NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

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

Bulging of a disc (called herniation) in the neck occurs when one or more of the spinal discs between the bones in the neck bursts and pushes against the spinal cord or nerve roots that run through the backbone. This herniation can cause pain in the neck, or pain, weakness and numbness in the arms and legs.

This procedure involves replacing damaged discs in the neck with artificial ones designed to act like natural neck discs.

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 December 2009.

Procedure name

- Prosthetic intervertebral disc replacement in the cervical spine

Specialty societies

- British Scoliosis Society
- British Association of Spinal Surgeons
- British Orthopaedic Association
- Society for Back Pain Research
- British Pain Society
- Society of British Neurological Surgeons

- Chartered Society of Physiotherapists
- British Chiropractic Association
- British Osteopathic Association
- British Cervical Spine Society

Description

Indications and current treatment

The procedure is used in patients with degenerative cervical disc disease, typically presenting as chronic spondylotic disease (associated with herniation of disc material, disc calcification and osteophyte formation emanating from the vertebral bodies). Symptoms may include neck pain, neck stiffness, limb paraesthesia and numbness or weakness of the limbs).

Conservative treatment options for acute radicular pain include analgesic medication, rest, physical therapy, and local injections.

Surgical intervention is reserved for those patients in whom permanent neurological damage is thought likely, or when conservative management fails to resolve symptoms. The current standard treatment is surgical decompression of the nerve root or spinal cord by cervical discectomy with or without vertebral body fusion (using iliac crest autograph and/or a variety of preformed spacers/cages).

It has been suggested that following cervical discectomy with or without fusion, lack of natural movement of the operated intervertebral joint may increase the mechanical load applied to adjacent joints, and could potentially accelerate their degeneration. On the basis of this hypothesis, artificial intervertebral discs have been developed with the aim of acting as a functional prosthetic replacement for the damaged disc. Replaced disc may help to reduce abnormal loading patterns on adjacent joints, and, consequently, the risk and speed of degeneration in adjacent levels. However there is uncertainty regarding the natural history of degenerative disease in adjacent discs.

What the procedure involves

Artificial intervertebral discs have been developed to act as a functional prosthetic replacement unit for intervertebral units in much the same way as prostheses have been developed for a variety of joints such as the hip or knee. The intention is to maintain movement at the spinal joint in the hope of reducing the need for subsequent operations. A number of devices have been developed for the cervical spine.

Under general anaesthesia the patient is placed in the supine position. The anterior cervical spine is exposed, and after standard decompression of the neural elements, an artificial disc prosthesis is placed between the vertebrae and anchored to them. Replacement of a failed intervertebral disc using a functional prosthesis aims to offer the same benefit as decompression while preserving motion at the operated segment thereby reducing abnormal stresses on adjacent disc levels associated with fusion procedures.

A number of different devices are available for this procedure.

List of studies included in the overview

This overview is based on 1554 patients from 3 randomised controlled trials[1,2,3,4], 2 non-randomised controlled studies[5,6], 1 case series[7] and 1 case report[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

The Neck Disability Index (NDI) questionnaire has 10 items concerning pain and activities of daily living including personal care, lifting, reading, headaches, concentration, work status, driving, sleeping and recreation. Scores are recorded out of 50 (or 100) with higher scores indicating greater disability.

A randomised controlled trial of 541 patients reported that mean NDI scores improved from baseline significantly more following prosthetic cervical disc insertion (55.7 to 20.7 points) than following fusion (56.4 to 26.8 points) at 3 months' follow-up ($p = 0.004$). However, at 6, 12 and 24 months' follow-up the difference between the groups was no longer statistically significant[1]. A randomised controlled trial of 209 patients reported that mean NDI score improved more following insertion of a prosthetic cervical disc than following fusion at 3 months' follow-up ($p = 0.05$) (absolute figures not reported). However, at 24 months' follow-up the mean NDI score was 21.4 points in the prosthetic cervical disc group and 20.5 points in the fusion group ($p = 1.00$)[4].

A randomised controlled trial of 463 patients reported that mean NDI score improved more in patients treated with a prosthetic cervical disc (51.4 to 16.2 points) than in patients treated by cervical fusion (50.2 to 19.2 points) at 24 months' follow-up ($p = 0.025$)[2].

A non-randomised controlled study of 140 patients reported that mean NDI score improved significantly more in patients treated with prosthetic cervical discs at multiple levels (52.2%) than in those requiring single-level treatment (37.6%)($p = 0.021$)(follow-up not reported)[5]. A case series of 54 patients (receiving a total of 77 prosthetic cervical discs) reported that mean NDI score improved from 19 points at baseline to 11 points at 1-year follow-up ($p < 0.0001$)[7].

Three randomised controlled trials of 541 patients[1], 463 patients[2] and 209 patients[4] respectively all reported that quality of life (as measured by the Short Form 36 physical and mental health components) improved significantly from baseline to 24 months' follow-up in both the prosthetic cervical disc and the fusion groups, however the difference between groups was not statistically significant.

A non-randomised controlled study of 146 patients reported that an excellent outcome (improvement in at least 80% of signs and symptoms) was achieved in 65% (32/49) of patients treated with a single-level cervical prosthesis at 24 months' follow-up, and 77% (20/26) of patients receiving discs at 2 levels at 12 months' follow-up[6].

Safety

Revision surgery / re-operation

A randomised controlled trial of 541 patients reported that revision surgery (reason not reported) was required in 0% (0/276) of patients in the prosthetic cervical disc group and 2% (5/265) of patients in the cervical fusion group at 2-year follow-up ($p = 0.028$)[1]. In the same study the rate of supplemental fixation in the neck (not otherwise defined) requiring additional surgery was significantly lower in the prosthetic disc group (0% [0/276]) than in the fusion group (3% [9/265]) ($p = 0.003$). A randomised controlled trial of 463 patients reported that the total rate of reoperation was significantly lower in the group of patients treated with a prosthetic cervical disc (5% [13/242]) than in the fusion group (8% [17/221]) at 2-year follow-up ($p = 0.045$)[3].

A non-randomised controlled study of 146 patients reported that reintervention was required in 3% (3/103) of patients in the single level group at 24 months and 9% (4/43) of patients in the 2-level group at 12 months' follow-up[6]. A non-randomised controlled study of 140 patients reported a similar rate of reoperation and serious adverse events between patients treated with a prosthetic cervical disc at a single level (4% [3/71]) and patients receiving a prosthesis at multiple cervical levels (3% [2/69]) (no further details provided and measurement of significance not reported)[5]

Intraoperative adverse events

A case report described fracture of the posterior central parts of the caudal C6 and the cranial C7 vertebrae during chiseling for prosthetic disc insertion. Sudden copious bleeding occurred and fragments were found compressing the posterior longitudinal ligament and the thecal sac[8]. Bleeding was controlled and the disc insertion was achieved without further complication.

