NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of prosthetic intervertebral disc replacement in the lumbar spine

As a person gets older, discs supporting the back bones can deteriorate because of wear and tear. Sometimes this causes such severe pain and disability that surgery is indicated; usually removal of the damaged disc. Prosthetic intervertebral disc replacement in the lumbar spine involves insertion of an artificial disc in the place of the damaged disc. Depending on the amount of damage, a person may have one or more discs replaced during the same operation.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2009.

Procedure name

- Lumbar disc replacement
- Lumbar disc prosthesis

Specialty societies

- British Association of Spinal Surgeons
- British Orthopaedic Association
- British Society of Neurological Surgeons

Description

Indications and current treatment

Symptomatic degenerative disc disease of the lumbar spine involves the intervertebral discs which support the spinal vertebrae. With age the discs lose their flexibility and elasticity and their height. This may cause prolapse (or herniation) of part of the disc, disturbing the normal mechanics of the spine and sometimes cause chronic low back and radicular pain. In most cases symptoms improve spontaneously over time. However, some patients with low back pain remain refractory to conservative treatment with medication, injections, and physical therapy. Some may require surgical removal of the protruding disc (discectomy). Discectomy and/or spinal fusion is the standard intervention for people with neurological complications (which are rare but may constitute a surgical emergency) or chronic intractable pain. A variety of percutaneous procedures have also been developed, including techniques using radiofrequency energy, laser treatment and electrothermal therapy.

Functional ability in patients with symptomatic degenerative disc disease is often evaluated using the Oswestry disability index (ODI) a 10-item questionnaire scoring from 0% to 100% (low scores better).

What the procedure involve

Artificial intervertebral discs are mobile spacers that attempt to maintain disc height and comfortable movement in the spinal column. The mobility of adjacent discs is theoretically protected, which could delay the onset of accelerated degenerative changes in adjacent levels.

Implantation of the prosthetic discs is carried out with the patient under general anaesthesia. The intervertebral space is accessed through an abdominal incision using a transperitoneal or retroperitoneal approach. Depending on the prosthesis used, the damaged native disc is partially or fully removed. The vertebral endplates and surrounding spinal ligaments are preserved and help to maintain implant stability. Multiple discs can be replaced during the same operation.

List of studies included in the overview

This overview is based on approximately 4000 patients from one systematic review[1], three randomised controlled trials[2,3,4], one non randomised controlled trial[5], and three case series[6,7,8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Efficacy

A randomised controlled trial of 304 patients (205 treated with a prosthetic lumbar disc) reported a significantly greater improvement from baseline in ODI score in patients implanted with a prosthetic disc than in patients treated by spinal fusion at 6-week, 3-month, and 6-month follow-up (absolute figures not reported)[4]. However at 12- and 24-month follow-up, the differences from baseline between the groups were no longer statistically significant.

A randomised controlled trial of 236 patients (161 treated with a prosthetic lumbar disc) reported a non significant difference in mean ODI score between the prosthetic disc group (23 points) and the fusion group (37 points) at 24-month follow-up (p = not significant). However, 69% of patients in the prosthetic disc group reported a >25% improvement from baseline ODI score, which was significantly more than the 55% of patients in the fusion group at 3-month follow-up (p = 0.040)[2]. In the same study, group mean quality of life scores (evaluated using the Short Form-36 questionnaire composite score of physical and mental health) improved by 86.6% in the prosthetic disc compared with 70.0% in the fusion group (p = 0.004) at 3-month follow-up. However, at 24-month follow-up, the difference was no longer statistically significant (p = 0.09).

A case series of 106 patients treated with a prosthetic lumbar disc reported that 42% (45/106) of patients had an ‘excellent’ clinical outcome, 40% (42/106) had a ‘good’ outcome, 8% (8/106) were rated ‘fair’, and 10% (11/106) had a ‘poor’ outcome with a follow-up of 13 years[6]. In the same study, 90% (86/96) of patients eligible for work at baseline had returned to work, and 78% (28/36) had returned to hard labour. In a case series of 100 patients treated with a prosthetic lumbar disc at single or multiple spinal levels, 92% (87/95) of eligible patients had returned to work at 11.3 years follow-up[7].

Safety

The randomised controlled trial of 304 patients reported that the rate of major neurological adverse events (not otherwise described) was higher after fusion surgery than a prosthetic disc implant (5.4% versus 2.4%; absolute figures and significance level not reported) at 42-day follow-up[4].

The randomised controlled trial of 236 patients reported that infection (not otherwise described) occurred in 3% (2/75) of patients treated by lumbar fusion and 0% (0/161) of patients treated with a prosthetic lumbar disc at 2 years follow up (significance level not reported)[2]. There were no instances of death, major vessel injury, neurological damage or nerve root injury in either group.

A randomised controlled trial of 67 patients reported that vertebral endplate fracture requiring further surgery occurred in 2% (1/44) of patients in the prosthetic lumbar disc group and 0% (0/23) patients in the fusion group at 2-year follow-up. Similarly, vascular injury to the left ilio-lumbar vessel during exposure of the anterior portion of the lumbar spine occurred in 2% (1/44) of

patients treated with a prosthetic lumbar disc and 0% of patients treated by lumbar fusion[3].

A non randomised controlled trial of 688 patients reported a need for reoperation within 2 years in 9% (52/589) of patients treated with a prosthetic lumbar disc compared with 10% (10/99) of patients treated by lumbar fusion ($p = 0.70$)[5].

A systematic review of 27 uncontrolled case series totalling 2490 patients treated with a prosthetic lumbar disc reported that degeneration (definition varied between studies included) in an adjacent intervertebral level occurred in 35% (314/926) of patients treated by fusion compared with 9% (31/313) of patients treated with a prosthetic lumbar disc ($p < 0.0001$) (length of follow-up varied between studies)[1]. In the same review, intervertebral disc disease (defined as clinically significant degeneration) was reported in 14% (173/1216) of patients treated by fusion compared with 1% (7/595) of patients treated with a prosthetic lumbar disc ($p < 0.001$).

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to prosthetic intervertebral lumbar disc replacement. Searches were conducted of the following databases, covering the period from their commencement to 11th November 2008 and updated to 31st March 2009: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy).

