difference in the incidence of adjacent segment disease following surgery, is unknown. No comparative long-term data have been reported that would allow a conclusion to be drawn on whether such a difference exists.
- The comparative reduction in the number of patients suffering chronic pain in the longer term is unknown. The clinical trial data cannot answer with any degree of certainty the existence of any long-term relative advantages of either procedure compared to non-surgical treatment.

Differences in cost between the procedures are driven by the difference in costs of the prostheses. It may be that the true cost of spinal fusion implants in Australia is less than that of arthroplasty prostheses, which would mean that AIDR is more expensive than spinal fusion for both cervical and lumbar surgeries.

Recommendations

On the basis of currently available evidence regarding safety, effectiveness and cost effectiveness, MSAC recommends 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 conservative therapy.

MSAC will review this recommendation in three years.

In the absence of adequate evidence of effectiveness, MSAC recommends that public funding for AIDR in the cervical spine should not be supported.

- The Minister for Health and Ageing accepted this recommendation on 6 June 2006. -

Appendix A MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake HTA work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of the MSAC comprises 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
Dr Stephen Blamey (Chair)	general surgery
Associate Professor John Atherton	cardiology
Professor Syd Bell	pathology
Dr Michael Cleary	emergency medicine
Dr Paul Craft	clinical epidemiology and oncology
Dr Kwun Fong	thoracic medicine
Dr Debra Graves	pathology
Professor Jane Hall	health economics
Professor John Horvath	medical advisor to the Department and Health Minister
Dr Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Dr Ray Kirk	health research
Associate Professor Donald Perry-Keene	endocrinology
Dr Ewa Piejko	general practice
Mrs Sheila Rimmer	consumer representative
Ms Samantha Robertson	Medicare Benefits Branch
Professor Jeffrey Robinson	obstetrics and gynaecology
Professor Ken Thomson	radiology
Dr Douglas Travis	urology

Appendix B Advisory Panel

Advisory Panel for MSAC application 1090
Artificial intervertebral disc replacement (total disc arthroplasty)

Professor Ken Thomson (Chair) MD Director of Radiology The Alfred Hospital Melbourne, VIC Foundation member Society of Minimally Invasive Therapy and the Interventional Radiology Society of Australasia, Council Member Royal Australian & New Zealand College of Radiologists	MSAC member
Ms Sheila Rimmer BSci Hons (Econ), MA (Political Science), AM Ranelagh, Darling Point, NSW	MSAC member
Associate Professor Les Barnsley BMed (Hons), FRACP, DipClinEpi, PhD Head Department of Rheumatology Concord, NSW	Nominated by the Australian Rheumatology Association
Ms Rebecca Coghlan Consumer Representative 37 Bulimba Rd Nedlands, WA 6009	Nominated by the Consumers' Health Forum of Australia
Dr Mark Davies MBBS, FRACS Neurosurgeon St George Private Hospital & Medical Centre Kogarah, NSW	Nominated by the Royal Australasian College of Surgeons

Dr Peter Lowthian MBBS, FRACP, FAFRM Rheumatologist Cabrini Medical Centre Malvern, VIC	Co-opted rheumatologist
Dr George Potter MBBS, FRACS (Orth), FRCS (Ed) (Orth), FA OrthA. Orthopaedic surgeon Adelaide, SA	Co-opted member
Dr Myron Rogers MBBS, FRACS (Neurosurgery) President Neurosurgical Society of Australasia, Member Spine Society of Australasia, Neurosurgeon Cabrini Medical Centre Malvern, VIC Austin Hospital, Heidelberg, VIC	Nominated by the Royal Australasian College of Surgeons
Professor Bryant Stokes AMRFD, MBBS, FRACS, FRCS Consultant Neurosurgeon St John of God Hospital Subiaco, WA	Co-opted member

Appendix C Indications and contraindications of AIDR

Based on advice from experts in the field, AIDR is indicated and contraindicated for the following patient groups in Australia.

Indications

Cervical region:

- radiculopathy or myelopathy secondary to anterior compression of cervical nerve roots or spinal cord;
- rarely, prevention of next level; disc failure; and
- rarely, chronic neck pain treated by multi-level cervical AIDR.

Lumbar region:

- significant axial back pain emanating from a degenerate disc with or without radiculopathy;
- pain and failure of conservative treatment for more than six weeks for radiculopathy and more than six months for lumbar disc replacement;
- pain alone for myelopathy or significant radicular motor deficits; and
- as an alternative to fusion in a young patient with (probable) discogenic back pain who has failed conservative management with particular psychological, physical and radiological criteria.

Contraindications

Cervical region:

- spinal infection, spinal neoplasm, spinal trauma, instability deformity eg kyphosis, severe osteoporosis, posterior nerve root or cord compression, anterior compression from osteophytes behind vertebral body, ossification of the posterior longitudinal ligament

Lumbar region:

- lumbar region: spinal infection, spinal neoplasm, spinal trauma, instability eg spondylolisthesis, deformity eg scoliosis, severe osteoporosis, spinal canal stenosis, pars defects, facet joint arthropathy, posterior nerve root compression, unfavourable pelvic or vascular anatomy or pathology, previous abdominal surgery.

Appendix D Search strategies

Table D1 Search strategy for Medline

Number	Search term
1	bryan.mp.
2	maverick.mp.
3	prestige.mp.
4	charite.mp.
5	prodisc.mp.
6	(pro adj disc).mp.
7	porous coated motion.mp.
8	or/1-7
9	(artificial or flexible or mobile or kinematic or endoprosth$ or replac$).mp.
10	"prostheses and implants"/ or implants, experimental/
11	prosthesis implantation/
12	arthroplasty, replacement/
13	arthroplasty.mp.
14	or/9-13
15	cervical vertebrae/ or lumbar vertebrae/
16	(spine or spinal or lumbar or cervical).mp.
17	vertebra$.mp.
18	(disc or discs or disk or disks).mp.
19	Intervertebral Disk/
20	(or/15-17) and (18 or 19)
21	14 and 20
22	8 or 21
23	limit 22 to humans

*=truncation symbol to represent a maximum of 3 letters at the end of a word segment.
dn=device trade name
de=Drug/Medical index terms (EMTREE, Embase's subject descriptors)
() nested terms to be searched together
and/or=Boolean operators "AND" and "OR".

Appendix E Internet sites searched

HTA agency websites

Agency for Healthcare Research and Quality – technology assessments (AHRQ) http://www.ahcpr.gov/clinic/techix.htm [Accessed 1 February 2005]

Alberta Heritage Foundation for Medical Research (AHFMR) http://www.ahfmr.ab.ca/hta/ [Accessed 1 February 2005]

Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) http://www.surgeons.org/asernip-s/ [Accessed 1 February 2005]

BCBS Technology Evaluation Center http://www.bcbs.com/tec/index.html [Accessed 1 February 2005]

Bundesaertekammer HTA [German] http://www.bundesaerztekammer.de/30/HTA/[Accessed 1 February 2005]

Canadian Coordinating Office for Health Technology Assessment (CCOHTA) http://www.ccohta.ca/ [Accessed 1 February 2005]

Catalan Agency for Health Technology Assessment and Research (CAHTA) http://www.aatrm.net/html/en/Du8/index.html [Accessed 4 February 2005]

CEDIT: Comité d'Evaluation et des Diffusion des Innovations Technologiques http://cedit.aphp.fr/english/index_present.html [Accessed 4 February 2005]

Center for Health Services and Policy Research (CHSPR) http://www.chspr.ubc.ca/ [Accessed 4 February 2005]

Danish Centre for Evaluation and Health Technology Assessment (DACEHTA) http://www.sst.dk/Planlaegning_og_behandling/Medicinsk_teknologivurdering.aspx?lang=en [Accessed 4 February 2005]

Deutsches Institut fur Medizinische Dokumentation und Information (DIMDI) http://www.dimdi.de/dynamic/en/index.html [Accessed 4 February 2005]

EUROSCAN: The European Information Network on New and Changing Health Technologies http://www.euroscan.bham.ac.uk/ [Accessed 4 February 2005]

Finnish Office for Health Care Technology Assessment http://www.stakes.fi/finohta/e/ [Accessed 4 February 2005]

Health Council of the Netherlands http://www.gr.nl/ [Accessed 4 February 2005]

HSTAT: Health Services/Technology Assessment Text http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat [Accessed 4 February 2005]

Health Technology Assessment (HTA) Database http://nhscrd.york.ac.uk/htahp.htm http://144.32.150.197/scripts/WEBC.EXE/NHSCRD/start (database) [Accessed 4 February 2005]

Institute for Clinical Systems Improvement (ICSI) http://www.icsi.org/index.asp [Accessed 4 February 2005]

Institute of Technology Assessment of the Austrian Academy of Science http://www.oeaw.ac.at/ita/welcome.htm [Accessed 4 February 2005]