A non-randomised controlled study of 146 patients reported that in the 2-level prosthetic cervical disc group a cerebral spinal fluid leak occurred during decompression surgery in 2% (1/43) of patients (not further described) [6].

Joint ossification

A case series of 54 patients receiving 77 prosthetic cervical discs between them reported that no heterotopic ossification was present around 34% (26/77) of implants, bridging ossification allowing movement of prosthesis in 10% (8/77), and complete fusion of the level in 9% (7/77) at 1-year follow-up[7].

Miscellaneous

A randomised controlled trial of 209 patients reported that adverse event success (no adverse event relating to implant or its implantation) was achieved in 97% (100/103) of patients in the prosthetic cervical disc group and 93% (99/106) of the cervical fusion group at 2-year follow-up ($p = 0.033$)[4].

A case report of 1 patient described chronic inflammatory debris as a result of hyper-reactivity to metal ions from the prosthesis at 9-month follow-up. Symptoms improved following revision surgery[9].

Overall success

A randomised controlled trial of 209 patients reported that overall success (defined as minimum clinically important >20% improvement in NDI score, neurological success, no serious adverse events, and no subsequent surgery or intervention) was achieved in 73.5% of the prosthetic disc group and 60.5% of the fusion group at 24 months' follow-up ($p = 0.047$)[4].

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to prosthetic intervertebral disc replacement in the cervical spine. Searches were conducted of the following databases, covering the period from their commencement to 14 April 2009, and updated to 25 January 2010: 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). Relevant published studies identified during consultation or resolution process that are published after this date may also be considered for inclusion.

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 cervical spine symptoms.
Intervention/test	Prosthetic intervertebral disc replacement in the cervical spine.
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

The Ontario Health Technology Advisory Committee (OHTAC) updated their recommendations on Artificial Disc Replacement (ADR) for Lumbar and Cervical Degenerative Disc Disease (DDD) in April 2006.

They produced the following recommendations on an evidence-based analysis.

'Currently there is no comparative research evaluating the effectiveness of cervical ADR. Because of this there was very low quality evidence to support the effectiveness of cervical ADR and to quantify the short or long-term rate of major complications. Comparative evidence from a Food and Drug Administrative (FDA) randomized controlled trial is expected to become available within the next 12 months' (Anderson 2008 and Heller 2009 studies in table 2 of this overview).

'Because of the uncertainty in the estimates of benefits, risks and burdens associated with cervical ADR, OHTAC does not recommend the use of cervical ADR to treat DDD over the use of other alternatives such as spinal fusion at this time.'

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

- Percutaneous endoscopic laser cervical discectomy. NICE interventional procedures guidance 303 (2009). Available from www.nice.org.uk/IPG303

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

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Mummaneni PV (2007)[1] **Randomised controlled trial** USA Study period: Oct 2002 to Aug 2004 Study population: patients with single-level disease. Age: 44 years (mean); Sex: 46% male. **n = 541 (276 prosthetic discs)** Inclusion criteria: single-level symptomatic degenerative disc disease. Intractable radiculopathy, myelopathy or both. Technique: insertion of a Prestige ST cervical disc versus fusion with ring allograft spacers and cervical plating system. **Follow-up: 2 years (median)** Conflict of interest: supported by manufacturer.	**Symptoms** NDI score improved significantly from baseline at all follow-up points in both groups. At 3 months' follow-up the mean change from baseline was greater in the artificial disc group (55.7 points to 20.7 points) than in the fusion group (56.4 points to 26.8 points) (p = 0.004). At 6, 12 and 24 months' follow-up the difference between the groups was no longer statistically significant. **Quality of life** The mean SF-36 mental and physical component scores improved significantly in both groups to 24 months' follow-up but the difference between groups was not statistically significant. **Return to work** Working status Prosthetic disc / Fusion Baseline: 66% / 63% 24 months' follow-up: 75% / 75% Median return to work time was 45 days in the prosthetic disc group and 61 days in the fusion group. **Operative characteristics** Group means Prosthetic disc / Fusion / p = Operative time (hrs): 1.6 / 1.4 / <0.001 Blood loss (ml): 60.1 / 57.5 / 0.635 Length of stay (days): 1.1 / 1.0 / 0.041 External orthosis (%): 31.2 / 59.1 / <0.009	**Complications** During the perioperative period adverse events occurred in 6% (17/276) of patients in the prosthetic disc group and 4% (11/265) of patients in the fusion group (measurement of significance not reported). Complications included dysphagia, dysphonia and spinal fluid leak in both groups. Additional surgery Prosthetic disc / Fusion / p = Revision: 0% (0/276) / 2% (5/265) / 0.028 Supplemental fixation: 0% (0/276) / 3% (9/265) / 0.003 Hardware removal: 2% (5/276) / 3% (9/265) / 0.287 Of the 5 patients in the prosthetic disc group requiring hardware removal 4 suffered persistent radiculopathy, and all had subsequent fusion. Surgery at adjacent level: 1% (3/276) / 3% (9/265) / 0.049* * calculated as the rate of adjacent level surgery by Kaplan-Meier analysis.	An FDA Investigational device exemption trial. Prospective follow-up. Computer randomisation at 1:1 ratio per site. Potential effect of learning curve in disc group No statistically significant difference between groups at baseline in clinical or demographic characteristics except for more alcohol users in the fusion group (p = 0.025). For patients who had reached 24 months' follow-up 86% (223/260) of the prosthetic disc group and 79% (198/251) of the fusion group had data available for analysis. Sensitivity analysis showed no effect of dropout when failure was assumed. Overall success (defined as >15 points' improvement in NDI score, neurological success, no serious adverse events and no subsequent surgery or intervention) was achieved in 79.3% of the prosthetic disc group and 67.8% of the fusion group at 24 months' follow-up (p = 0.0053) (non-inferiority).