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with degenerative (herniated) lumbar discs
Intervention/test	Prosthetic intervertebral lumbar disc replacement.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Non-rigid stabilisation techniques for the treatment of low back pain. NICE interventional procedures guidance 183 (2006). Available from www.nice.org.uk/IPG183
- Prosthetic intervertebral disc replacement in the cervical spine. NICE interventional procedures guidance 143 (2005). Available from www.nice.org.uk/IPG143
- Prosthetic intervertebral disc replacement (current guidance). NICE interventional procedures guidance 100 (2004). Available from www.nice.org.uk/IPG100
- Percutaneous intradiscal radiofrequency thermocoagulation for lower back pain. NICE interventional procedures guidance 083 (2004). Available from www.nice.org.uk/IPG083
- Percutaneous intradiscal electrothermal therapy for low back pain. NICE interventional procedures guidance 081 (2004). Available from www.nice.org.uk/IPG081
- Laser lumbar discectomy. NICE interventional procedures guidance 027 (2003). Available from www.nice.org.uk/IPG1027

Clinical Guidelines

- A clinical guideline on low back pain is in development. For more information see www.nice.org.uk/guidance

Table 2 Summary of key efficacy and safety findings on prosthetic intervertebral disc replacement in the lumbar spine

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;

Study details	Key efficacy findings	Key safety findings	Comments
Harrop J S (2008)[1] **Systematic review** USA Study period: not reported Study population: demographic characteristics not reported. **n = 2490 (758 lumbar prosthesis) from 27 studies – no controlled trial.** Inclusion criteria: Not reported Technique: Implantation of Charité disc (various models) or Prodisc (various models) versusaArthrodesis. **Follow-up: Not reported – varied between studies** Conflict of interest: Supported by grant from manufacturer		**Complications** **Adjacent segment degeneration (asymptomatic)** This was classified as progression of radiographic degeneration of the adjacent functional spinal unit to the index procedure during the follow up period. 19 of 27 studies reported on the incidence of lumbar adjacent segment degeneration, 14 after arthrodesis and 5 after arthroplasty. Degeneration (follow-up not reported): Arthrodesis 35% (314/926); Arthroplasty 9% (31/313); p= <0.0001 When arthrodesis versus arthroplasty was the only factor included in the analysis, the OR for developing degeneration was 4.67 (95% CI 3.19 to 7.05). In multivariate analysis, arthrodesis (OR 2.55 95% CI 1.50 to 4.51) (p = 0.0008), age at surgery (OR 20.45 95% CI 7.62 to 55.56) (p < 0.0001), and length of follow-up (OR 2.98 95% CI 1.46 to 6.08) (p = 0.0025) were independent predictors of the development of degeneration. Gender was not a significant factor. **Adjacent segment disease (symptomatic)** This was classified as the clinical presence of symptoms which correlates to degenerative disease adjacent to the index level with the radiographic presence of disease. 16 of 27 studies reported on the incidence of lumbar ASD (clinically significant degeneration), 12 after arthrodesis and 4 after arthroplasty. ASD (follow-up not reported): Arthrodesis 14% (173/1216); Arthroplasty 1% (7/595); p= <0.0001 When arthrodesis and arthroplasty was the only factor included in the analysis, the OR for developing ASD was 13.93 (95% CI 7.01 to 32.96). Multivariate analysis reported that arthrodesis (OR 17.69 95% CI 8.12 to 44.19) (p < 0.0001) and male gender (OR 3.07 95% CI 1.63 to 6.33) (p = 0.0019) were independent predictors of the development of SD. Conversely, mean length of follow-up was inversely associated with ASD (OR 0.25 95% CI 0.05 to 0.85) (p = 0.0453). Mean age was not a significant factor.		MEDLINE search only. Indexes were used for cross reference. Studies graded on hierarchy (I-V) but no quality assessment undertaken. No primary studies of comparative design were included. Analysis involved pooled groups and crude event rates with potentially different patient populations. Multivariate analyses assessed the influence of confounding variables. However, not all studies identified were used in multivariate analysis. Authors state that this analysis supports the need for further randomised controlled trials between fusion and arthroplasty

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;

Study details	Key efficacy findings	Key safety findings	Comments
Geisler F H (2004)[4] **RCT** USA Study period: Not reported Study population: single level degenerative disc disease at L4-L5 or L5-S1 confirmed by magnetic resonance imaging and provocative discography. Other demographic characteristics not reported. **n = 304 (205 lumbar prosthesis)** Inclusion criteria: ODI score ≥ 30 and back pain ≥ 40 on VAS with no radicular component. Failed non operative treatment of 6 months. Technique: Implantation of Charité III disc following complete discectomy and removal of the cartilaginous endplates, with fluoroscopic control for alignment. No back brace necessary. Compared with fusion using BAK cages implanted according to manufacturer's instructions. **Follow-up: 2 years (median)** Conflict of interest: All authors have financial interests in the device used.	**Functional ability** The mean change in ODI scores from baseline was significantly greater in patients treated with a prosthetic lumbar disc Charité than in the fusion group at 6-week, 3-month and 6-month follow-up(data not presented). At 12 months the change from baseline was not significantly different between the groups (p = 0.1388) nor was it at 24 months (p = 0.5439) (absolute figures not reported). Using the FDA requirement for the study of a 25% improvement in ODI score. 62% of patients treated with a prosthetic lumbar discCharité had a 25% improvement at 24 months compared with 49% in the fusion group (p = 0.0354) **Pain** There was no significant difference between the groups with respect to neurological status and change in VAS from baseline at 24-month follow-up.	**Complications** Major neurological events (not otherwise defined) occurred in 4.9% (10/205) patients treated with a prosthetic lumbar discCharité and 4% (4/99) of the fusion patients at 2-year follow-up. At 42 days following surgery there were more major neurological events in the fusion group 5.4% vs the Charitéprosthetic lumbar disc group 2.4% (5.4% vs. 2.4%; absolute figures not reported)	FDA device exemption trial Patients randomised to prosthesis at a 2:1 ratio There were no differences in baseline clinical or demographic characteristics between the study groups. The spinal levels treated did not differ between the groups. Clinicians treated 5 patients each using the prosthetic disc procedure during a training phase before randomisation. Some outcomes of changes in the pain VAS and ODI are compared with meta-analysis of results from spinal fusion literature, and may not represent clinical or demographic equivalence between groups. No device failure analysis provided.

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Zigler J (2007)[2]

RCT

USA

Study period: Oct 2001 to Jun 2003

Study population: single-level degenerative disc disease at L3-S1. Age = 39 years (mean), Sex = 49% male.

n = 236 (161 lumbar prosthesis)

Inclusion criteria: Back and or radicular pain. Radiographically confirmed instability, decreased disc height, scarring of annulus fibrosis, herniated nucleus pulposus, or vacuum phenomenon, ODI low back pain score ≥ 40. Failed conservative treatment of 6 months.

Technique: Implantation of ProDisc-L via mini-open retroperitoneal approach following complete discectomy and removal of the cartilaginous endplates, with fluoroscopic control, versus circumferential fusion.