Clinical trial register websites

CentreWatch clinical trials listing service http://www.centerwatch.com/ [Accessed 4 February 2005]

ClinicalTrials.com http://www.clinicaltrials.com/ [Accessed 4 February 2005]

ClinicalTrials.gov http://www.clinicaltrials.gov/ [Accessed 4 February 2005]

Current Controlled Trials http://www.controlled-trials.com/ [Accessed 4 February 2005]

NHMRC Clinical Trials Centre http://www.ctc.usyd.edu.au/trials/registry/registry.htm [Accessed 4 February 2005

Society for Clinical Trials http://www.sctweb.org/ [Accessed 4 February 2005]

TrialsCentral http://www.trialscentral.org/ [Accessed 4 February 2005]

UK The National Research Register http://www.update-software.com/national/ [Accessed 4 February 2005]

The Cochrane Central Register of Controlled Trials http://www.mrw.interscience.wiley.com/cochrane/cochrane_search_fs.html [Accessed 4 February 2005]

Appendix F Data from case series of lumbar AIDR

Lumbar case series

The search identified no comparative studies of lumbar AIDR and non-surgical treatment. Thus, the best evidence available for this population group was from prospective case series of consecutively selected patients undergoing lumbar AIDR. Twenty-five case series were identified, 14 published in English and 11 published in other languages (listed below). The non-English studies have not been translated or included in the current review.

Alessi GF, Cornette W, Noens B et al, 2004. 'Postoperatieve results of the dynamic lumbar disc prosthesis'. *Tijdschrift voor Geneeskunde* 60 (14–15), 1004–1012.

Buttner-Janz K & Schellnack K, 1988. 'Principle and initial results with the Charite Modular type SB cartilage disk endoprosthesis'. *Magyar Traumatologia, Orthopaedia Es Helyreallito Sebeszet* 31 (2) 136–140.

Buttner-Janz K, Hahn S, Schikora K & Link HD, 2002. 'Basic principles of successful implantation of the SB Charite model LINK intervertebral disk endoprosthesis'. *Orthopade* 31 (5) 441–453.

Cakir B, Schmidt R, Huch K, Puhl W & Richter M, 2004. 'Sagittal alignment and segmental range of motion after total disc replacement of the lumbar spine'. *Zeitschrift fur Orthopadie und Ihre Grenzgebiete* 142 (2) 159–165.

David T, 2002. 'Surgical technique, indications and complications of total lumbar disk protheses'. *Revue de Chirurgie Orthopedique et Reparatrice de l'Appareil Moteur* 88 (5 SUPPL.) 59

Hopf C, Heeckt H & Beske C, 2002. 'Disc replacement with the SB Charite endoposthesis - experience, preliminary results and comments after 35 prospectively performed operations'. *Zeitschrift fur Orthopadie und Ihre Grenzgebiete* 140 (5) 485–491.

Hopf C, Heeckt H & Beske C, 2004. 'Indication, biomechanics and results of arteficial disk replacement'. *Zeitschrift fur Orthopadie und Ihre Grenzgebiete* 142 (2) 153

Lemaire J-P, 2002a. 'SB Charite III intervertebral disk prothesis: Results of more than 10 year follow-up'. *Revue de Chirurgie Orthopedique et Reparatrice de l'Appareil Moteur* 88 (5 SUPPL.) 64–67.

Lemaire J-P, 2002b. 'SB Charite III intervertebral disk prothesis: Biochemical, clinical and radiological correlations with a series of 100 cases over 10 years follow-up'. *RACHIS* 14 (4/5) 271–285.

Ogon M, Chavanne A, Meissner J & Becker S, 2004. 'Disc arthroplasty for patients who are suffering from painful degenerative disc disease'. *Journal fur Mineralstoffwechsel* 11 (3) 7–12.

Wittig C, Muller RT, Staude HW, 1989. 'Bandscheibenprosthese SB Charite, erfolge und misserfolge an hand von fruhergebnisse'. *Med Orthop Technik* 109 70–74.

Lemaire (2002a) may have reported results from Lemaire (2002b).

Mayer et al (2002) reported results for a group of 34 patients, of which a subset of 26 appear to have been reported in another study (Mayer & Wiechert 2002). Thus, results from Mayer & Wiechert (2002) have not been reported herein.

Critical appraisal of case series

Critical appraisal of the case series are presented in Table F1. Nine case series reported on the use of the SB Charité™ disc, four on the use of the ProDisc and one on the use of the Acroflex disc. One study each was conducted in Israel, Italy, UK, The Netherlands, Australia and one multi-centre study was conducted at sites in the USA and Europe. Four studies were conducted in France, two in Germany and two in China. The follow-up in each of the studies ranged from a mean of 11.9 months (Griffith et al 1994) to 8.7 years (Huang et al 2003). The number of males enrolled in each study was similar and, where reported, ranged from 34.0 per cent (Tropiano et al 2003) to 64.8 per cent (Lemaire et al 1997). The mean ages of participants were also similar ranging, where reported from 36 years (Cinotti et al 1996) to 48 years (Sott & Harrison 2000).

Table F1 Descriptive characteristics of case series for lumbar AIDR after failed non-surgical treatment

Study	Location	Enrolment period	Outcome measures	Time of follow-up	Study population			
					n	Losses to follow-up	№ male (%)	Age (years)
SB Charité™ III								
Caspi et al (2003)[a]	Israel	Not reported	Clinical outcomes and radiographs	48 months	20 (23 discs)	0	11 (55.0)	Range: 24–50
Cinotti et al (1996)[b]	Italy	Not reported	Spinal ROM, nerve root tension tests, motor strength, pain, need for analgesics, ability to resume work and daily activities	2–5 years Mean: 3.2 years	46 (56 discs)	0	21 (45.7)	Mean: 36 Range: 27–44
David (1993)[a]	France	Not reported	Clinical results, average mobility (radiographs)	12–37 months Mean: 19 months	22 (29 discs)	0	13 (59.1)	Mean: 37 Range: 27–50
Griffith et al (1994)[a,c]	Multicentre: US, Germany, The Netherlands	1987–1991	Work status, pain, neurologic status, walking ability, lumbar mobility	Model III 1–37 months Mean: 11.9 months	93 (139 discs)	3[d]	50 (53.8)	Overall: Mean (SD): 43.0 (7.3) Male: Mean: 43.7 Range: 25–59 Female: Mean: 42.3 Range: 27–56
Lemaire et al (1997)[a]	France	Not reported	Modified Stauffer-Coventry rating scale incorporating return time and quality of work recovery for scoring – relative gain (defined as absolute gain/ maximal gain minus pre-operative score). Results considered good when >70% and poor when <60%	Mean 51 months	105 (154 discs)	0	68 (64.8)	Mean: 39.2 Range: 24–50

Table F1 (cont'd) **Descriptive characteristics of case series for lumbar AIDR after failed non-surgical treatment**

Study	Location	Enrolment period	Outcome measures	Time of follow-up	Study population			
					n	Losses to follow-up	№ male (%)	Age (years)
SB Charité™ III (cont)								
Sott & Harrison (2000)	UK	1992–1998	Clinical outcome (published criteria), ROM (via radiology)	18–68 months Mean: 48 months	14 (15 discs)	0	8 (57.1)	Mean: 48 Range: 31–61
Su et al (2003)	China	Apr 1998–Apr 2000	Clinical outcome: 4-point scale ranging from excellent to poor; radiological evaluation of ROM	17–41 months Mean: 26 months	31 (37 discs)	0	Not reported	Mean: 43.5 Range: 32–55
Xu et al (2004)[a]	China	Feb 1999–Jun 2002	Lumbar spine stability, intervertebral motor scope, intervertebral space height and intervertebral foramen size, clinical evaluation	3–38 months Mean: 18.6 months	34 (41 discs)	0	20 (58.8)	Mean: 41.1 Range: 21–65
Zeegers et al (1999)	The Netherlands	Jun 1989–Jun 1991	Radiography to assess lumbar degeneration: No, minor or definite Clinical response to surgery: Good, fair, poor	2 years	50 (75 discs)	4	20 (40.0)	Mean: 43 Range: 24–59
ProDisc								
Bertagnoli & Kumar (2002)	Germany	Not reported	Radiological outcomes: Degeneration and ROM, ODI, SF-36, pain using VAS	3 months to 2 years	108 (134 discs)	0	58 (53.7)	Mean: 42 Range: 34–65
Huang et al (2003)	France	Mar 1990-–Sep 1993	Radiographic evaluation of post-operative flexion-extension ROM and junctional degeneration	Mean 8.7 years	64 (42 with 58 discs)	Excluded n=16, 3 deceased, 3 lost	23/42 (54.8)	Mean: 45.2 Range: 25–63
Mayer et al (2002)	Germany	Jun 2000–Mar 2002	VAS, ODI, SF-36, clinical parameters, radiographs	24 months Mean (SD): 5.8 (3.0) months	34	0, but follow-up time not lapsed at time of reporting	12 (35.3)	Mean: 44 Range: 25.2–65.4