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Heller JG (2009)[2] and Anderson PA (2008)[3] **Randomised controlled trial** USA Study period: May 2002 to Oct 2004 Study population: patients with radiculopathy or myelopathy with single level disease. Age: 45 years (mean); Sex: 48% male. **n = 463 (242 prosthetic discs)** Inclusion criteria: radiculopathy or myelopathy secondary to disc herniation not responding to 6 weeks of non-operative management. No marked spondylosis, or reduction of disc space >50%. Technique: insertion of a Bryan cervical disc versus standardised fusion with allograft and single anterior plating system. **Follow-up: 2 years (median)** Conflict of interest: supported by manufacturer.	**Symptoms** The NDI questionnaire has ten items concerning pain and activities of daily living including personal care, lifting, reading, headaches, concentration, work status, driving, sleeping and recreation. Higher scores represent greater disability. NDI score improved significantly from baseline at all follow-up points in both groups. At 24 months' follow-up the mean change from baseline was greater in the artificial disc group (51.4 points to 16.2 points) than in the fusion group (50.2 points to 19.2 points) (p = 0.025). At 24 months' follow-up the mean change in neck pain score from baseline was greater in the artificial disc group (75.4 points to 23.0 points) than in the fusion group (74.8 points to 30.3 points) (p = 0.009). Neurological success (maintenance or improvement from baseline) was achieved in 93.9% of patients in the prosthetic disc group and 20.2% of patients in the fusion group (p = 0.111). **Quality of life** The mean SF-36 mental and physical component scores improved significantly in both groups to 24 months' follow-up but the difference between groups was not significant at this time. **Return to work** There were no statistically significant differences between the groups in the proportion of patients who had returned to work at 24 months' follow-up: 76.8% in the prosthetic disc group and 73.6% in the fusion group (measurement of significance not reported).	**Complications** Overall there were more adverse events related to the operation in the prosthetic disc group (34% [82/242]) than in the fusion group (29% [64/221]) (p = 0.023). Medical events possibly or directly related to the operation occurring within 6 weeks of procedure Outcome / Prosthetic disc / Fusion Cardiovascular 5 0 Gastrointestinal 6 5 Infection 4 3 Allergy 6 4 Psychiatric 0 4 Pulmonary 6 7 Genitourinary 0 0 Musculoskeletal 1 4 Endocrine 1 3 Central nervous system 7 4 Death 0 0 Total 15% (36/242) 15% (34/221) p = 0.07 between the group for total events. Neurological event at up to 3 years' follow-up Outcome / Prosthetic disc / Fusion Sensory upper 15% (37/242) 16% (36/221) Motor loss upper 3% (7/242) 4% (8/221) Myelopathy <1% (1/242) 2% (4/221) Sensory lower 2% (6/242) <1% (1/221) Total 21% (50/242) 22% (49/221) p = 0.125 between the groups for total events.	30 participating centers, with 65 surgeons undertaking procedures. An FDA Investigational device exemption trial. Central randomisation in blocks of four by site. Patient follow-up was 93.1% complete at 12 months and 91.6% complete at 24 months. Clinical and demographic characteristics were the same between groups at baseline except for SF-36 mental health component (p = 0.0410) and range of motion (p < 0.001) which were worse in the prosthetic disc group, and body mass index (p = 0.027) which was worse in the fusion group. Overall success (defined as >15 points' improvement in NDI score, neurological success, no serious adverse events and no subsequent surgery or intervention) was achieved in 82.6% of the prosthetic disc group and 72.7% of the fusion group at 24 months' follow-up (p = 0.010) (non-inferiority).

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Heller JG (2009) and Anderson PA (2008) continued		WHO grade 3 or 4 events Outcome: Prosthetic disc / Fusion / p = Medical: 17% (41/242) / 15% (33/221) / 0.09 Surgical: 1% (3/242) / 1% (2/221) / 0.12 Severe neck /arm pain: 7% (16/242) / 13% (28/221) / N/R Thoracolumbar complication: 4% (10/242) / 4% (8/221) / N/R Headache: 1% (3/242) / 1% (3/221) / N/R Pseudoarthrosis: 0% (0/242) / 3% (6/221) / N/R Total symptoms: 12% (29/242) / 20% (45/221) / 0.0003 Total: 30% (73/242) / 36% (80/221) / 0.012 **Reoperation** Rate of reoperation in the cervical spine Site: Prosthetic disc / Fusion / p = Index level: 2% (6/242) / 4% (8/221) / 0.056 Adjacent: 2% (6/242) / 3% (7/221) / 0.12 Both: <1% (1/242) / 1% (2/221) / N/R Total: 5% (13/242) / 8% (17/221) / 0.045	

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Murrey D (2009)[4] **Randomised controlled trial** USA Study period: Aug 2003 to Oct 2004 Study population: patients with single-level disease. Age: 43 years (mean); Sex: 45% male. **n = 209 (103 prosthetic discs)** Inclusion criteria: single-level symptomatic degenerative disc disease. Debilitating radiculopathy unresponsive to non-operative treatment for 6 weeks. NDI score of 30% or more. Technique: insertion of a ProDisc C cervical disc versus anterior cervical discectomy and fusion with allograft bone spacers and cervical fixed angle plate. **Follow-up: 2 years (median)** Conflict of interest: supported by manufacturer.	**Symptoms** Neurological success (maintenance or improvement in sensory, motor and reflex function) was achieved in 90.9% of the prosthetic disc group and 88.0% of the fusion group at 24 months' follow-up (p = 0.638). NDI score improved significantly from baseline at all follow-up points in both groups. At 3 months' follow-up the mean change from baseline was greater in the artificial disc group than in the fusion group (absolute figures not reported) (p = 0.05). At 24 months' follow-up the mean score in the prosthetic disc group was 21.4 ± 20.1 points, and in the fusion group 20.5 ± 18.4 points (p = 1.000). A minimum clinically important difference in pain (reduction of >20% in VAS score from baseline) was reported in 87.9% of the prosthetic disc group patients and 86.9% of the fusion group (p = 1.0) (absolute figures not reported). **Quality of life** The mean SF-36 mental and physical component scores improved significantly in both groups to 24 months' follow-up but the difference between groups was not significant at this time (p = 0.094). **Operative characteristics** Group means (and standard deviation) Operative time (min): Prosthetic disc 98.7 (47); Fusion 107.2 (36); p = 0.0078 Blood loss (ml): Prosthetic disc 63.5 (50.3); Fusion 83.5 (64.9); p = 0.0094 Length of stay (days): Prosthetic disc 1.3 (0.83); Fusion 1.4 (1.18); p = 0.7882	**Complications** Adverse event success (no adverse event relating to the implant or its implantation) was achieved in 97% (100/103) of patients in the prosthetic disc group and 93% (99/106) of patients in the fusion group (p = 0.33). Of the 3 patients who did not achieve success in the prosthetic disc group 2 had persistent pain (one elected for device removal and fusion), and 1 had a dural tear. Device success (no revision, removal or reoperation) was achieved in 98% (101/103) of patients in the prosthetic disc group and 92% (97/106) of patients in the fusion group (p = 0.033)	An FDA Investigational device exemption trial. Prospective follow-up. Computer randomisation at 1:1 ratio per site. Medication regimen was not specified in the study protocol but collected by class of drug. Follow-up was 98% in the prosthetic disc group and 95% in the fusion group at 24 months' follow-up. No statistically significant difference between groups at baseline in clinical or demographic characteristics. Overall success (defined as minimum clinically important >20% improvement in NDI score, neurological success, no serious adverse events and no subsequent surgery or intervention) was achieved in 73.5% of the prosthetic disc group and 60.5% of the fusion group at 24 months' follow-up (p = 0.047) (superiority).