Follow-up: 2 years (median)

Conflict of interest: One or more author has financial interests in the device used.</td>
<td>Functional ability
In both groups the change in ODI score from baseline was significant at all time points
Score (points) estimated from figure, p value indicates difference between groups in change from baseline
<table>
<tr><th></th><th>Baseline</th><th>6 weeks</th><th>6 months</th><th>24 months</th></tr>
<tr><td>Prosthetic</td><td>63</td><td>41</td><td>35</td><td>32</td></tr>
<tr><td>Fusion</td><td>62</td><td>49</td><td>41</td><td>37</td></tr>
<tr><td>p=</td><td>N/S</td><td>≤ 0.02</td><td>≤ 0.02</td><td>N/S</td></tr>
</table>
A improvement in ODI score from baseline of >25% was achieved in a significantly greater proportion of patients in the prosthetic disc group (69.1%) than in the fusion group (54.9%) (p = 0.0396) (absolute figures not reported)
At 24-month follow-up, 92.4% of patients in the prosthetic disc group were in employment compared to 85.1% of the fusion group (p = 0.0485).
Pain
There was a significant reduction from baseline in pain as rated on a 10-cm VAS scale in both groups at 24-months follow-up. However the difference between the prosthetic disc group (39 mm improvement) and the fusion group (32 mm improvement) was not statistically significant (p = 0.08).
Quality of life
Patient satisfaction, as assessed by VAS, was significantly greater following prosthetic disc surgery (76.7 ± 29.2 mm) than following fusion (67.3 ± 31.5 mm) at 24-month follow-up (p = 0.0015)
Short Form-36 score % change from baseline scores, composite score of physical and mental health.
<table>
<tr><th></th><th>6 weeks</th><th>3 months</th><th>6 months</th><th>24 months</th></tr>
<tr><td>Prosthetic</td><td>72.1%</td><td>86.6%</td><td>80.4%</td><td>79.2%</td></tr>
<tr><td>Fusion</td><td>56.9%</td><td>70.0%</td><td>75.0%</td><td>70.0%</td></tr>
<tr><td>p=</td><td>0.0183</td><td>0.0036</td><td>0.2333</td><td>0.0943</td></tr>
</table>
,</td>
<td>Complications
Device failure occurred in 4% (6/161) of the prosthetic disc group (4 migrations, 1 technical error, 1 supplemental fixation due to failure to resolve pain), and in 3% (2/75) of the fusion group (2 required reoperation due to failure to resolve pain). Follow-up period to failure or measure of significance not reported.
<table>
<tr><th></th><th>Prosthetic disc</th><th>Fusion</th></tr>
<tr><td>Blood loss > 1500 ml</td><td>0%</td><td>3% (2/75)</td></tr>
<tr><td>Retrograde ejaculation</td><td>1% (2/161)</td><td>0%</td></tr>
<tr><td>Infection (not otherwise described)</td><td>0% (0/161)</td><td>3% (2/75)</td></tr>
<tr><td>Deep vein thrombosis (all managed medically)</td><td>1% (2/161)</td><td>1% (1/75)</td></tr>
</table>
There were no complications (major vessel injury, neurological damage, nerve root injury, or death) in either treatment group.</td>
<td>FDA investigational device exemption trial; 17 participating sites, procedures performed by 38 surgeons all with clinical practice based in adult spinal surgery.

Clinicians treated 5 patients each in a training phase before randomisation.

Sample size calculation based on 12.5% power. Randomisation based in fixed blocks of 6 patients in 2:1 ratio. No details provided of concealment method or blinding.

Radiographic outcomes evaluated independently.

No significant difference between the 2 groups at baseline with respect to demographic or clinical characteristics

Follow-up was 98.2% at 2 years, with no significant difference in the proportion in each group.</td>
</tr>
</table>

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Zigler J (2007) continued	**Overall success** Using the FDA definition of success using a composite score of ODI score (15 point improvement), device success, neurological status, Short Form-36 score, and radiographic assessment there was a greater proportion of patients with overall success in the prosthetic disc group (53.4%) than in the fusion group (40.8%) at 2-year follow-up (p=0.044). **Operative characteristics** Mean blood loss was significantly lower during the fusion procedure 465 ± 444 ml (n=75), than during the prosthetic disc insertion procedure 204 ± 231 ml (n=160) (p < 0.0001). Conversely, the mean length of hospital admission was significantly shorter following the disc procedure 3.5 ± 1.29)days (n = 161), than following the fusion procedure 4.4 ± 1.54 days (n = 75) (p = 0.0001)		

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Sasso R C (2008)[3]

RCT

USA

Study period: Not reported

Study population: single level degenerative disc disease at L1-S1. Age = 38 years (mean), Sex = 49% male.

n = 67 (44 lumbar prosthesis)

Inclusion criteria: More axial than radicular pain. DDD confirmed radiographically with translational or angular instability, or decreased disc height. VAS and ODI low back pain score ≥ 40. Failed conservative treatment of 6 months.

Technique: Implantation of FlexiCore disc via mini-open retroperitoneal approach following complete discectomy and removal of the cartilaginous endplates, with radiographic control; versus circumferential fusion using a femoral ring allograft.

Follow-up: 2 years (median)