Table F1 (cont'd) **Descriptive characteristics of case series for lumbar AIDR after failed non-surgical treatment**

Study	Location	Enrolment period	Outcome measures	Time of follow-up	Study population			
					n	Losses to follow-up	№ male (%)	Age (years)
ProDisc (cont)								
Tropiano et al (2003)	France	Dec 1999–Dec 2001	VAS for pain intensity, ODI Qualitative scales: Quality of life, return to work, patient satisfaction, radiographic evaluation	1–2 years Mean: 1.4 years	53	0	18 (34.0)	Mean: 45 Range: 28–67
Acroflex								
Fraser et al (2004)	Australia	Pilot 1: 1998–1999 Pilot 2: Feb–Dec 2000	VAS for self assessment of pain, radiological outcomes, SF-36,Low Back Outcome Score (LBOS), ODI	2 years	28	0	14 (50.0)	Mean: 41 Range: 30–54

[a] Studies did not explicitly state that participants were required to have failed non-operative treatment, however the participants had symptoms for many years
[b] Study did not explicitly state that participants were required to have failed non-operative treatment or the duration of symptoms
[c] Study presented results for SB Charité™ Models I, II and III. 93 participants received SB Charité™ Model III
[d] Reported as lost to follow-up or had not been seen for follow-up

Table F2 presents the inclusion and exclusion criteria used to enrol participants in each of the studies.

Table F2 Patient selection criteria for case series for lumbar AIDR after failed non-surgical treatment

Study	Inclusion	Exclusion
SB Charité™ III		
Caspi et al (2003)	Low back pain with or without radicular pain for at least 5 years	Not reported
Cinotti et al (1996)	Degenerated disc at one or two levels and a painful discography at the same levels	• Degenerative changes of the facet joints (as seen on CT or MRI scans) • Disc degeneration adjacent to a fused area • Spondylolisthesis
David (1993)	Lumbar and/or radicular chronic pain for many years with clinical signs of disc pathology and/or instability	Not reported
Griffith et al (1994)	Not reported	Not reported
Lemaire et al (1997)	Low back pain and radicular pain	Not reported
Sott & Harrison (2000)	• Long-standing lumbar pain • Clinical/radiological signs of degenerative lumbar disc disease • Several previous physiotherapy or chiropractor treatment courses	Not reported
Su et al (2003)	• Lumbar intervertebral disc degeneration or recurrent degeneration complicated with – narrowing of intervertebral space – affected walking function • Unsatisfactory non-surgical treatment	Not reported
Xu et al (2004)	Diagnosed with degenerative diseases of the lumbar intervertebral disc and received AIDR	All cases that were in accordance with degenerative diseases of lumbar intervertebral disc and did not receive AIDR
Zeegers et al (1999)	• Medically refractory lumbar discopathies • Failed conservative management	Predominant symptoms or deficits in the legs that could be related to involvement of nerve roots

Table F2 (cont'd) Patient selection criteria for case series for lumbar AIDR after failed non-surgical treatment

Study	Inclusion	Exclusion
ProDisc		
Bertagnoli & Kumar (2002)	• Previous conservative treatment for at least 6 months • Positive pre-operative response to discography	• Severe osteoporosis • Physiological dysfunction • History of previous disc infection • Severe posterior element pathologies • Fracture of the vertebra • Tumour
Huang et al (2003)	• Disc degeneration with discogenic pain • Failed at least 6 months of conservative management	Post-hoc: Incomplete radiographic documentation
Mayer et al (2002)	• Mono- or bi-segmental lumbar disc degeneration and post-operative disc degeneration • Failed at least 6 months of conservative therapy (extensive inpatient and outpatient physiotherapy including fluoroscopy-guided infiltrations pre-operatively)	• Translational instability (eg, spondylolisthesis, spinal stenosis, significant osteoarthritis of the facet joints, deformities, infection, tumour) • Previous fusion attempts in affected levels • Pregnancy • Incomplete worker's compensation procedures • Unwillingness to comply with follow-up visits
Tropiano et al (2003)	• Disc degeneration • Failed spine surgery • At least 6 months of severe back pain refractory to non-surgical treatment	• Chronic disease of major organ system • History of local infection • Pregnancy • Associated facet degeneration • History of abdominal or retroperitoneal surgery near planned approach • Osteoporosis or osteopaenia • Structural spinal deformities • Postoperative absence of posterior elements
Acroflex		
Fraser et al (2004)	• Disc degeneration (1–2 levels) at L4-L5 or L5-S1 levels • Pain refractory to at least 6 months of conservative therapy • Provocation discography demonstrating internal disc disruption • Aged 30–55 years • Informed consent given • Willingness to comply with follow-up	• Previous lumbar surgery • Lumbosacral angle too steep to allow direct anterior approach, central or lateral recess spinal stenosis, spondylolisthesis, systemic disease that would impact on condition, morbid obesity, structural scoliosis • Alcohol and/or drug abuse • 3 or more positive Waddell signs • Psychiatric disorder or mental condition that would impair ability to complete follow-up • Involvement in litigation related to the spinal condition

Validity of case series

The validity assessment of the case series are presented in Table F3.

Table F3 Validity characteristics of case series for lumbar AIDR after failed non-surgical treatment

Study	Design	Participants consecutively enrolled	Explicit inclusion/ exclusion criteria	Outcomes assessed in all participants	Outcomes assessed using objective criteria	Outcomes assessed in a blinded manner	Uniform follow-up	Indication uniform across participants
SB Charité™ III								
Caspi et al (2003)	Not reported	Not reported	Exclusion criteria not explicit	Yes	Unclear	Not reported	Yes 48 months	Yes
Cinotti et al (1996)	Not reported	Not reported	Yes	Yes	Unclear	Not reported. Participants evaluated by one of authors who did not participate in the surgery and had no affiliation with the hospital where surgery took place	No Range: 2–5 years	Yes
David (1993)	Prospective	Not reported	Exclusion criteria not explicit	Yes	Unclear; radiographic criteria objective	Not reported	No Range: 12–37 months	Yes
Griffith et al (1994)	Retrospective	Not reported	Inclusion and exclusion criteria not explicit	Yes	Unclear, pain subjective	Not reported	No	Unclear
Lemaire et al (1997)	Not reported	Not reported	Inclusion and exclusion criteria not explicit	Yes	Unclear	Not reported	Unlikely as mean reported	Yes
Sott & Harrison (2000)	Prospective	Not reported	No	Yes	Unclear	Not reported	No Range: 18–68 months	Yes
Su et al (2003)	Not reported	Not reported	Exclusion criteria not explicit	Yes	Unclear if clinical outcome scale objective (local scale)	Not reported	No Range: 17–41 months	Unclear

Table F3 (cont'd) **Validity characteristics of case series for lumbar AIDR after failed non-surgical treatment**

Study	Design	Participants consecutively enrolled	Explicit inclusion/ exclusion criteria	Outcomes assessed in all participants	Outcomes assessed using objective criteria	Outcomes assessed in a blinded manner	Uniform follow-up	Indication uniform across participants
SB Charité™ III (cont)								
Xu et al (2004)	Not reported	No. Participitants selected from those diagnosed with intervertebral DDDs	Reported poorly defined inclusion and exclusion criteria	No	Unclear: Radiographic criteria objective, clinical criteria subjective	Not reported	No Range: 3–38 months	Unclear
Zeegers et al (1999)	Prospective	Yes (report of first series of 50/350)	Yes	n=4 lost to follow-up not reported	Unclear: Radiographic criteria objective, clinical criteria subjective	Not reported	Yes	Unclear (need clinical opinion)
ProDisc								
Bertagnoli & Kumar (2002)	Prospective	Not reported	Yes	Yes	Unclear for radiological outcomes, yes for ODI, VAS, SF-36	Not reported	No Range: 3 months to 2 years	Broad indications
Huang et al (2003)	Retrospective	Not reported	No, exclusion post-hoc	16 excluded due to incomplete records, 3 deceased, 3 lost to follow-up	Yes	Not reported	Unlikely as mean reported	Yes
Mayer et al (2002)	Prospective	Yes	Yes	8 had not finished the first 3-month post-operative interval at time of reporting	Some outcomes eg VAS and ODI	Not reported	No Mean (SD) 5.8 (3.0) month follow-up	Yes

Table F3 (cont'd) **Validity characteristics of case series for lumbar AIDR after failed non-surgical treatment**