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Pimenta L (2007)[5] **Non-randomised controlled trial** Brazil Study period: not reported Study population: patients with single- or multiple-level disease. Age: 46 years (mean); Sex: 40% male. **n = 140 (71 single-level, 69 multiple-level)** Inclusion criteria: discogenic radiculopathy with radiographically confirmed cervical spondylosis, disc herniation, pseudoarthritis or failed fusion, failed cervical cage unresponsive to non-operative treatment for 6 weeks. Technique: insertion of a porous coated motion cervical disc at 1 level versus multiple levels (up to 4 levels). **Follow-up: 26 months (mean)** Conflict of interest: supported by manufacturer.	**Symptoms** Neurological success was evaluated using the NDI and a VAS. Mean NDI scores improved significantly more in the multiple-level group (52.2%) than in the single-level group (37.6%) ($p = 0.021$) (follow-up period not reported). Mean VAS scores improved more in the multiple-level group (65.9%) than in the single-level group (58.4%) (follow-up period and measurement of significance not reported). Outcome assessment by Odom's criteria i.e. Excellent = improvement in 80% of signs and symptoms Good = improvement in 70% of signs and symptoms Fair = improvement in 50% of signs and symptoms Poor = improvement in less than 50% of signs and symptoms | | Excellent | Good | Fair | Poor | | --- | --- | --- | --- | --- | | Single-level | 14% | 44% | 32% | 10% | | Multiple-level | 9% | 30% | 55% | 6% | **Operative characteristics** Mean estimated blood loss was 20 ml greater, length of procedure 39 minutes longer and length of stay 6.1 hours longer in the multiple-level group ($p < 0.05$ for all).	**Complications** There were no deaths, infections or iatrogenic neurological progression in either study group. There rate of reoperation and serious adverse events was similar in the single-level group (4% [3/71]) and the multiple-level group (3% [2/69]) (no further details provided and measurement of significance not reported). Within the whole series (single- and multiple-level) there were 4 dural tears during the decompression part of the procedure. Overall reoperation was required following 2% (5/229) of procedures, 4 for revised prosthetic implant and 1 conversion to fusion. Heterotopic ossification (class 4) (not otherwise defined) occurred in 1% (1/71) of patients in the single-level group.	Consecutive patient accrual. 21 patients had adjacent segment disease at baseline 12 in the single-level treatment group and 9 in the multiple-level group. No statistically significant difference between groups at baseline in clinical or demographic characteristics. Authors state that a prospective study to determine differential resulting disc degeneration has yet been performed or reported.

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Goffin J (2003) [6] **Non-randomised controlled study** International Study period: 2000 / 2001 onwards Study population: patients with degenerative disc disease, either disc herniation or spondylosis with radiculopathy or myelopathy. Age: 26 - 79 years (range); Sex: 46% male. **n = 146** (103 single-level prosthesis, 43 bi-level) Inclusion criteria: not reported. Technique: insertion of Bryan disc. **Follow-up: single-level to 24 months; bi-level to 12 months** Conflict of interest: supported by manufacturer.	**Symptoms and signs** Improvements in surgeon-assessed motor strength, reflex and sensory signs, and patient-reported symptoms were recorded as follows. Assessment by 40 neurological tests and subjective patient assessment of 15 symptoms. • Excellent = improvement in at least 80% of signs and symptoms • Good = improvement in at least 70% of signs and symptoms • Fair = improvement in at least 50% of signs and symptoms • Poor = improvement in less than 50% of signs and symptoms Excellent / Good / Fair / Poor Single-level: 65% (32/49) / 4% (2/49) / 20% (10/49) / 10% (5/49) Bi-level: 77% (20/26) / 4% (1/26) / 15% (4/26) / 4% (1/26) **Range of motion**. The flexion and extension range of motion was greater than 2 degrees in 93% (43/46) of patients following single-level disc replacement and in 86% (42/49) patients having bi-level surgery. **Quality of life assessment** The SF-36 health survey (physical component) showed baseline scores in the single-level group to be 36.1 ± 6.4, and at 24 months postoperatively 46.8 ± 10.9. For the bi-level replacement groups the scores were 37.4 ± 7.2 at baseline and 47.0 ± 10.7 at 12 months.	**Surgical complications** Following single-level surgery reintervention was required in 3% (3/103) of cases. This was for evacuation of a prevertebral haematoma, posterior foraminotomy for residual symptoms and posterior decompression to treat residual myelopathic symptoms. In the bi-level study group there was a cerebral spinal fluid leak during decompression surgery in 2% (1/43) of cases, and reintervention was required in 9% (4/43) of cases. These were an evacuation of epidural haematoma and of prevertebral haematoma, repair of a pharyngeal tear from intubation and anterior decompression for ongoing nerve root compression. **Device position** There was no instance of device subsidence into the vertebral endplates. Device migration (not otherwise defined) was found in 2% (2/103) of patients undergoing single-level disc replacement and 2% (1/43) of patients having artificial discs placed at two levels. However no migration greater than 3.5 mm was reported	Consecutive patients Operative time was calculated from the third and subsequent cases at each centre. Authors state that 5-year follow-up is necessary to evaluate long-term performance of the prosthesis. No data were provided regarding comparative efficacy between participating sites. A small number of patients went through to 24-month follow-up in the single-level group or 12-month follow-up in bi-level group. Careful patient selection was used, with those included having failed on conservative treatment for at least 6 weeks, and exclusion of patients with instability or previous spinal surgery.

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Goffin J (2003) continued	**Operative data** Operative time for the single-level procedure was 125 ± 51 minutes, and for bi-level surgery 158 ±53 minutes. The length of stay for patients undergoing the procedures was 3.5 ± 2.2 days following single-level surgery and 3.6 ± 6.2 days for bi-level surgery.		