Conflict of interest: supported by manufacturer.</td>
<td>Functional ability
Mean ODI group scores (measurement of significance not reported)
<table>
<tr><th></th><th>Baseline</th><th>6 weeks</th><th>6 months</th><th>24 months</th></tr>
<tr><td>Prosthetic</td><td>62 (n=44)</td><td>36 (n=42)</td><td>25 (n=37)</td><td>6 (n=11)</td></tr>
<tr><td>Fusion</td><td>58(n=23)</td><td>50(n=20)</td><td>25(n=17)</td><td>12(n=7)</td></tr>
</table>
Pain
Mean VAS group scores (measurement of significance not reported)
<table>
<tr><th></th><th>Baseline</th><th>6 weeks</th><th>6 months</th><th>24 months</th></tr>
<tr><td>Prosthetic</td><td>85 (n=44)</td><td>36 (n=42)</td><td>33 (n=37)</td><td>16 (n=11)</td></tr>
<tr><td>Fusion</td><td>82 (n=23)</td><td>43 (n=20)</td><td>26 (n=17)</td><td>20 (n=8)</td></tr>
</table>
Operative characteristics
Mean or median group scores
<table>
<tr><th></th><th>Operative time (min)</th><th>Blood loss (ml)</th><th>Length of stay (days)</th></tr>
<tr><td>Prosthetic</td><td>82</td><td>97</td><td>2</td></tr>
<tr><td>Fusion</td><td>179</td><td>179</td><td>3</td></tr>
<tr><td>p=</td><td><0.001</td><td><0.02</td><td><0.005</td></tr>
</table>
Radiographic evaluation
This was undertaken by an independent laboratory at 6-week follow-up in the prosthetic disc group.
<table>
<tr><th></th><th>Baseline</th><th>6 weeks</th></tr>
<tr><td>Angular rotation</td><td>2.8°</td><td>3.8°</td></tr>
<tr><td>Lateral bending</td><td>4.7°</td><td>4.2°</td></tr>
</table>
</td>
<td>Complications
<table>
<tr><th></th><th>Prosthetic</th><th>Fusion</th></tr>
<tr><td>Serious events requiring surgery</td><td></td><td></td></tr>
<tr><td>Wound infection</td><td>2% (1/44)</td><td>13%(3/23)</td></tr>
<tr><td>Low back pain requiring removal of hardware</td><td>0%</td><td>23% (5/23)</td></tr>
<tr><td>Low back pain requiring fusion</td><td>2% (1/44)</td><td>0%</td></tr>
<tr><td>Radicular leg pain</td><td>5% (2/44)</td><td>0%</td></tr>
<tr><td>Haematoma</td><td>2% (1/44)</td><td>0%</td></tr>
<tr><td>Endplate fracture</td><td>2% (1/44)</td><td>0%</td></tr>
<tr><td>Hard ware migration</td><td>2% (1/44)</td><td>0%</td></tr>
<tr><td>Vascular injury</td><td>2% (1/44)</td><td>0%</td></tr>
</table>
<table>
<tr><th></th><th>Prosthetic</th><th>Fusion</th></tr>
<tr><td>Serious events not requiring surgery</td><td></td><td></td></tr>
<tr><td>Stridor / hypoxia</td><td>2% (1/44)</td><td>0%</td></tr>
<tr><td>Tachyarrythmia</td><td>2% (1/44)</td><td>0%</td></tr>
<tr><td>Pulmonary embolisation</td><td>0%</td><td>4% (1/23)</td></tr>
<tr><td>Extraperitoneal seroma</td><td>0%</td><td>4% (1/23)</td></tr>
</table>
</td>
<td>Two participating centres.

Initial results of 67 patients from 501 patients recruited.

Randomisation in 2:1 ratio.

Four patients in the prosthetic disc group and 5 patients in the fusion group withdrew from the study before surgery, and one patient broke protocol and received fusion.

P values are not reported for clinical outcomes. This is probably due to this publication being an early report of an ongoing larger trial which was powered to require a larger study population.</td>
</tr>
</table>

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;

Study details	Key efficacy findings	Key safety findings	Comments
McAfee P C (2006)[5] **Non randomised controlled study** USA Study period: Not reported Study population: single level degenerative disc disease at L5-S1 or L4-L5 . Age = not reported, Sex = not reported. **n = 688 (589 prosthetic disc)** Inclusion criteria: Not reported Technique: Implantation of Charité disc versus anterior interbody lumbar fusion using the same approach **Follow-up: Minimum 2 years** Conflict of interest: supported by manufacturer.	Efficacy outcomes were not reported on.	**Complications** Reoperation: Prosthetic (n=589) 9% (52/589); Fusion (n=99) 10% (10/99) (No significant difference between the groups p = 0.70) Mean time to reoperation: Prosthetic 266 days; Fusion 423 days Devices removed: Prosthetic 4% (24/589); Fusion 1% (1/99) Vessel injury during index procedure (not described): Prosthetic 3% (20/589); Fusion 2% (2/99) (measurement of significance not reported)	14 participating centres The prosthetic disc group comprises patients allocated to this treatment as part of a randomized controlled trial plus additional non randomised patients (the first 5 procedures at each site), and additional patients. Some patients the same as Geisler (2006) but additional patients are reported here.

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;

Study details	Key efficacy findings	Key safety findings	Comments
David T (2007)[6] **Case series** France Study period: Jan 1989 to Nov 1995 Study population: Single-level DDD with or without radiculopathy at L5-S1 (n=82), L4-L5 (n=25), or L3-L4 (n=1). Age = 36 years, Sex = 42% male. 44 patients had received previous lumbar procedures at the index level before surgery. **n = 106** Inclusion criteria: Refractive to non operative treatment for 6 months. Technique: Implantation of SB Charité III disc, via anterior retroperitoneal approach with imaging control. No postoperative bracing and active physiotherapy at 6-day follow-up. **Follow-up: 13.2 years (mean)** Conflict of interest: Author has interest in manufacturer.	**Functional ability** Clinical outcome was measured by a modified Stauffer-Coventry classification Outcome – Description – % Excellent – No pain, normal life and sporting activities, no treatment or medication – 42% (45/106) Good – Occasional pain, some medication, change to a lighter job – 40% (42/106) Fair – Constant pain with treatment or medication but better than baseline – 8% (8/106) Poor – No improvement or worse than baseline – 10% (11/106) Of the 96 patients eligible to work at baseline 90% (86/96) had returned to work, and 78% (28/36) had returned to hard labour. Mean ROM was 10.1° for flexion-extension, and 4.4° for lateral bending. **Operative characteristics** Mean operative time was 90 minutes. No blood transfusions were required.	**Complications** Period of follow up not reported for each Surgical – Rate Secondary procedure (fusion) due to continued symptoms – 8% (8/106) Secondary replacement prosthetic disc due to device failure – 3% (3/106) Index level – non surgical Partial device ossification* – 4% (4/106) Complete device ossification and spontaneous fusion – 2% (2/106) Subsidence with spontaneous fusion – 1% (1/106) Subsidence without spontaneous fusion * – 1% (1/06) Adjacent level Disc herniation – microdiscetomy – 2% (2/106) Spinal stenosis – decompression and fusion – 1% (1/106) *Not clinically relevant	Single centre study Retrospective chart review 2 patients lost to follow up – died due to unrelated causes. The remainder were all followed up. 44 patients had received previous lumbar procedures at the index level before surgery Authors state that proper indications play a vital role in clinical success.