Study	Design	Participants consecutively enrolled	Explicit inclusion/ exclusion criteria	Outcomes assessed in all participants	Outcomes assessed using objective criteria	Outcomes assessed in a blinded manner	Uniform follow-up	Indication uniform across participants
ProDisc								
Tropiano et al (2003)	Prospective	Not reported	Yes	Yes	Some scales ODI, VAS	Unclear, but assessors did not participate in selection, surgery or post-operative care	No Range: 1–2 years	Yes
Acroflex								
Fraser et al (2004)	Prospective	Not reported	Yes	Yes	ODI, VAS, LBO	Not reported	Yes	Yes

Results of case series

The results reported in the case series are summarised in Table F4. Each of the case series reported different outcome measures. Seven studies (Bertagnoli & Kumar 2002, Caspi et al 2003, Cinotti et al 1996, David 1993, Sott & Harrison 2000, Su et al 2003, Xu et al 2004) reported clinical outcomes, rated as excellent, good, fair or poor. It is unclear how these clinical outcomes were measured and whether these were subjective or objective measures. Seven studies (Bertagnoli & Kumar 2002, Cinotti et al 1996, Griffith et al 1994, Huang et al 2003, Su et al 2003, Tropiano et al 2003, Xu et al 2004) reported ROM, three studies reported ODI scores (Fraser et al 2004, Mayer et al 2002, Tropiano et al 2003) and two studies reported VAS pain scores (Mayer et al 2002, Tropiano et al 2003). These data are difficult to interpret without a parallel comparison group of participants who received lumbar fusion or standard non-surgical treatment.

Table F4 Results of case series for lumbar AIDR

Study	№ or proportion of participants with reported results	Length of follow-up	Outcomes
SB Charité™ III			
Caspi et al (2003)	20 (23 discs)	48 months	• Clinical results: Fair 3/20, good 4/20, excellent 11/20, poor 4/20 (1 participant underwent secondary fusion and another is waiting for surgery) • Participants recovery in terms of occupation: Completely disabled 4/20, resumed physical labour 1/20, returned to light and sedentary work 15/20
Cinotti et al (1996)	46 (56 discs)	Mean: 3.2 years Range: 2–5 years	• Clinical results: Excellent 11/46, good 18/46, fair 14/46, poor 3/46 • Patient satisfaction: Great benefit 14/46, great but not complete benefit 17/46, mild improvement 12/46, no improvement or worsening 3/46 • ROM: 12° in participants receiving central or posterior placement of disc and 5° in participants receiving placement anteriorly • No DDD evident in adjacent levels in 10 participants undergoing MRI at follow-up
David (1993)	22 (29 discs)	Mean: 19 months	Clinical results (modified Stauffer-Coventry): Excellent 3/22, good 12/22, fair 6/22, bad (one secondary fusion) 2/22
Griffith et al (1994)	93 (139 discs)	Mean (SD): 11.9 (3.8) months Range: 1–37 months for Model III	• VAS (change in pain intensity from baseline to last follow-up): Right leg pain – increased 7/71, decreased 31/71, unchanged 21/71; Left leg pain – increased 4/71, decreased 35/71, unchanged 18/71; Back pain – increased 7/71, decreased 47/71, unchanged 9/71 • Resolution of neurologic weakness 17/21 • Walking status (self-reported, change from baseline): Improved 28/71, decreased 2/71, unchanged 41/71 • ROM (change from baseline): Lumbar flexion – increased 76/93, decreased 7/93, unchanged 9/93 Lumbar extension – increased 68/93, decreased 9/93, unchanged 16/93
Lemaire et al (1997)	105 (154 discs)	Mean: 51 months	• Average final relative gain was 82.18% (n=105). Mean increased over time with 48.3% at 3 months and 72.82% at 12 months • Relative gain: >70% (89/105), 60-70% (6/105), <60% (16/105) • Improvement in radicular pain 101/105, improvement in low back pain 95/105 3 months after surgery

Table F4 (cont'd) Results of case series for lumbar AIDR

Study	№ or proportion of participants with reported results	Length of follow-up	Outcomes
SB Charité™ III (cont'd)			
Sott & Harrison (2000)	14 (15 discs)	Mean: 48 months	• Clinical outcome: Good 10/14, fair 2/14, poor 1/14; aged <45 years (n=7) and aged >45 years (n=7), good in 5, fair in 1, poor in 1 • Maximal ROM between extension and flexion: 10°
Su et al (2003)	31/31 (37 discs)	Mean: 26 months	• Clinical outcome: Excellent 23/31, good, 6/31, fair 2/31 • Postoperative mobility: 4.0° anterior flexion, 5.1° posterior extension (pre-operative not reported)
Xu et al (2004)	34 (41 discs)	Mean: 18.6 months Range: 3–38 months	• Lumbar spine stability: No abnormal dislocation of the operated level was found in post-operative lumbar radiographs in participants with lumbar disc herniation (n=4) • Intervertebral motor scope L4-L5 segment replacement Mean (SD) (n=25): Anteflexion: Baseline 10.2° (2.1°), follow-up 9.8° (1.7°) Posterior extension: Baseline 5.6° (1.3°), follow-up 5.1° (1.1°) • Intervertebral space height and intervertebral foramen size were not significantly different pre- and post-operatively for L4–L5 disc replacements (n=25) • Clinical evaluation: Excellent 27/34, good 4/34, fair 3/34, poor 0/34
Zeegers et al (1999)	46/50 (75 discs)	2 years	• Positive clinical result (good or fair): 32/46 (70%); ITT: 64% • Age <45 years only factor statistically associated with a positive clinical result (chi-square test) • Subjective reporting of outcome: – 30/46 (ITT 60%) reported reduction of low back pain – 38/46 (ITT 76%) report no regrets with surgery • 38/50 completed 2-year radiographic follow-up. 28/38 (ITT 56%) had a good technical result and 9/39 had a fair result based on authors' criteria
ProDisc			
Bertagnoli & Kumar (2002)	108/108	3 months – 2 years	• Clinical outcome: Excellent (98/108), good (8/108), fair (2/108), poor (0/108) • ROM: Increased in all patients post-operatively at operated levels • VAS, ODI, SF-36 not reported
Huang et al (2003)	42/64 (58 prostheses)	Mean: 8.7 years	• Flexion-extension motion of ≥2°: 38/58 discs (66%) • Mean ROM (all levels): 3.8° • Radiographic signs of junctional disc degeneration: 10/42 (24%) • Association between AIDR ROM patient factors: Female gender associated with failure to achieve 2° of motion
Mayer et al (2002)	26/34 participants (37 implants)	Mean: 5.8 months	• Mean VAS score: 6.3 pre-operatively vs 2.4 post-operatively (Mean reduction: 3.9, Range: –8.4 to +7.5) • ODI score: mean (SD) postoperative reduction of 11.5 (9.6) points, range -27 to +12 • Subjective ratings: At last follow-up, 76% reported no back pain and 82.6% 'satisfied' or 'completely satisfied' • Radiology: No loosening or migration of implants, no change in the function of the implant

Table F4 (cont'd) Results of case series for lumbar AIDR

Study	№ or proportion of participants with reported results	Length of follow-up	Outcomes
ProDisc (cont'd)			
Tropiano et al (2003)	53	Mean: 1.4 years	• VAS scores – Mean(SD) – Baseline vs 1.4 year follow-up: VAS lumbar: Poor, 7.4 (2.5) vs excellent, 1.3 (1.78) VAS radicular: Fair 6.7 (2.99) vs excellent, 1.9 (2.59) • ODI (%) pre-operative vs 1.4 years: Severe disability, 56 (8.21) vs minimal disability, 14 (7.38) • Operated at L5-S1: ROM mean 8° (range 2°–12°); L4-L5 mean 10° (range 8°–18°°); no change in lordosis following AIDR • Patient satisfaction: Entirely satisfied, n=46 (87%); satisfied, n=7 (13%); not satisfied, n=0 • Activities of daily living: Full, n=38 (72%); slightly limited, n=15 (28%)
Acroflex			
Fraser et al (2004)	28/28	2 years	• Mean ODI baseline vs 24 months: 49.3 vs 34.4 • Mean LBO score baseline vs 24 months: 17.7 vs 33.0 • VAS and specific SF-36 outcomes not reported

Abbreviations: ITT, intention to treat; LBO, low back outcome

Case series can be a useful study design to identify prognostic factors that influence outcomes. Huang et al (2003) reported failure of the disc prosthesis to achieve at least a 2° ROM in 44 per cent of participants. The authors performed statistical analyses to identify female gender, but not age, weight, number of levels implanted, level implanted and history of spinal surgery, as prognostic factors that may lead to this failure. Zeegers et al (1999) assessed the relationship between several factors and the clinical outcome of surgery and reported that only age less than 45 years was statistically associated with a positive clinical outcome.

Discussion of case series

The results reported in the identified case series are difficult to interpret in the absence of a control group of participants receiving lumbar fusion or non-surgical treatment. However, where reported, most studies found improvements compared with baseline levels.