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale

Study details	Key efficacy findings	Key safety findings	Comments
Mehran C (2006)[7] **Case series** Germany and Czech Republic Study period: not reported Study population: patients with degenerative disc disease. Age: not reported; Sex: not reported. Single-level n = 34; multiple-level n = 20. **n = 54 (77 prosthetic discs)** Inclusion criteria: disc herniation or other degenerative changes at C3–4 to C6–7 with neurological deficit or arm / neck pain. Technique: insertion of ProDisc C prosthetic disc following discectomy and decompression. Soft neck collar for 1–2 days post surgery. **Follow-up: 1 year** Conflict of interest: none.	**Symptoms** Mean NDI score improved from 19 points at baseline to 11 points at 1-year follow-up ($p < 0.0001$). Mean VAS score (0 to 10) for arm pain improved from 6.1 at baseline to 1.8 at 1-year follow-up ($p < 0.0001$). Mean VAS score (0 to 10) for neck pain improved from 5.4 at baseline to 2.4 at 1-year follow-up ($p < 0.0001$).	**Complications** HO was graded using a modified McAfee scale. Grade 0: No HO present Grade 1: HO in front of the vertebral body but not in the interdiscal space Grade 2: HO growing in the disc space, possibly affecting the function of prosthesis Grade 3: Bridging ossification which still allows movement of prosthesis. Grade 4: Complete fusion of the segment without movement in flexion or extension. At 1-year follow-up Rate (n = 77 discs) Grade 0: 34% (26/77) 15 single; 11 multiple Grade 1: 8% (6/77) 1 single; 5 multiple Grade 2: 39% (30/77) 13 single; 17 multiple Grade 3: 10% (8/77) 3 single; 5 multiple Grade 4: 9% (7/77) 2 single; 5 multiple There rate of HO was significantly greater in the multiple-level patients than the single-level patients ($p = 0.0116$). High grade HO did not correlate with efficacy outcome for NDI score ($r = –0.090$, $p = 0.88$) or VAS score ($r = –0.044$, $p = 0.75$ for neck pain; $r = –0.127$, $p = 0.36$ for arm pain).	Prospective study. 2 study centres (part of a wider European multicentre study). All surgeons had minimum 5 years' experience in cervical fusion. Two independent clinicians performed all analyses.

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Shim CS (2007)[8] **Case report** South Korea Study period: not reported Study population: patient with huge parmedian disc herniation confirmed by computed tomography scan. Right upper extremity numbness and pain for 2 months unresponsive to medication, physiotherapy and acupuncture. Age: 32 years; Sex: male. Single-level herniation at C6–7, with some degenerative changes at C56. **n = 1** Inclusion criteria: not reported Technique: insertion of ProDisc C prosthetic disc following discectomy **Follow-up: 3 months** Conflict of interest: supported by a grant from a foundation.	Following discectomy and removal of herniated fragments chiselling was done with a keel-cutting chisel followed by a box-cutting chisel. With further mallet impaction to advance the chisel slightly deeper sudden copious bleeding occurred. This was controlled by gelfoam pledgets. Once bleeding was controlled it was observed that posterior central parts of the caudal C6 and cranial C7 vertebrae were fractured; bony fragments were compressing the posterior longitudinal ligament and the thecal sac. The displaced bony fragments were removed; the paths for the keel made in the bony endplates were not damaged and insertion of the prosthetic disc was possible. The rest of the procedure was completed without incident. Postoperative computed tomography scans indicated that posterior portions of the C6 and C7 vertebral bodies were removed and the prosthetic disc was in place. X-ray at 3 months' follow-up showed good position of prosthesis without migration; the patient had improvement in motor weakness, and no numbness or pain.		'Denominator' number of procedures undertaken at the institution not reported. Operator experience not described. Authors state that surgery was done following the established surgical instructions. Possible explanations for fracture are not discussed.

Abbreviations used: HO, heterotopic ossification, NDI, Neck Disability Index; SF-36, Short Form 36; VAS, visual analogue scale			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Cavanaugh (2009)[9] **Case report** South Korea Study period: not reported Study population: patient with herniated intervertebral disc at C5–C6 level. Age: 39 years; Sex: female. **n = 1** Inclusion criteria: not reported Technique: insertion of prosthetic disc following discectomy **Follow-up: 9 months** Conflict of interest: not reported	Cervical disc arthroplasty for herniated intervertebral disc at C5–C6 level was uneventful during surgery and in the immediate postoperative period. Recurrence of symptoms began 9 months after the procedure and failed to respond to conservative measurements. Imaging revealed soft-tissue mass posterior to the implanted disc encroaching the spinal cord. Surgical explantation and exploration of the disc space revealed a thick layer of abnormal hyaline cartilaginous tissue with chronic inflammatory debris as a result of hyper-reactivity to metal ions. The patient had complete resolution of symptoms after revision surgery.		'Denominator' number of procedures undertaken at the institution not reported. Operator experience not described.

Validity and generalisability of the studies

- FDA device exemption studies include a composite overall success outcome based on both efficacy and safety parameters which cannot easily be categorised into either section; in addition each specific outcome is also reported separately.
- FDA device exemption studies use non-inferiority analysis to compare overall success rather than superiority analysis (except in one study).
- There are less data available concerning the use of 2-level (or multi-level) prostheses.
- Little long-term data are available, particularly in relation to potential reduction in adjacent level degeneration.
- NDI score is sometimes scored out of 50 and sometimes out of 100.

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 A Casey (Society of British Neurological Surgeons), Mr JNA Gibson (British Cervical Spine Society), Mr RJC Laing (British Cervical Spine Society), Mr RD Strachan (British Pain Society).

- Opinion was split on the current status of this procedure. One Specialist Adviser classified it as novel and of uncertain safety and efficacy; 1 as a minor variation of an existing procedure; and 2 as established and no longer new.
- The main comparator is discectomy and cervical fusion.
- Anecdotal adverse events relating to this procedure include paraplegia, disc extrusion following trauma, fusion of prosthesis, implant migration or loosening, vertebral fractures, segmental kyphosis, and inadequate decompression.

- Adverse events listed by the Specialist Advisers to be reported in the literature include delayed hyper-reactivity to metal ions after cervical disc arthroplasty, vertical split fracture of the vertebral body, sagittal split fractures in multilevel cervical arthroplasty, posterior avulsion fracture at adjacent vertebral body.
- Theoretical adverse events might include infection, explant surgery, neurological injury, infection, migration and displacement of prosthesis into the spinal canal, disc debris causing inflammatory response and discs wearing and osteolysis.
- The key efficacy outcomes for this procedure were thought to be the NDI, VAS arm and neck pain scores, SF-36 score, technical success / revision rate, range of movement and reduction in rate of adjacent level disease in 5 to 10 years.