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;

Study details	Key efficacy findings	Key safety findings	Comments
Lemaire J-P (2005)[7] **Case series** France Study period: Feb 1989 to Dec 1993 Study population: Single- or multiple-level DDD without radiculopathy. Age = 40 years, Sex = 41% male. Mean duration of symptoms = 6 years. **n = 100 (147 discs)** Inclusion criteria: Refractive to non operative treatment. Instability ruled out radiographically Technique: Implantation of Charité disc (model not described) at L3-L4, L4-L5, or L5-S1 via anterior retroperitoneal approach with imaging control. **Follow-up: 11.3 years (mean)** Conflict of interest: Supported by manufacturer.	**Functional ability** Clinical outcome was measured by a modified Stauffer-Coventry classification Outcome / Description / % Excellent / Improvement in score over baseline >70% / 62% (62/100) Good / Improvement in score over baseline >60% <70% / 28% (28/100) Poor / Improvement in score over baseline <60% / 10% (10/100) There was no significant difference in results between patients treated at a single level and those treated at multiple levels. Of the 95 patients eligible to work at baseline 92% (87/95) had returned to work. Mean ROM was 10.3° in flexion-extension and 5.4° in lateral bending.	**Complications** Length of follow-up not reported for each Surgical / Rate Secondary procedure (fusion) / 5% (5/100) Articular arthritis / 4% (4/100) Ossification / 2% (2/100) Adjacent level degeneration / 2% (2/100) Neurologic (n=1 paralysis at L4 requiring ligomentoplasty, n=1 not described) / 2% (2/100) Subsidence (secondary to trauma) / 2% (2/100) Perioperative vascular injury (repaired without sequelae) / 2% (2/100) Sexual dysfunction (resolved spontaneously at 12 months / 1% (1/100) Acute leg ischaemia / 1% (1/100)	107 patients treated 6 patients lost to follow up – due to relocation and 1 died due to unrelated causes. The remainder were all followed up. 44 patients had received previous lumbar procedures at the index level before surgery. 3 patients treated with concomitant fusion at a different level during surgery. Main clinical outcome score not well described. Radiological assessment undertaken independently

Abbreviations used: ASD, adjacent segment disease; DDD, degenerative disc disease; FDA: Food and Drug Administration; ODI, Oswestry disability index; OR, odds ratio; ROM, range of motion; VAS, visual analogue scale;

Study details	Key efficacy findings	Key safety findings	Comments
Punt I M (2008)[8] **Case series** The Netherlands Study period: 1989 to 2005 Study population: Single- or multiple-level DDD with or without radiculopathy. Age = 41 years, Sex = 45% male. Mean duration of symptoms = 6 years. **n = 75 (with complications)** Inclusion criteria: not reported Technique: Implantation of Charité disc (various designs) at L2-L3, L3-L4, L4-L5, or L5-S1. **Follow-up: 7 years (mean)** Conflict of interest: Not reported	**Functional ability following revision surgery** Of 10 patients treated with fusion 3% (3/10) achieved a clinically important (>25%) increase in ODI score. Of 13 patients treated with prosthetic disc removal and fusion, 46% (6/13) achieved a clinically important (>25%) increase in ODI score.	**Complications – index procedure** 61% (46/75) of these patients required one or more salvage operations after the index disc implant procedure. 29% (22/75) of patients treated with lumbar fusion with the artificial disc left in place, and in 32% (24/75) of patients the disc was removed and fusion performed. Mean period between insertion and removal of the prosthetic lumbar disc was 8 years 11 months. Late complications n= Subsidence 39 Disc prosthesis too small 24 Adjacent disc degeneration 36 Degenerative scoliosis 11 Facet joint degeneration 25 Anterior disc migration 6 Posterior disc migration 2 Device failure 10 Excessive wear 5 Severe osteolysis 1 Subluxation of the disc core 1 **Complications – revision procedure** Two patients in the fusion group developed pseudo arthrosis postoperatively. In the disc removal group, deep vein thrombosis occurred in 1 patient, decreased sensitivity in the groin and upper leg in 2 patients, and severe pain in 2 patients (resolving in 1 patient).	Patients with complications or residual pain presenting at 1 clinic. From approximately 1000 patients treated with a prosthetic lumbar disc. Precise denominator figure for complications following index procedure are not available. Two patients received a non rigid stabilisation device during revision surgery.

Validity and generalisability of the studies

- The intervention has varied between and within studies in terms of the technology used and the number of lumbar levels treated.
- Studies with longer follow-up have used older devices for the procedure.
- Few objective outcomes measurements of efficacy have been reported, and a number of different subjective scales have been used across the studies.

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr L Breakwell, (British Association of Spinal Surgeons), Mr G Marsh (British Association of Spinal Surgeons), Mr G Findlay (Society of British Neurological Surgeons), Mr R Ross (Society of British Neurological Surgeons), Mr S Ross (Society of British Neurological Surgeons).

- Four of the Specialist Advisers considered this procedure to be novel and of uncertain safety and efficacy, while one classified it as a minor variation on an established procedure.
- Anecdotal or published adverse event following this procedure include vascular injury, spinal endplate fracture, retrograde ejaculation, failure to control symptoms, device subsidence and wear debris from the device.
- Additional theoretical adverse events may include nerve injury (including cauda equine injury), bowel injury, haemorrhage, infection, impaired bladder function and device failure requiring revision surgery.
- All Specialist Advisers considered lumbar spinal fusion to be the main comparator; however, one also suggested that intensive multidisciplinary team-led rehabilitation programmes may be an alternative.
- Training may include workshop and/or cadaveric training, and first cases undertaken with an experienced surgeon. The procedure requires specialist

knowledge of anterior approaches to the lumbar spine, and may require vascular surgical support.

- The key efficacy outcomes for this procedure include pain relief (measured by VAS or ODI), disability, return to work, quality of life and avoiding additional procedures.
- Patient selection is of paramount importance, as in all forms of lumbar surgery
- The possible advantage of this surgery is to preserve spine movement and reduce the development of adjacent segment disease, although there is no certainty that this is a real clinical problem.
- Very few long-term outcomes have been reported.
- One Specialist Adviser commented that the procedure should only be performed in the context of an ongoing prospective randomised study.
- If the procedure was found to be safe and efficacious, three of the Specialist Advisers thought that it would be offered at a minority of UK hospitals, but at least 10.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme sent 60 questionnaires to 3 trusts for distribution to patients who had the procedure (or their carers). NICE received 26 completed questionnaires, however only 11 of these were from patients who had a lumbar disc prosthesis.

The Patient Commentators' views on the procedure were consistent with the published evidence and the opinions of the Specialist Advisers.

Issues for consideration by IPAC

- Considerable new data available since initial overview was considered, with many studies published very recently.
- Some overlap and duplicate publication of the same patients. This is described where known.
- Baseline disease severity varied between studies.
- Although there are randomised studies available in the evidence base, the comparator itself (spinal fusion) is a treatment with limited evidence base and/or agreed indications.

References

1 Harrop JS, Youssef JA, Maltenfort M et al. (2008) Lumbar adjacent segment degeneration and disease after arthrodesis and total disc arthroplasty. Spine 33:1701-1707.

2 Zigler J, Delamarter R, Spivak JM et al. (2007) Results of the prospective, randomized, multicenter food and drug administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease. Spine 32:1155-1162.

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

4 Geisler FH, Blumenthal SL, Guyer RD et al. (2004) Neurological complications of lumbar artificial disc replacement and comparison of clinical results with those related to lumbar arthrodesis in the literature: results of a multicenter, prospective, randomized investigational device exemption study of Charité intervertebral disc. Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2004. Journal of Neurosurgery: Spine 1:143-154.