Appendix G Trials and studies identified in the review of economic literature

Technology	Comparator	Citation	Type of economic evaluation	Country (Trial)
Lumbar fusion or ligamentous stabilisation	Intensive rehabilitation	Fairbank et al. 'A UK multi-centre trial-based cost-utility analysis of surgical stabilisation of the lumbar spine versus intensive rehabilitation for treatment of chronic low back pain patients.' 2004. SpineWeek 2004 (Porto) (abstract)	Cost-effectiveness analysis	UK (The Spine Stabilisation Trial)
Lumbar fusion	Non-surgical treatment[a]	Fritzell et al. 'Cost-effectiveness of lumbar fusion and non-surgical treatment for chronic low back pain in the Swedish Lumbar Spine Study.' *Spine* 2004; 29(4): 421–434	Cost-effectiveness analysis	Sweden (The Swedish Lumbar Spine Study
Lumbar fusion	None	Katz. 'Lumbar spinal fusion. Surgical rates, costs and complications.' *Spine* 1995; 24(S): 78S–83S	Cost analysis	US
AIDR	Spinal fusion	Singh et al. 'Assessing the potential impact of total disc arthroplasty on surgeon practice patterns in North America.' *Spine Journal* 2004; 4(6): 195S–201S	Market analysis	US

[a] Not further defined in the publication

Appendix H Comments on the economic sections of the Application to MSAC for AIDR

Review of the literature on the cost-effectiveness of AIDR

The Application included the search strategies and results of a literature review conducted to identify relevant publications. Non-surgical treatment was not included in the review as it was not considered an appropriate comparator. The approach taken by the Applicant to conduct the literature review was considered inadequate because of the non-usage of economic databases. An independent systematic review of the literature was performed by the evaluators to identify publications on the cost-effectiveness of cervical AIDR and cervical fusion, lumbar AIDR and lumbar fusion, and lumbar AIDR and non-surgical treatment. The evaluators' review is described in 'What are the economic considerations?'.

Critical appraisal of the cost-effectiveness analysis in the Application

Cost-effectiveness analyses (CEAs) using Excel spreadsheets were conducted separately for lumbar AIDR and cervical AIDR. No CEA was performed for non-surgical treatment, which was not considered an appropriate comparator. The perspective adopted in the analyses was that of the health sector. A discount rate of five per cent per annum was applied to both costs and benefits. The robustness of the CEA results for cervical AIDR was verified using a one-way sensitivity analysis.

Definition and measurement of costs

Direct costs included in the CEAs are health care costs, covering the costs of hospital care, prostheses and medical fees if the procedures are performed in the private sector. The cost of hospital care is based on resources required for:

- DRG I09A (spinal fusion with catastrophic or severe complications or co-morbidities); and
- DRG I09B (spinal fusion with no catastrophic or severe complications or co-morbidities).

Cost data and the number of separations come from the NHCDC 2001-2002 (Australian Government DoHA 2004c). The Application makes no adjustment for the changes in the price of health services since 2001 (totalling 22.8% to the March quarter, 2005) (Australian Bureau of Statistics 2005) and the possible increase in the number of spinal fusions. Medical fees are taken from the MBS Book May 2004 edition (DoHA 2004d) and include fees for the surgeon, surgical assistance and anaesthesia management. The MBS items used to calculate medical fees are listed in Tables 10.2.2.2 and 10.2.5.1 of the Application for lumbar and cervical procedures, respectively.

The DoHA has advised that items 40300 (laminectomy for removal of intervertebral disc or discs) and 40301 (microsurgical discectomy of intervertebral disc or discs) are not

payable for either spinal fusion or AIDR, and that the multi-operation rule is applicable in both spinal fusion and AIDR (see note T8.5 on p158 of the MBS November 2004). Under this rule, the fees for two or more operations listed in Group T8 (other than Subgroup 12 of that group), performed on a patient on the one occasion (except as provided in paragraph T8.5.3) are calculated by the following rule:

- 100 per cent for the item with the greatest schedule fee;
- plus 50 per cent for the item with the next greatest schedule fee;
- plus 25 per cent for each other item.

The use of incorrect MBS items and the non-application of the multi-operation rule have resulted in an overestimation of medical fees for both procedures. In addition the Application erroneously includes item 40330 (spinal rhizolysis) for AIDR. According to advice from the DoHA, the item is not relevant for reimbursement of this technology and should be removed. The Application also incorrectly uses item 20670 (initiation of management of anaesthesia for extensive spine and/or spinal cord procedures) in the calculation of medical fees for single-level cervical procedures. Note T10.23 on p180 of the MBS Book November 2004 states that this item is applicable for multiple levels only and the correct item for all single level cervical procedures is 20600. Appendices I and J list medical fees applicable for AIDR and spinal fusion.

The cost of prostheses used in AIDR and spinal fusion is the average selling price provided by the suppliers. The Application gives itemised costing of prostheses used in cervical fusion but not those used in lumbar fusion. It is assumed that the cost given in the Application is the price for 2004. For both cervical and lumbar fusion, the prostheses included are for an interbody fusion method which is more costly than the screws and rods (lumbar fusion), and screws and plates (cervical fusion) methods. According to information provided by the Advisory Panel, the prosthesis cost differential between the two methods could range from $4,000 (single level) to $8,000 (two levels) for lumbar fusion and $700 (single level) to $2,200 (two levels) for cervical fusion. This finding is supported by the literature on spinal fusion. Fritzell et al (2004) reported that costs for interbody fusion increase 103 per cent compared with non-instrumented posterolateral fusion. NHCDC data and Medicare claim data for items 48654–48675 for the periods 2001–2002 and 2002–2003 indicate that interbody fusion represents 21.7 per cent and 23.9 per cent, respectively, of spinal fusion. Given that item 48660 is also applicable for AIDR, these estimates are considered to be conservative. Hence the use of an interbody fusion method as the basis for cost comparison has the effect of inflating the cost of spinal fusion in favour of AIDR.

Rehabilitation costs after discharge from hospital were not taken into account in the CEAs. These might include the costs of physiotherapy, pain medications, nursing care and GP consultation. If the consumption of these health care services differs between patients undergoing spinal fusion and AIDR, then the non-inclusion would impact on the total cost of the procedures. Data are lacking on the costs of rehabilitation following surgery with either procedure.

Definition and measurement of benefits

The clinical benefit used in the comparison of lumbar AIDR with lumbar fusion is the overall success rate, defined as the achievement of all four primary efficacy measures:

- reduction in the ODI (>25% improvement compared to baseline);
- absence of any device failures requiring revision, re-operation or removal;
- absence of major complications; and
- maintenance or improvement of neurological status at 24 months.

The Application argues that this outcome best reflects the comparative clinical effectiveness of lumbar AIDR versus lumbar fusion. Data used in the comparison came from the pivotal Charité™ RCT which had a follow-up period of 24 months, although not all randomised patients had reached this time point when data were analysed.

For the comparison of cervical AIDR with cervical fusion, the reduction in the development of adjacent segment disease (ASD), and consequent reduction in pain and YLD, are the benefits taken into account in the analysis. Data used in the analysis came from a case series of cervical fusion with a sample size of 50 (Gore & Sepic 1998).

Assumptions used in the cost-effectiveness analysis

Key assumptions used in the CEAs are presented in Table H1. Assumptions 13–18 are applicable for cervical analysis only. The majority of assumptions are either not evidence based or were taken from studies of low methodological quality. The value of variables 5, 6 and 8 were altered in the CEA of cervical AIDR versus cervical fusion. The use of assumption 11 biases the cervical analysis in favour of AIDR.