- Indications for this treatment remain not entirely clear.

- Not all discs are necessarily equal and their use should be governed by clinical studies, not just CE marking.

- There are no additional concerns about the safety of this procedure than for standard decompression and fusion.

- A dedicated training course is required on technical aspects of the procedure.

- Uncertainty remains over whether the artificial disc will protect adjacent segments.

- Some believe that many disc replacements will ultimately fuse. The procedure may be no better than fusion in the long term (>10 years) and long term data are needed.

- The impact on the NHS could be moderate if the procedure replaces cervical fusion.

Patient Commentators' opinions

NICE was unable to gather patient commentary for this procedure

Issues for consideration by IPAC

- There has been a considerable increase in available data since the committee first considered this procedure.
- A number of abstracts / posters relating to research in cervical prosthetic discs (including a range of new devices) were included at the 9th Annual Symposium on Motion Preservation Technology. None of these reported on additional adverse events that are not described elsewhere in this overview.
- Most patients recruited in the studies included in the overview had pain refractory to non-surgical treatment.
- There are no data / evidence about the main intended / aimed for outcome and rationale for this procedure, i.e. on reduction of risk of progression of degenerative disease in adjacent to those replaced intervertebral joints.

References

1 Mummaneni PV, Burkus JK, Haid RW et al. (2007) Clinical and radiographic analysis of cervical disc arthroplasty compared with allograft fusion: a randomized controlled clinical trial.. Journal of Neurosurgery Spine 6:198–209

2 Heller JG, Sasso RC, Papadopoulos SM et al. (2009) Comparison of BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion: clinical and radiographic results of a randomized, controlled, clinical trial. Spine 34:101–8

3 Anderson PA, Sasso RC, and Riew KD. (2008) Comparison of adverse events between the bryan artificial cervical disc and anterior cervical arthrodesis. Spine 33:1305–13

4 Murrey D, Janssen M, Delamarter R et al. (2009) Results of the prospective, randomized, controlled multicenter Food and Drug Administration investigational device exemption study of the ProDisc-C total disc replacement versus anterior discectomy and fusion for the treatment of 1-level symptomatic cervical disc disease. Spine Journal 9:275–86

5 Pimenta L, McAfee PC, Cappuccino A et al. (2007) Superiority of multilevel cervical arthroplasty outcomes versus single-level outcomes: 229 consecutive PCM prostheses. Spine 32:1337–45

6 Goffin J, Van CF, van LJ et al. (2003) Intermediate follow-up after treatment of degenerative disc disease with the Bryan Cervical Disc Prosthesis: single-level and bi-level. Spine (Phila.Pa.1976.) 28:2673–8

7 Mehren C, Suchomel P, Grochulla F et al. (2006) Heterotopic ossification in total cervical artificial disc replacement. Spine 31:2802–7

8 Shim CS, Shin HD, and Lee SH. (2007) Posterior avulsion fracture at adjacent vertebral body during cervical disc replacement with ProDisc-C: a case report. Journal of Spinal Disorders & Techniques 20:468–72

9 Cavanaugh DA, Nunley PD, Kerr EJ. (2009) Delayed hyper-reactivity to metal ions after cervical disc arthroplasty. Spine 34:E262-E265

Appendix A: Additional papers on prosthetic intervertebral disc replacement in the cervical 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
Anderson PA, Sasso RC, Rouleau JP et al. (2004) The Bryan Cervical Disc: wear properties and early clinical results. Spine 4 (6:Suppl): 309S	n = 136 FU = 1 year	The in vivo and in vitro wear properties are satisfactory for the expected duration of life of the prosthesis. The early clinical results are satisfactory and equal to fusion.	Larger studies included in table 2
Bertagnoli R, Yue JJ, Pfeiffer F, et al. (2005) Early results after ProDisc-C cervical disc replacement. Journal of Neurosurgery Spine 2(4):403–10	n = 16 FU = 1 year	Analysis of preliminary results involving ProDisc-C arthroplasty indicates significant improvement in pain and functional outcome scores. No spontaneous fusions at the level of surgery or at adjacent levels were noted. Long-term follow-up studies will be necessary before more definitive treatment recommendations can be formulated.	Larger studies included in table 2
Coric D, Finger F, Boltes P (2006) Prospective randomized controlled study of the Bryan Cervical Disc: early clinical results from a single investigational site. Journal of Neurosurgery Spine 4(1):31–5	n = 33 (17 discs) FU = 2 years	The preliminary results documented at this investigational site are encouraging. Evaluation of data acquired in the Bryan disc treatment group showed that improvements in the clinical parameters were similar to those in the fusion group. Additionally in the artificial disc-treated group, there was radiographic evidence that motion was maintained.	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Cheng, L., Nie, L., Zhang, L., and Hou, Y. (2009) Fusion versus Bryan Cervical Disc in two-level cervical disc disease: a prospective, randomised study. International Orthopaedics 33 (5) 1347-1351	n=65 (31 discs) FU=2 years	Bryan artificial cervical disc replacement seems reliable and safe in the treatment of patients with two-level cervical disc disease	Larger studies are included in table 2.
Duggal N, Pickett GE, Mitsis DK et al. (2004) Early clinical and biomechanical results following cervical arthroplasty. Neurosurgical Focus 17(3):E9	n = 26 FU = 1 year	The Bryan artificial cervical disc provided in vivo functional spinal motion at the treated level. Overall cervical spinal motion was not significantly altered. Sagittal rotation did not change significantly at any level after surgery.	Larger studies included in table 2
Heidecke V, Burkert W, Brucke M et al. (2008) Intervertebral disc replacement for cervical degenerative disease - clinical results and functional outcome at two years in patients implanted with the Bryan cervical disc prosthesis. Acta Neurochirurgica 150(5):453–9	n = 54 FU = N/R	Implantation of the Bryan disc resulted in excellent or good neurological outcome in all patients. The surgical technique was safe and without complications. 12% of the implanted Bryan discs lost mobility at two years.	Larger studies included in table 2
Kim, H. K., Kim, M. H., Cho, D. S., (2009) Surgical outcome of cervical arthroplasty using bryan(r). Journal of Korean Neurosurgical Society 46 (6) 532-537.	n = 52 FU = 29 months	Arthroplasty using the Bryan(R) disc seemed to be safe and provided encouraging clinical and radiologic outcome in our study. Although the early results are promising, this is a relatively new approach, therefore long-term follow up studies are required to prove its efficacy and its ability to prevent adjacent segment disease	Larger studies are included in table 2.
Kim SW, Shin JH, Arbatin JJ et al. (2008) Effects of a cervical disc prosthesis on maintaining sagittal alignment of the functional spinal unit and overall sagittal balance of the cervical spine. European Spine Journal 17(1):20–9	n = 47 FU = 2 years	The Bryan disc preserves motion of the FSU. Although the preoperative lordosis (or kyphosis) of the functional spinal unit could not always be maintained during the follow-up period, the overall sagittal balance of the cervical spine was usually preserved.	Larger studies included in table 2 Non-clinical outcomes