5 Kellner M, Yassouridis A, Hua Y et al. (2002) Intravenous C-type natriuretic peptide augments behavioral and endocrine effects of cholecystokinin tetrapeptide in healthy men. Journal of Psychiatric Research 36:1-6.

6 David T. (2007) Long-term results of one-level lumbar arthroplasty: minimum 10-year follow-up of the CHARITÉ artificial disc in 106 patients. Spine 32:661-666.

7 Lemaire J-P, Carrier H, Ali E-H et al. (2005) Clinical and radiological outcomes with the Charité[trademark] artificial disc: A 10-year minimum follow-up. Journal of Spinal Disorders and Techniques 18:353-359.

8 Punt IM, Visser VM, van Rhijn LW et al. (2008) Complications and reoperations of the SB Charité lumbar disc prosthesis: experience in 75 patients. European Spine Journal 17:36-43.

Appendix A: Additional papers on prosthetic intervertebral disc replacement in the lumbar spine

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Aunoble S, Donkersloot P, Le Huec JC. (2004) Dislocations with intervertebral disc prosthesis: two case reports.[see comment]. European Spine Journal 13:464-467.	Case report n=2 FU=4 and 19 months	Prosthesis dislocation treated with surgical revision resulting in good clinical outcome	Larger studies included in table 2
Bertagnoli R, Kumar S. (2002) Indications for full prosthetic disc arthroplasty: a correlation of clinical outcome against a variety of indications. European Spine Journal 11: Suppl-6.	Case series n=108 FU=N/R	Mean time to return to daily activities was 2.3 weeks. No implant failures or complications due to surgery	Larger studies included in table 2
Bertagnoli R, Yue JJ, Shah RV et al. (2005) The treatment of disabling single-level lumbar discogenic low back pain with total disc arthroplasty utilizing the Prodisc prosthesis: a prospective study with 2-year minimum follow-up. Spine 30:2230-2236.	Case series n=115 FU=2 years minimum	Procedure is a safe and efficacious treatment for debilitating low back pain.	Larger studies included in table 2
Bertagnoli R, Yue JJ, Kershaw T et al. (2006) Lumbar total disc arthroplasty utilizing the ProDisc prosthesis in smokers versus nonsmokers: a prospective study with 2-year minimum follow-up. Spine 31:992-997.	Case series n=22 FU=34.6 months	Significant improvements in ODI score observed at 3 months and maintained to 2 years.	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bertagnoli R, Yue JJ, Fenk-Mayer A et al. (2006) Treatment of symptomatic adjacent-segment degeneration after lumbar fusion with total disc arthroplasty by using the prodisc prosthesis: a prospective study with 2-year minimum follow up. Journal of Neurosurgery Spine 4:91-97	Case series n=20 FU=2 years minimum	Significant improvements in ODI and patient satisfaction at 3 months in patients with previous fusion and degeneration at adjacent level.	Larger studies included in table 2
Caspi I, Levinkopf M, and Nerubay J. (2003) Results of lumbar disk prosthesis after a follow-up period of 48 months. *Israel Medical Association Journal* 5:9-11.	Case series n=20 FU=2 years	Contradictions to surgery appear to be the principal cause of failure rather than the prosthesis itself	Larger studies included in table 2
Chung SS, Lee CS, and Kang CS. (2006) Lumbar total disc replacement using ProDisc II: a prospective study with a 2-year minimum follow-up. Journal of Spinal Disorders & Techniques 19:411-415.	Case series n=38 FU=minimum 2 years	Success rate of 94% based on Food and Drug Administration criteria.	Larger studies included in table 2 Studies with longer follow-up are included in table 2
David T. (2005) Revision of a Charité artificial disc 9.5 years in vivo to a new Charité artificial disc: case report and explant analysis. European Spine Journal 14:507-511	Case report n=1 FU=N/R	Case report of revision surgery at 9.5 years follow up due to device failure.	Larger studies included in table 2
Freeman BJC, Davenport J. (2006) Total disc replacement in the lumbar spine: A systematic review of the literature. European Spine Journal 15 (Suppl 3):S439-S447	Systematic review n=20 studies FU=varied	Descriptive synthesis of published studies. Well designed prospective randomised controlled trials will be required before approval and widespread use of this technology.	Larger studies included in table 2
Geisler, F. H., Guyer, R. D., Blumenthal, S. L et al (2008) Patient selection for lumbar arthroplasty and arthrodesis: the effect of revision surgery in a controlled, multicenter, randomized study. Journal of neurosurgery.Spine 8 (1) 13-16..	RCT n=N/R FU=2 years	7.1% of patients who had a secondary stabilisation procedure had poor clinical improvement	Subgroup analysis of same patients reports in Geisler (2004) included in table 2.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Gioia G, Mandelli D, Randelli F. (2007) The Charité III Artificial Disc lumbar disc prosthesis: Assessment of medium-term results. Journal of Orthopaedics and Traumatology 8:134-139	Case series N=36 FU=6.9 years	Mean ODI score fell from 44% to 9%.	Larger studies included in table 2
Richard D. Guyer, Paul C. McAfee, Robert J. Banco et al (2009) Prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITÉ artificial disc versus lumbar fusion: Five-year follow-up The spine journal. 9 (5), 374-386	RCT n=133 FU=5 years	The results of this five-year, prospective, randomized multicenter study are consistent with the two-year reports of noninferiority of CHARITÉ artificial disc vs. ALIF	Same study as Geisler (2004) included in table 2
Guyer RD, Siddiqui S, Zigler JE et al. (2008) Lumbar spinal arthroplasty: analysis of one center's twenty best and twenty worst clinical outcomes. Spine 33:2566-2569.	Non randomised controlled trial n=40 FU=2 years	Comparison of factors relating to good or bad outcome. Length of time off work at baseline was the only factor related to outcome.	Larger studies included in table 2
Hannibal M, Thomas DJ, Low J et al. (2007) ProDisc-L total disc replacement: a comparison of 1-level versus 2-level arthroplasty patients with a minimum 2-year follow-up. Spine 32:2322-2326.	Non randomised controlled trial n=59 FU=2 years minimum	No significant difference in clinical outcomes for patients treated at 1 or 2 spinal levels.	Larger studies included in table 2
Huang RC, Girardi FP, Cammisa Jr FP et al. (2003) Long-term flexion-extension range of motion of the prodisc total disc replacement. Journal of Spinal Disorders & Techniques 16:435-440,	Case series n=42 FU=8.7 years	Mean range of motion in the spine was 3.8 degrees.	Larger studies included in table 2
Jeon SH, Choi WG, Lee SH (2008) Anterior revision of a dislocated ProDisc prosthesis at the L4-5 level. Journal of Spinal Disorders & Techniques 21:448-450,	Case report n=1 FU=2.5 years	Patient recovered from revision surgery for a dislocated prosthetic disc without sequelae and symptoms improved.	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Kafer W, Clessienne CB, Daxle M et al. (2008) Posterior component impingement after lumbar total disc replacement: a radiographic analysis of 66 ProDisc-L prostheses in 56 patients. Spine 33:2444-2449.	Case series n=56 FU=3 years	Posterior component impingement was seen in a considerable number of implants.	Larger studies included in table 2
Kim DH, Ryu KS, Kim MK et al. (2007) Factors influencing segmental range of motion after lumbar total disc replacement using the ProDisc II prosthesis. Journal of Neurosurgery: Spine 7:131-138.	Case series n=32 FU=2 years minimum	Range of movement did not improve as much when used at L5-S1 level.	Larger studies included in table 2