Table H1 Key assumptions used in the cost-effectiveness analyses

№	Variable	Value	Source	Comment
1	Time horizon of the CEA for cervical fusion	21 years	Gore & Sepic (1998)	The value used is the follow-up period of a case series by Gore & Sepic (1998)
2	Time horizon of the CEA for lumbar fusion	10 years	Not stated	Probably reasonable according to the FDA Orthopaedic and Rehabilitation Devices Panel
3	Proportion of two-level cervical fusions	22%	Gore & Sepic (1998), Hillibrand et al (1999), Geisler et al (1998)	These studies are case series reporting a range of proportion from 7.5% to 34%
4	Re-operation for ASD in patients with cervical fusion	2% per year	Gore & Sepic (1998)	This is a case series and hence results are susceptible to bias
5	Reduction in the number of two-level cervical fusions as a result of AIDR	50%	Suppliers' Medical Advisory Board	Evidence is lacking
6	Reduction in the number of patients requiring re-operation for ASD, as a result of having cervical or lumbar AIDR	50%	Suppliers' Medical Advisory Board	Evidence is lacking
7	Re-operation for ASD in the lumbar spinal region	4% per year	Not stated	Evidence is lacking
8	Reduction in the number of patients suffering chronic pain following cervical AIDR	50%	Suppliers' Medical Advisory Board	Evidence is lacking. It would appear that this assumption is overly optimistic. Porchet & Metcalf (2004) reported no significant differences between treatment groups at 24 months follow-up for neck disability index, neck pain, arm pain and neurological status.
9	Number and type of prostheses required for a lumbar spinal fusion	4 pedicle screws, 4 set screws, 2 rods, 2 interbody spacers	Not stated	Reasonable according to advice from the Advisory Panel
10	Number and type of prostheses required for a single-level cervical spinal fusion	1 cage	Not stated	Reasonable according to advice from the Advisory Panel
11	Number and type of prostheses required for a two-level cervical spinal fusion	2 cages, 1 plate, 4 screws	Not stated	According to the Advisory Panel, only the cages are required. By including other hardware the Application overestimates the cost of prostheses by $3,750
12	Hospitalisation cost	Same for both procedures regardless of anatomical site	Charité™ trial	NHCDC data do not differentiate between lumbar and cervical fusion. Data on the cost of AIDR in Australia are not available at present
13	Average age at operation	45	Gore & Sepic (1998)	
14	Average time for pain to recur (years)	7.2	Gore & Sepic (1998)	Low quality evidence
15	Average time for pain to recur after re-operation (years)	3.5	Gore & Sepic (1998)	Low quality evidence
16	Quality of life when there is no medical problem	0.97	Fryback et al (1993)	

Table H1 (cont'd) Key assumptions used in the cost-effectiveness analyses

№	Variable	Value	Source	Comment
17	Quality of life when there is chronic back pain	0.79	Fryback et al (1993)	
18	Disability weight for back pain	0.125	Matthers et al (1999)	
19	Operating time for spinal fusion (cervical and lumbar)	3 hours	Suppliers' Medical Advisory Board	A range of mean operative times has been reported: 83 minutes for one-level and 97 minutes for two-level cervical interbody procedures (Agrillo et al 2002), 160 minutes for lumbar interbody fusion (Haid et al 2004)
20	Operating time for AIDR (cervical and lumbar)	2.5 hours	Suppliers' Medical Advisory Board	The Charité™ RCT reported no significant difference in operative time between the study groups while the ProDisc trial suggests that operative time for AIDR is significantly shorter than fusion (75 and 218 minutes, respectively, $p<0.01$). Alessi et al (2004) reported operating time varying between 75 and 160 minutes

Unit cost used in the CEAs

The unit cost used in the analyses according to resource type is tabulated in Table H2. In this section, prices have been revised to the 2005 level to account for the changes in the price of health care services and presented as a weighted average in the third column. The latest data available (2002–2003) are used in the calculations (Australian Government DoHA 2004a). Unit cost for item 9 has been corrected according to advice from the Advisory Panel.

Table H2 Unit cost by resource item

№	Resource item	Unit cost in Application	Correct unit cost
1	Cost of hospitalisation for lumbar AIDR	Public hospital: $15,096 Private hospital: $7,528	$11,184[a], source: NHCDC AN-DRG I09A I09B
2	Cost of hospitalisation for lumbar fusion	Public hospital: $15,096 Private hospital: $7,528	$11,184[a], source: NHCDC AN-DRG I09A I09B
3	Cost of hospitalisation for cervical AIDR	Public hospital: $15,096 Private hospital: $7,528	$11,184[a], source: NHCDC AN-DRG I09A I09B
4	Cost of hospitalisation for cervical fusion	Public hospital: $15,096 Private hospital: $7,528	$11,184[a], source: NHCDC AN-DRG I09A I09B
5	Cost of prostheses for lumbar AIDR	$9,833	$11,514[a], source: Sponsors' price
6	Cost of prostheses for one level lumbar fusion	$13,861	$14,227[a], source: Sponsors' price
7	Cost of prostheses for cervical AIDR	$11,439	$13,395[a], source: Sponsors' price
8	Cost of prostheses for one-level cervical fusion	$3,000	$3,000, source: Sponsors' price
9	Cost of prostheses for two-level cervical fusion	$9,750	$6,000, source: Sponsors' price (unnecessary implants are not included according to advice from the Advisory Panel)

[a] Weighted average

Results of the cost-effectiveness analyses

Lumbar AIDR versus lumbar fusion

Table H3 suggests that as well as gaining a higher success rate, there is a potential saving of $2,715 per separation if lumbar AIDR is performed instead of lumbar fusion. Other economic benefits claimed by the Application are a further saving of $3,911 per patient over a ten-year horizon due to the reduction in operation for ASD and a potential reduction in length of stay and theatre time (not further quantified). The discounted saving amount is estimated to be slightly lower, at $3,627 per separation, if the weighted average costs of hospitalisation and prostheses are used in the calculation.

The accuracy of these estimates depends on:

- the assumption that the procedure cost is the same for fusion and AIDR;
- the validity and generalisability of results from the Charité™ trial; and
- the validity of assumptions used.

In addition, the hospitalisation costs for both lumbar fusion and lumbar AIDR might be underestimated because NHCDC cost data cover both instrumented and non-instrumented procedures.

Table H3 Cost effectiveness of lumbar AIDR versus lumbar fusion

Source of cost	Lumbar fusion	Lumbar AIDR
Hospitalisation per separation	$11,184	$11,184
Medical fees	$1,443	$1,441
Prostheses per separation	$14,227	$11,514
Total per separation	**$26,854**	**$24,139**

It should be noted that efficacy data came from one RCT that was yet to evaluate all randomised patients at 24 months. Additionally, concerns have been raised about the sponsors' application of the intention-to-treat principle in the analysis of the trial. An FDA re-analysis of the trial using the conservative single imputation last-observation-carried-forward method reported that the success rate for the Charité™ patients ranged from 54 to 68 per cent, whereas that for the BAK group ranged from 50 to 70 per cent (FDA 2004), indicating little difference in short-term outcomes between the control and intervention groups.

Furthermore, when the four primary efficacy endpoints that make up the composite success outcome were examined, only the difference in the improvement of ODI scale approached statistical significance (p=0.054). Additionally, the Charité™ group had a higher rate of life-threatening adverse events (15% versus 9%) and device-related adverse events (7.3% versus 4.0%). However, the BAK group had a higher incidence of device failures (8.1% versus 4.9%) (FDA 2004). The discounted saving of $3,627 per separation due to a reduction in the incidence of ASD is based on low quality evidence and hence is subject to uncertainty. The saving of $2,715 per separation might not be realised if treating the adverse events or revising implant devices is costly or results in much poorer quality of life for affected patients.

Cervical AIDR versus cervical fusion

Table H4 presents the weighted average cost per separation for one-level cervical fusion and AIDR. Given that the hospitalisation cost is assumed to be the same for both procedures, the incremental cost of $8,727 is almost entirely due to the higher cost of the AIDR prostheses. As in the case for lumbar AIDR, the cost of rehabilitation has not been considered by the Applicant. The predicted incremental cost might change if the rehabilitation cost differs between the two groups or the cost of prostheses has been incorrectly estimated.

Table H4 Incremental cost of one level cervical AIDR

Source of cost	Fusion (one level)	AIDR	Incremental cost
Hospitalisation	$11,184	$11,184	$0
Prostheses	$3,000	$11,439	$8,439
Medical fees	$1,116	$1,404	$288
Total cost	**$15,300**	**$24,027**	**$8,727**

The Application claims that cervical AIDR would reduce the incidence of ASD by 50 per cent, therefore resulting in a reduction in the number of cervical operations involving two levels. Over a time horizon of 21 years, this would lead to a cost offset of $541 per separation.

The incremental gain in quality of life is shown in Table H5. Results in this table should be interpreted with caution because they are based on very low quality evidence. The costs (discounted) for various quality of life outcomes are shown in Table H6. They are based on the sponsors' assumption that AIDR would reduce chronic pain and disability by 50 per cent. A central issue in interpreting the results presented is the plausibility of the percentage pain reduction. Results for various outcomes, including quality of life measures, from the only RCT comparing cervical AIDR with cervical fusion, the ACDPI trial (Porchet and Metcalf 2004), suggest that differences between the two groups are not statistically significant. It would appear that the sponsor's assumption is not evidence based and is biased against cervical fusion.