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Kim SH, Shin HC, Shin DA et al. (2007) Early clinical experience with the mobi-C disc prosthesis. Yonsei Medical Journal 48(3):457–64	n = 23 FU = 6 months	Mobi-C disc prosthesis provided a favourable clinical and radiological outcome in this study. However, long-term follow-up studies are required to prove its efficacy and ability to prevent adjacent segment disease.	Larger studies included in table 2
Kim SW, Limson MA, Kim SB et al. (2007) Comparison of radiographic changes after ACDF versus Bryan disc arthroplasty in single and bi-level cases. European Spine Journal 18(2):218–31	n = 105 (51 discs) FU = 20 months	A longer period of evaluation is needed, to see if all these radiographic changes will translate to symptomatic adjacent level disease.	Larger studies included in table 2 Non-clinical outcomes
Lafuente J, Casey ATH, Petzold A et al. (2005) The Bryan cervical disc prosthesis as an alternative to arthrodesis in the treatment of cervical spondylosis: 46 consecutive cases. Journal of Bone & Joint Surgery, British Volume 87B(4):508–13	n = 46 FU = 1 year	The Bryan cervical disc prosthesis seems reliable and safe in the treatment of patients with cervical spondylosis.	Larger studies included in table 2
Leung CH, Ma WK, Poon WS (2007) Bryan artificial cervical disc arthroplasty in a patient with Klippel-Feil syndrome. Hong Kong Medical Journal 13(5):399–402	n = 1 FU = 2 weeks	We report a case where a Bryan artificial cervical disc arthroplasty was used to maintain and preserve the mobility and function of the cervical motion segments adjacent to fused vertebral lesions in a 33-year-old woman with Klippel-Feil syndrome who presented with chronic neck pain and signs of early myelopathy.	Larger studies included in table 2
Leung C, Casey AT, Goffin J et al. (2005) Clinical significance of heterotopic ossification in cervical disc replacement: a prospective multicenter clinical trial. Neurosurgery 57(4):759–63	n = 90 FU = 1 year	There is a strong association of the occurrence of HO with subsequent loss of movement of the implanted cervical artificial disc. We have found that sex and age are two possible risk factors in the development of HO after cervical disc replacement.	Larger studies included in table 2
Ma W-H, Xu R-M, Huang L et al. (2007) Artificial cervical disc replacement for the treatment of cervical spondylotic radiculopathy and myelopathy. Journal of Clinical Rehabilitative Tissue Engineering Research 11(36):7295–8	n = 17 FU = 6 months	Artificial cervical disc replacement can obviously improve the symptoms of patients, and has good therapeutic effects in the treatment of cervical syndrome.	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Nabhan A, Steudel WI, Nabhan A et al. (2007) Segmental kinematics and adjacent level degeneration following disc replacement versus fusion: RCT with three years of follow-up. Journal of Long-Term Effects of Medical Implants 17(3):229–36	n = 49 (25 discs) FU = 3 years	The range of motion of the treated segment with prosthesis remained unchanged 3 years after surgery in comparison to the 1-year result. The prosthesis shows a significant segmental motion in contrast to the fusion group at each examination time.	Larger studies included in table 2
Peng, C. W., Quirnoa, M., Bendo, et al. (2009) Effect of intervertebral disc height on postoperative motion and clinical outcomes after Prodisc-C cervical disc replacement. Spine Journal: Official Journal of the North American Spine Society 9 (7) 551-555	n=166 FU=2years	Patients with greater disc collapse of less than 4mm preoperative disc height benefit more in ROM after TDR	Comparison based on baseline clinical characteristics Larger studies are included in table 2.
Peng-Fei S, Yu-Hua J (2008) Cervical disc prosthesis replacement and interbody fusion: a comparative study. International Orthopaedics 32(1): 103–6	n = 24 FU = 17 months	The short follow-up time does not support the advantage of the cervical disc prosthesis. The clinical effect and the maintenance of the function of the motion of the intervertebral space are no better than the interbody fusion.	Larger studies included in table 2
Pickett GE, Rouleau JP, Duggal N (2005) Kinematic analysis of the cervical spine following implantation of an artificial cervical disc. Spine 30(17):1949–54	n = 20 FU = 2 years	The Bryan artificial cervical disc provided in vivo functional spinal motion at the operated level, reproducing the preoperative kinematics of the spondylotic disc.	Larger studies included in table 2
Ramadan AS, Mitulescu A, Schmitt, P (2007) Total cervical disc replacement with the Discocerv (Cervidisc Evolution) cervical prosthesis: Early results of a second generation. European Journal of Orthopaedic Surgery and Traumatology 17(6): 513–20	n = 17 FU = 5 months	Early results with Discocerv Cervidisc Evolution cervical prosthesis are encouraging. However, further follow-up on a larger group is necessary to confirm these findings.	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Rohl, K. and Rohrich, F. (2009) Artificial disc versus spinal fusion in the treatment of cervical spine degenerations in tetraplegics: a comparison of clinical results. Spinal Cord 47 (9) 705-708	n=24 FU=6 months	Usage of prostheses results in improved total mobility of the cervical spine in comparison with the outcomes of a fusion. This study also confirmed these results in tetraplegics	Studies with longer follow up are included in table 2.
Sekhon LH, Sears W, Duggal N (2005) Cervical arthroplasty after previous surgery: results of treating 24 discs in 15 patients. Journal of Neurosurgery Spine 3(5): 335–41	n = 15 FU = 24 months	Issues such as accelerated device-related wear and the use of arthroplasty after aggressive facetectomy resection will need further study; however, in carefully selected patients who have undergone previous surgery cervical arthroplasty may provide an additional tool in the management of cervical disc disease.	Larger studies included in table 2
Sekhon LH (2004) Two-level artificial disc placement for spondylotic cervical myelopathy. Journal of Clinical Neuroscience 11(4):412–15	n = 1 FU = 11 months	This is the first two-level case reported in the literature and opens the way for the possible future management of multilevel cervical cord compression in a way that maintains cervical motion, avoids donor site bone graft problems and may reduce the incidence of adjacent segment disease.	Larger studies included in table 2