Leahy M, Zigler JE, Ohnmeiss DD et al. (2008) Comparison of results of total disc replacement in postdiscectomy patients versus patients with no previous lumbar surgery. Spine 33:1690-1694.	Non randomised controlled trial n=87 FU=2 years	Outcome following prosthetic disc insertion is not compromised by a history of previous discectomy.	Larger studies included in table 2
Leivseth G, Braaten S, Frobin W. et al. (2006) Mobility of lumbar segments instrumented with a ProDisc II prosthesis: a two-year follow-up study. Spine 31:1726-1733.	Case series n=41 FU=2 years minimum	Procedure fails to restore normal segmental rotational motion	Larger studies included in table 2
Levin DA, Bendo JA, Quirno M et al. (2007) Comparative charge analysis of one- and two-level lumbar total disc arthroplasty versus circumferential lumbar fusion. Spine 32:2905-2909.	Randomised controlled trial n=53 (36 discs) FU=29 to 32 months	Significantly shorter operating tiem with prosthetic disc insertion than fusion.	Larger studies included in table 2 Most patients reported in Zigler (2007) in table 2
Marshman LA, Friesem T, Rampersaud YR et al. (2008) Subsidence and malplacement with the Oblique Maverick Lumbar Disc Arthroplasty: technical note. Spine Journal: Official Journal of the North American Spine Society 8:650-655.	Non randomised controlled trial n=14 FU=N/R	Comparison of insertion approaches.	Larger studies included in table 2
Park CK, Ryu KS, Jee WH (2008) Degenerative changes of discs and facet joints in lumbar total disc replacement using ProDisc II: minimum two-year follow-up. Spine 33:1755-1761.	Case series n=32 FU=32 months	Degenerative changes in the discs and facets at adjacent level appears to be minimal.	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Patel VV, Andrews C, Pradhan BB et al. (2006) Computed tomography assessment of the accuracy of in vivo placement of artificial discs in the lumbar spine including radiographic and clinical consequences. Spine 31:948-953.	Case series n=52 FU=41.5 weeks	Device location was < 1.2 mm from the centre point and < 12 degrees of rotation from midline.	Larger studies included in table 2
Pazmino PR, Regan JJ. (2008) Revision strategies involving lumbar artificial disc replacement. *Seminars in Spine Surgery* 20 (1): 34-45.	Case series n=20 FU=N/R	Anterior revision surgery can be performed safely.	Larger studies included in table 2
Putzier M, Funk JF, Schneider SV et al. (2006) Charité total disc replacement-clinical and radiographical results after an average follow-up of 17 years.[see comment]. European Spine Journal 15:183-195.	Case series n=53 FU=17.3 years	No significant difference between implant types found in terms of clinical outcome.	Larger studies included in table 2
Ross R, Mirza AH, Norris HE et al. (2007) Survival and clinical outcome of SB Charité III disc replacement for back pain. *Journal of Bone & Joint Surgery - British Volume* 89:785-789.	Case series N=160 FU=N/R	Mean improvement in OID score was 14%.	Larger studies included in table 2
Schroven I, Dorofey D. (2006) Intervertebral prosthesis versus anterior lumbar interbody fusion: one-year results of a prospective non-randomised study. Acta Orthopaedica Belgica 72:83-86.	Non randomized controlled tral n=24 (14 discs) FU=12 months	ODI index improved more at 12 months following prosthetic disc than fusion.	Larger studies included in table 2
Schulte TL, Lerner T, Hackenberg L et al. (2007) Acquired spondylolysis after implantation of a lumbar ProDisc II prosthesis: case report and review of the literature. Spine 32:E645-E648.	Case report n=1 FU=14 months	Case report of a patient with spondylolysis with a good clinical outcome.	Larger studies included in table 2
Shim CS, Lee S, Maeng DH et al. (2005) Vertical split fracture of the vertebral body following total disc replacement using ProDisc: report of two cases. Journal of Spinal Disorders & Techniques 18:465-469.	Case report n=2 FU=3 months	Report of vertebral split fractures following prosthetic disk replacement .	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Shim CS, Lee SH, Shin HD et al. (2007) CHARITÉCharité versus ProDisc: a comparative study of a minimum 3-year follow-up. Spine 32:1012-1018.	Non randomised controlled trial n=57 FU=38.4 months	Mean percentage change in ODI score was 78.9% using one type of disc and 75.8% with another.	Larger studies included in table 2
Siepe CJ, Mayer HM Wiechert K et al. (2006) Clinical results of total lumbar disc replacement with ProDisc II: three-year results for different indications. Spine 31: 1923-1932.	Case series n=92 FU=34 months	Beneficial clinical results in a highly selected group of patients with DDD.	Larger studies included in table 2
Siepe CJ, Wiechert K, Khattab MF et al. (2007) Total lumbar disc replacement in athletes: clinical results, return to sport and athletic performance. European Spine Journal 16:1001-1013.	Case series n=39 FU=26.3 months	Preoperative participation in sport is a strong predictor of successful outcome.	Larger studies included in table 2
Stieber JR, Donald GD, III. (2006) Early failure of lumbar disc replacement: case report and review of the literature. [Review] [24 refs]. Journal of Spinal Disorders & Techniques 19:55-60.	Case report n=1 FU=3 weeks	Report of a device failure. Explanted and revised to lumbar fusion.	Larger studies included in table 2
Su P-Q, Huang D-S, Li C-H et al. (2003) Significance of recovering spinal motion and carrying ability by artificial lumbar intervertebral disc replacement. Chinese Journal of Clinical Rehabilitation 7:2828-2829.	Case series n= FU=		Larger studies included in table 2
Tortolani PJ, Cunningham BW, Eng M et al. (2007) Prevalence of heterotopic ossification following total disc replacement. A prospective, randomized study of two hundred and seventy-six patients. Journal of Bone & Joint Surgery - American Volume 89:82-88.	Case series n=276 FU=N/R	Heterotopic ossification occurred in 4.3% of patients.	Same patients as reported in Geisler (2004) in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Tropiano P, Huang RC, Girardi FP et al. (2003) Lumbar disc replacement: preliminary results with ProDisc II after a minimum follow-up period of 1 year. Journal of Spinal Disorders & Techniques 16:362-368	Case series N=53 FU=1 year minimum	Satisfactory results in 90% of patients who had undergone previous surgery, reoperation required in 6% of patients.	Larger studies included in table 2
Tropiano P, Huang RC, Girardi FP et al. (2005) Lumbar total disc replacement. Seven to eleven-year follow-up. Journal of Bone & Joint Surgery - American Volume 87:490-496.	Case series n=64 FU=8.7 years	Procedure appears effective and safe for the treatment of symptomatic degenerative disc disease.	Larger studies included in table 2
Trouillier H, Kern P, Refior HJ et al. (2006) A prospective morphological study of facet joint integrity following intervertebral disc replacement with the CHARITÉCharité Artificial Disc. European Spine Journal 15:174-182.	Case series n=13 FU=12 months	Clinical outcomes scores were improved at 6 and 12 months compared to baseline.	Larger studies included in table 2
Wagner WH, Regan JJ, Leary SP et al. (2006) Access strategies for revision or explantation of the Charité lumbar artificial disc replacement. *Journal of Vascular Surgery* 44 (6): 1266-1272	Case series n=19 FU=7 months	Prosthesis successfully removed in all patients.	Larger studies included in table 2
Warachit P. (2008) Results of Charité artificial lumbar disc replacement: experience in 43 Thais. Journal of the Medical Association of Thailand 91:1212-1217.	Case series n=43 FU=2 years	Good short-term outcomes.	Larger studies included in table 2