Table H5 Predicted incremental gain in quality of life in patients undergoing cervical AIDR

Outcomes	Fusion	AIDR	Incremental gain
Cumulative total years with pain	6.99	3.49	3.49
Discounted cumulative total years with pain	4.33	2.16	2.16
Cumulative QALYs lost	1.26	0.63	0.63
Discounted cumulative QALYs lost	0.78	0.39	0.39
Cumulative total years with pain	**6.99**	**3.49**	**3.49**

Abbreviation: QALY, quality adjusted life-year

Table H6 Incremental cost per year of pain avoided, QALY gained and YLD avoided

Outcome	Cost
Incremental cost per year of pain avoided	$3,902
Incremental cost per QALY gained	$21,676
Incremental cost per YLD avoided	$31,214

Abbreviation: QALY, quality adjusted life-year; YLD, years lived with disability

Appendix I Medical fees for AIDR

Item	Service	Schedule fee	% claimable[a]	Fee to be claimed
Lumbar, one level				
48660	Spinal fusion (anterior interbody) to cervical, thoracic or lumbar regions – 1 level	$918.65	100	$918.65
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 49642–48675 applies – 1 or 2 levels	$798.85	50	$399.43
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20630	Initiation of management of anaesthesia for procedures in lumbar region	$134.80	100	$134.80
23120	Anaesthesia perfusion time units (2.46–3.00 hours)	$202.20	100	$202.20
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$263.62	100	$263.62
Total fees				$1,955.09
Cervical, one level				
48660	Spinal fusion (anterior interbody) to cervical, thoracic or lumbar regions – 1 level	$918.65	100	$918.65
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 49642–48675 applies – 1 or 2 levels	$798.85	50	$399.43
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20600	Initiation of management of anaesthesia for procedures on cervical spine and/or cord	$168.50	100	$168.50
23120	Anaesthesia perfusion time units (2.46–3.00 hours)	$202.20	100	$202.20
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$263.62	100	$263.62
Total fees				$1,988.79
Lumbar, two levels				
48669	Spinal fusion (anterior interbody) to cervical, thoracic or lumbar regions – more than 1 level	$1,238.20	100	$1,238.20
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 49642–48675 applies – 1 or 2 levels	$798.85	50	$399.43
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20670	Initiation of management of anaesthesia for extensive spine and/or spinal cord procedures	$219.05	100	$219.05
23140	Anaesthesia perfusion time units (3.15–3.30 hours) (14 basic units)	$235.90	100	$235.90
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$327.53	100	$327.53
Total fees				$2,456.50

Item	Service	Schedule fee	% claimable[a]	Fee to be claimed
Cervical, two levels				
48669	Spinal fusion (anterior interbody) to cervical, thoracic or lumbar regions – more than 1 level	$1,238.20	100	$1,238.20
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 49642–48675 applies – 1 or 2 levels	$798.85	50	$399.43
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20670	Initiation of management of anaesthesia for extensive spine and/or spinal cord procedures	$219.05	100	$219.05
23140	Anaesthesia perfusion time units (3.15–3.30 hours) (14 basic units)	$235.90	100	$235.90
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$327.53		$327.53
Total fees				$2,456.50
Weighted average medical fees for lumbar AIDR				$2,040.83
Weighted average medical fees for cervical AIDR				$2,068.77

[a] Multiple operation formula applied

Appendix J Medical fees for spinal fusion

Item	Service	Schedule fee	% claimable[a]	Fee to be claimed
Lumbar, one level				
Screws plus rod				
48648	Bone graft (postero-lateral fusion) – 1 or 2 levels	$918.65	100	$918.65
40330	Spinal rhizolysis	$810.30	50	$405.15
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 48642–48675 applies – 1 or 2 levels	$798.85	25	$199.71
47726	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – small quantity	$119.85	25	$29.96
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20630	Initiation of management of anaesthesia for procedures in lumbar region	$134.80	100	$134.80
23120	Anaesthesia perfusion time units (2.46–3.00 hours)	$202.20	100	$202.20
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$304.70	100	$304.70
Total fees				$2,231.58
Interbody cage				
48654	Spinal fusion (posterior interbody)	$918.65	100	$918.65
40300	Laminectomy for removal of invertebral disc or discs	$810.30	50	$405.15
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 48642–48675 applies – 1 or 2 levels	$798.85	25	$199.71
47726	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – small quantity	$119.85	25	$29.96
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20630	Initiation of management of anaesthesia for procedures in lumbar region	$134.80	100	$134.80
23120	Anaesthesia perfusion time units (2.46–3.00 hours)	$202.20	100	$202.20
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$310.70	100	$310.70
Total fees				$2,237.57
Weighted average cost of medical fees for lumbar procedures – one level				$1,851.11

Item	Service	Schedule fee	% claimable[a]	Fee to be claimed
Cervical, one level				
Non-instrumented fusion				
40332	Cervical decompression, including anterior fusion, 1 level	$1,322.25	100	$1,322.25
47726	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – small quantity	$119.85	50	$59.93
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20600	Initiation of management of anaesthesia for procedures on cervical spine and/or cord	$168.50	100	$168.50
23120	Anaesthesia perfusion time units (2.46–3.00 hours)	$202.20	100	$202.20
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$276.44	100	$276.44
Total fees				$2,065.71
Screws and plate				
40332	Cervical decompression, including anterior fusion, 1 level	$1,322.25	100	$1,322.25
47726	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – small quantity	$119.85	50	$59.93
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20670	Initiation of management of anaesthesia for extensive spine and/or spinal cord procedures	$219.05	100	$219.05
23140	Anaesthesia perfusion time units (3.15–3.30 hours) (14 basic units)	$235.90	100	$235.90
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$276.44	100	$276.44
Total fees				$2,149.96
Interbody cage				
48660	Spinal fusion (anterior interbody) to cervical, thoracic or lumbar regions – 1 level	$918.65	100	$918.65
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 48642–48675 applies – 1 or 2 levels	$798.85	50	$399.43
47726	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – small quantity	$119.85	25	$29.96
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20600	Initiation of management of anaesthesia for procedures on cervical spine and/or cord	$168.50	100	$168.50
23120	Anaesthesia perfusion time units (2.46–3.00 hours)	$202.20	100	$202.20
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$269.61	100	$269.61
Total fees				$2,024.75

Item	Service	Schedule fee	% claimable[a]	Fee to be claimed
Interbody cage, plate and screws				
40332	Cervical decompression, including anterior fusion, 1 level	$1,322.25	100	$1,322.25
47726	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – small quantity	$119.85	50	$59.93
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20670	Initiation of management of anaesthesia for extensive spine and/or spinal cord procedures	$219.05	100	$219.05
23140	Anaesthesia perfusion time units (3.15–3.30 hours) (14 basic units)	$235.90	100	$235.90
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$276.44	100	$276.44
Total fees				$2,149.96
Average medical fees for cervical interbody procedures				$2,087.35
Average medical fees for cervical non-instrumented, and screw and plate procedures				$2,107.84
Weighted average cost of medical fees for cervical procedures – one level				$1,743.52
Lumbar, two levels				
Screws plus rod				
48648	Postero-lateral fusion – 1 or 2 levels	$918.65	100	$918.65
40330	Spinal rhizolysis	$810.30	50	$405.15
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 48642–48675 applies – 1 or 2 levels	$798.85	25	$199.71
47729	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – large quantity	$199.75	25	$49.94
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20670	Initiation of management of anaesthesia for extensive spine and/or spinal cord procedures	$219.05	100	$219.05
23140	Anaesthesia perfusion time units (3.15-3.30 hours) (14 basic units)	$235.90	100	$235.90
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$314.69	100	$314.69
Total fees				$2,379.49

Item	Service	Schedule fee	% claimable[a]	Fee to be claimed
Interbody cage				
48657	Spinal fusion (posterior interbody) with laminectomy, more than one level	$1,278.15	100	$1,278.15
40330	Spinal rhizolysis	$810.30	50	$405.15
48684	Spine, segmental internal fixation of, other than for scoliosis, being a service associated with a service to which any one of items 48642–48675 applies – 1 or 2 levels	$798.85	25	$199.71
47729	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – large quantity	$199.75	25	$49.94
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20670	Initiation of management of anaesthesia for extensive spine and/or spinal cord procedures	$219.05	100	$219.05
23140	Anaesthesia perfusion time units (3.15–3.30 hours) (14 basic units)	$235.90	100	$235.90
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$386.59	100	$386.59
Total fees				$2,810.89
Weighted average cost of medical fees for lumbar procedures – two levels				$423.71
Weighted average cost of medical fees for lumbar procedures				$2,274.82
Cervical, two levels				
Screws plus plate				
40335	Cervical decompression, including anterior fusion, more than one level	$1,642.25	100	$1,642.25
47729	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – large quantity	$199.75	50	$99.88
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$36.40
20670	Initiation of management of anaesthesia for extensive spine and/or spinal cord procedures	$219.05	100	$219.05
23140	Anaesthesia perfusion time units (3.15–3.30 hours) (14 basic units)	$235.90	100	$235.90
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$348.43	100	$348.43
Total fees				$2,581.90
Interbody cage				
40335	Cervical decompression, including anterior fusion, more than one level	$1,642.25	100	$1,642.25
47726	Bone graft, harvesting of, via separate incision in conjunction with another service – autogenous – large	$199.75	50	$99.88
17603	Examination of a patient in preparation for the administration of an anaesthetic	$36.40	100	$219.05
20670	Initiation of management of anaesthesia for extensive spine and/or spinal cord procedures	$219.05	100	$219.05
23140	Anaesthesia perfusion time units (3.15–3.30 hours) (14 basic units)	$235.90	100	$235.90
51303	Assistance at any operation identified by the word "assist" for which the fee exceeds $473.75	$348.43	100	$348.43
Total fees				$2,764.55
Weighted average cost of medical fees for cervical procedures – two levels				$448.63
Weighted average cost of medical fees for cervical procedures				$2,192.15