Appendix B: Related NICE guidance for prosthetic intervertebral disc replacement in the lumar spine

Guidance	Recommendations
Interventional procedures	**Prosthetic intervertebral disc replacement (CURRENT GUIDANCE). NICE interventional procedures guidance 100 (2004)** 1.1 Current evidence on the safety and efficacy of prosthetic intervertebral disc replacement appears adequate to support the use of this procedure. However, there is little evidence on outcomes beyond 2–3 years and collection of long-term data is therefore particularly important. 1.2 Clinicians wishing to undertake prosthetic intervertebral disc replacement should take the following actions. • Ensure that patients understand the uncertainty about the procedure's long term efficacy and provide them with clear written information. Use of the Institute's *Information for the Public* is recommended. • Audit and review clinical outcomes of all patients having prosthetic intervertebral disc replacement. 1.3 Publication of longer-term efficacy outcomes will be useful in reducing the current uncertainty. The Institute may review the procedure upon publication of further evidence **Prosthetic intervertebral disc replacement in the cervical spine. NICE interventional procedures guidance 143 (2005)** 1.1 Current evidence suggests that there are no major safety concerns about the use of prosthetic intervertebral disc replacement in the cervical spine, and there is evidence of short-term efficacy. Clinicians wishing to undertake this procedure should take the following actions. • Ensure that patients understand the long-term uncertainties about the procedure and the alternative treatment options. In addition, use of the Institute's Information for the public is recommended. • Audit and review clinical outcomes of all patients having prosthetic intervertebral disc replacement in the cervical spine. 1.2 This procedure should only be performed in specialist units where surgery of the cervical spine is regularly undertaken **Non-rigid stabilisation techniques for the treatment of low back pain NICE interventional procedures guidance 183**

	(2006) 1.1 Limited evidence suggests that non-rigid stabilisation procedures for the treatment of low back pain provide clinical benefit for a proportion of patients with intractable back pain. Current evidence on the safety of these procedures is unclear and involves a variety of different devices and outcome measures. Therefore, these procedures should only be used with special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake non-rigid stabilisation techniques for the treatment of low back pain should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the benefits of these procedures and the alternative treatment options, and provide them with clear written information. In addition, use of the Institute's 'Understanding NICE guidance' is recommended • Audit and review clinical outcomes of all patients undergoing non-rigid stabilisation procedures for the treatment of low back pain. 1.3 Publication of further research will be useful provided that the outcome measures and comparators are well defined. The Institute may review the procedure upon publication of further evidence.

Appendix C: Literature search for prosthetic intervertebral disc replacement in the lumbar spine

Database	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	11/11/08	Issue 4, 2008	0
Database of Abstracts of Reviews of Effects – DARE (CRD website)	11/11/08	N/A	4
HTA database (CRD website)	11/11/08	N/A	1
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	11/11/08	Issue 4, 2008	57
MEDLINE (Ovid)	11/11/08	1950 to October Week 5 2008	28
MEDLINE In-Process (Ovid)	11/11/08	November 10, 2008	70
EMBASE (Ovid)	11/11/08	1980 to 2008 Week 45	48
CINAHL (Search 2.0, NLH)	11/11/08	1981 to present	25
Current Contents (CBIB)	11/11/08	1995 to date	28

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Database: Medline - 1950 to October Week 5 2008

Strategy used:

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1 Prosthesis Implantation/ (4866)
2 (Prosthe$ adj3 Implant$).tw. (5904)
3 1 or 2 (10581)
4 Intervertebral Disk/su (1785)
5 Intervertebral Disk Displacement/su (5764)
6 (Intervertebral$ adj3 Dis#$ adj3 (Replacement$ or Displacement$ or Hernia$)).tw. (1175)
7 exp Diskectomy/ (2193)
8 Dis#ectom$.tw. (2583)
9 or/4-8 (9309)
10 3 and 9 (138)
11 (Prosthe$ adj3 intervertebra$ adj3 dis#$).tw. (38)
12 (Artificial$ adj3 intervertebra$ adj3 dis#$).tw. (27)
13 Charité$.tw. (487)
14 ProDis#$.tw. (94)
15 Acromed$.tw. (64)
16 Acroflex$.tw. (6)
17 or/10-16 (788)
18 Animals/ (4373282)

19	Humans/ (10774807)
20	18 not (18 and 19) (3282008)
21	17 not 20 (747)
22	200210$.ed. (44532)
23	200211$.ed. (40555)
24	200212$.ed. (45692)
25	2003$.ed. (872073)
26	2004$.ed. (821080)
27	2005$.ed. (618802)
28	2006$.ed. (664823)
29	2007$.ed. (795440)
30	2008$.ed. (597127)
31	or/22-30 (4500124)
32	21 and 31 (401)
33	200805$.ed. (53212)
34	200806$.ed. (55838)
35	200807$.ed. (59646)
36	200808$.ed. (58777)
37	200809$.ed. (61584)
38	200810$.ed. (56322)
39	200811$.ed. (0)
40	or/33-39 (345379)
41	32 and 40 (28)