[a] Multiple operation formula applied

Appendix K Cost of prostheses provided by the sponsors

AIDR	Unit cost	Upper limit of unit cost	Number needed	Total cost	Upper limit of total cost
Lumbar, one level	$9,833	$9,833	1	$9,833	$9,833
Lumbar, two level	$9,833	$9,833	2	$19,666	$19,666
Cervical, one level	$11,439	$11,439	1	$11,439	$11,439
Cervical, two level	$11,439	$11,439	2	$22,878	$22,878
Weighted average cost of prostheses for lumbar procedures					$11,514
Weighted average cost of prostheses for cervical procedures					$13,395
Spinal fusion	**Unit cost**	**Upper limit of unit cost**	**Number needed**	**Subtotal**	**Upper limit of subtotal**
Lumbar, one level					
Screws plus rods					
Pedicle screw	$1,515	$1,515	4	$6,061	$6,061
Set screw	$558	$558	4	$2,233	$2,233
Rod	$311	$311	2	$622	$622
Total				$8,916	$8,916
Interbody cage					
Screws and rods as above				$8,916	$8,916
Interbody cage	$2,472	$2,472	2	$4,944	$4,944
Total				$13,860	$13,860
Lumbar, two levels					
Screws plus rods					
Pedicle screw	$1,515	$1,515	4	$6,060	$6,060
Set screw	$558	$558	4	$2,232	$2,232
Rod	$311	$311	2	$622	$622
Crosslink	$1,400	$1,400	1	$1,400	$1,400
Total				$10,314	$10,314
Interbody cage					
Screws and rods as above				$10,314	$10,314
Interbody cage	$2,472	$2,472	4	$9,888	$9,888
Total				$20,202	$20,202
Cervical, one level					
Non-instrumented: no prosthesis needed					
Screws and plate					
Plate	$2,450	$2,450	1	$2,450	$2,450
Screws	$325	$325	4	$1,300	$1,300
Total				$3,750	$3,750
Interbody cage					
Cage	$3,000	$3,000	1	$3,000	$3,000
Total				$3,000	$3,000

Spinal fusion	Unit cost	Upper limit of unit cost	Number needed	Subtotal	Upper limit of subtotal
Interbody cage, screws and plate					
Plate	$2,450	$2,450	1	$2,450	$2,450
Screws	$325	$325	4	$1,300	$1,300
Interbody cage	$3,000	$3,000	1	$3,000	$3,000
Total				$6,750	$6,750
Average cost of one-level interbody prostheses				$4,875	$4,875
Cervical, two levels					
Screws and plate					
Plate	$2,450	$2,450	1	$2,450	$2,450
Screws	$325	$325	4	$1,300	$1,300
Total				$3,750	$3,750
Interbody cage					
Cage	$3,000	$3,000	2	$6,000	$6,000
Weighted average cost of lumbar fusion prostheses		$10,475			
Weighted average cost of cervical fusion prostheses		$4,050.36			

Appendix L Cost of hospitalisation

System	Number of separations		Total average cost		Cost of prostheses	
	AR-DRG I10A	AR-DRG I10B	AR-DRG I10A	AR-DRG I10B	AR-DRG I10A	AR-DRG I10B
Public	444	1024	$26,655	$13,156	$4,024	$2,659
Private	497	3027	$22,822	$13,794	$9,007	$6,494

Source: NHCDC 2002–2003
AR-DRG I10A: spinal fusion with catastrophic or severe comorbidities and complications
AR-DRG I10B: spinal fusion without catastrophic or severe comorbidities and complications

Number of separations in public hospitals	1,468
Number of separations in private hospitals	3,524
Proportion of separations in the public sector	29.4%
Proportion of separations in the private sector	70.6%
Proportion of AR-DRG I10A in public hospitals	30.2%
Proportion of AR-DRG I10B in public hospitals	69.8%
Proportion of AR-DRG I10A in private hospitals	14.1%
Proportion of AR-DRG I10B in private hospitals	85.9%
Average cost of hospitalisation in public hospitals	$14,167
Average cost of hospitalisation in private hospitals	$8,219
Weighted average cost of hospitalisation	$9,968
Weighted average cost of hospitalisation, adjusted for inflation (totalling 12.2% to March 2005)	$11,184

Appendix M Cost comparison base case

When both screw and rod/plate fusion system and interbody fusion system are included		
Lumbar procedures		
Base case	**Spinal fusion**	**AIDR**
Weighted average cost of hospitalisation	$11,184	$11,184
Weighted average cost of medical fees	$1,606	$1,621
Weighted average cost of prostheses	$10,475	$11,514
Total cost	$23,265	$24,319
Incremental cost		$1,054
Cervical procedures		
Base case	**Spinal fusion**	**AIDR**
Weighted average cost of hospitalisation	$11,184	$11,184
Weighted average cost of medical fees	$1,548	$1,641
Weighted average cost of prostheses	$4,050	$13,395
Total cost	$16,782	$26,220
Incremental cost		$9,438
When only interbody fusion system is considered		
Lumbar procedures		
Base case	**Spinal fusion**	**AIDR**
Weighted average cost of hospitalisation	$11,184	$11,184
Weighted average cost of medical fees	$1,649	$1,621
Weighted average cost of prostheses	$14,944	$11,514
Total cost	$27,777	$24,319
Incremental cost	$3,458	
Cervical procedures		
Base case	**Spinal fusion**	**AIDR**
Weighted average cost of hospitalisation	$11,184	$11,184
Weighted average cost of medical fees	$1,519	$1,641
Weighted average cost of prostheses	$5,067	$13,395
Total cost	$17,770	$26,220
Incremental cost		$8,450

Appendix N Cost of prostheses provided by other industry sources

AIDR	Minimum price	Maximum price
Lumbar, one level	$8,000	$15,882
Lumbar, two level	$16,000	$31,764
Cervical, one level	$10,800	$14,000
Cervical, two level	$21,600	$28,000
Spinal fusion	**Minimum price**	**Maximum price**
Lumbar, one level		
Screws plus rods		
Pedicle screw	$1,200	$1,705
Set screw	$165	$199
Rod	$400	$521
Interbody cage		
Screws and rods as above		
Interbody cage	$2,000	$4,018
Lumbar, two levels		
Screws plus rods		
Pedicle screw	$1,200	$1,705
Set screw	$165	$199
Rod	$400	$521
Crosslink	$1,400	$1,400
Interbody cage		
Screws and rods as above		
Interbody cage	$2,000	$4,018
Cervical, one level		
Non-instrumented (no prosthesis needed)		
Screws and plate		
Plate	$800	$1,608
Screws	$217	$262
Interbody cage		
Cage	$1,500	$3,145
Interbody cage, screws and plate		
Plate	$800	$1,608
Screws	$217	$262
Interbody cage	$1,500	$3,145

Spinal fusion	Minimum price	Maximum price
Cervical, two levels		
Screws and plate		
Plate	$900	$1,608
Screws	$217	$262
Interbody cage		
Cage	$1,500	$3,145

Appendix O Studies included in this review

Cervical

RCTs

Artificial Cervical Disc Primary Indication Study (ACDPI), unpublished.

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Lumbar

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Less than 10 participants

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Case series

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Inappropriate participant group

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Lumbar

RCTs, results reported elsewhere

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Narrative review

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Abbreviations

AIDR	artificial intervertebral disc replacement
AIHW	Australian Institute of Health and Welfare
ASD	adjacent segment disease
BMI	body mass index
BMP	bone morphogenic protein
CEA	cost effectiveness analysis
CI	confidence interval
DDD	degenerative disc disease
DoHA	Department of Health and Ageing
DRG	Diagnosis Related Groups
FDA	Food and Drug Administration
HTA	health technology assessment
ITT	intention to treat
LBO	low back outcome
LBOS	low back outcome score
MCS	mental composite score
MSAC	Medical Services Advisory Committee
NDI	neck disability index
NICE	National Institute for Clinical Excellence
NNT(H)	number needed to treat to harm
ODI	Oswestry disability index
PCM	porous coated motion
PCS	physical component score
QALY	quality adjusted life-year
RD	risk difference
RCT	randomised controlled trial
ROM	range of motion
RR	relative risk
VAS	visual analogue scale
YLD	years lived with disability

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