Sekhon LH (2003) Cervical arthroplasty in the management of spondylotic myelopathy. Journal of Spinal Disorders & Techniques 16(4):307–13	n = 7 FU = 6 months	All patients had a good or excellent operative outcome (either 'minimum persistence of preoperative symptoms able to carry out daily occupation without significant interference' or 'all preoperative symptoms relieved, able to carry out daily occupations without impairment').	Larger studies included in table 2 Potentially the same patients as reported in Sekhon (2005).
Shin DA, Yi S, Yoon DH (2009) Artificial disc replacement combined with fusion versus two-level fusion in cervical two-level disc disease. Spine 34 (11) 1153-1159.	n = 40 (20 disc) FU = 2 years	HS is superior to 2-ACDF in terms of better NDI recovery, less postoperative neck pain, faster C2-C7 ROM recovery, and less adjacent ROM increase.	Larger studies included in table 2.
Pickett GE, Sekhon LH, Sears WR et al. (2006) Complications with cervical arthroplasty. Journal of Neurosurgery Spine 4(2):98–105	n = 74 FU = N/R	The Bryan prosthesis was effective in maintaining spinal motion. Major perioperative and device-related complications were infrequent.	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Porchet F, Metcalf NH (2004) Clinical outcomes with the Prestige II cervical disc: preliminary results from a prospective randomized clinical trial. Neurosurg Focus 17(3):E6	n = 55 FU = up to 24 months	There was statistical equivalence in arm pain frequency and intensity score between the study groups.	Larger studies included in table 2
Robertson JT, Papadopoulos SM, Traynelis VC (2005) Assessment of adjacent-segment disease in patients treated with cervical fusion or arthroplasty: a prospective 2-year study. Journal of Neurosurgery Spine 3(6):417–23	n = 228 (74 discs) FU = 2 years	In comparing these prospective studies the authors demonstrated that maintaining motion rather than fusion will prevent symptomatic adjacent-disc disease and will decrease adjacent-level radiological indicators of disease at a 24-month postoperative interval.	Larger studies included in table 2
Robertson JT, Metcalf N. H (2004) Long-term outcome after implantation of the Prestige I disc in an end-stage indication: 4-year results from a pilot study. Neurosurgical Focus 17(3):E10	n = 17 FU = to 4 years	In this report the authors demonstrate the clinical viability of the Prestige I cervical disc system at long-term postoperative intervals, even in the more severe biomechanical environment of end-stage disease.	Larger studies included in table 2 Potentially the same patients as reported in Robertson (2005).
Sahoo PK, Bhatoe HS (2006) Cervical disc replacement for spondylotic myeloradiculopathy. Medical Journal Armed Forces India 62(2):112–15	n = 20 FU = 2 years	Cervical disc replacement for cervical disc prolapse with myeloradiculopathy represents an exciting new technology. Patients treated with the Bryan cervical disc prosthesis for single-level cervical disc prolapse showed good to excellent improvement in neurological deficit. Clinically and radiologically maintenance of motion was found during follow-up.	Larger studies included in table 2
Sears WR, Duggal N, Sekhon LH et al. (2007) Segmental malalignment with the Bryan Cervical Disc prosthesis-contributing factors. Journal of Spinal Disorders and Techniques 20(2):111–17	n = 67 FU = N/R	Although the prescribed surgical technique is relatively standardised, it seems likely that a number of surgical variables, particularly those leading to loss of disc space height and affecting annular tension, are important.	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, Park HJ et al. (2006) Early clinical and radiologic outcomes of cervical arthroplasty with Bryan Cervical Disc prosthesis. Journal of Spinal Disorders & Techniques 19(7):465–70	n = 47 FU = 6 months	For the present, it seems preferable to exclude the patient who already has significant segmental kyphosis from disc arthroplasty with Bryan Cervical Disc prosthesis.	Larger studies included in table 2
Wang Y, Zhang X, Xiao S et al. (2006) Clinical report of cervical arthroplasty in management of spondylotic myelopathy in Chinese. Journal of Orthopaedic Surgery 1:13	n = 83 FU = 1 year	Byran cervical disc prosthesis restored motion to the level of the intact segment in flexion-extension and lateral bending in postoperative images. At the same time, it can achieve good anterior decompression treatment effect and immediate stability in replaced 1 or 2 levels.	Larger studies included in table 2
Wenger M, Hoonacker P, Zacee B et al. (2009) Bryan cervical disc prostheses: preservation of function over time. Journal of Clinical Neuroscience 16(2):220–5	n = 25 FU = 22 months	With our protocol, 28 of 29 cervical disc prostheses in 25 consecutive patients were mobile after an average of 22.3+/-9.4 months. Prosthesis motion was physiological and very similar to that of the healthy adjacent segments. Long-term studies including larger numbers of patients are required to validate our initial observations.	Larger studies included in table 2 Non-clinical outcomes
Wigfield CC, Gill SS, Nelson RJ, Metcalf NH, Robertson JT (2002) The new Frenchay artificial cervical joint: Results from a two-year pilot study. Spine 27(22):15	n = 15 FU = 24 months	The mean angulation of motion segment was 7.5 degrees (range 1–15 degrees) at baseline, and this was maintained following surgery as 6.5 degrees (range 3–12 degrees).	Larger studies included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Xu, J. X., Zhang, Y. Z., Shen, Y., et al. (2009) Effect of modified techniques in bryan cervical disc arthroplasty. Spine 34 (10) 1012-1017	n=39 FU=6 months	The modified techniques can improve the outcomes of the cervical arthroplasty with Bryan disc and prevent the unexpected imbalance and motion of cervical spine	Comparison of two different techniques for the same procedure Larger studies are included in table 2.
Yi, S., Lee, D. Y., Ahn, P. G., et al (2009) Radiologically documented adjacent-segment degeneration after cervical arthroplasty: characteristics and review of cases.Surgical Neurology 72 (4) 325-329	n=72 FU=16 months	The rate of adjacent-segment degeneration was higher than that observed in previous studies.	Larger studies are included in table 2.
Yi, S., Lim, J. H., Choi, K. S., et al (2009) Comparison of anterior cervical foraminotomy vs arthroplasty for unilateral cervical radiculopathy. Surgical Neurology 71 (6) 677-680	n=28 (15 discs) FU=not reported	In unilateral cervical radiculopathy, arthroplasty and ACF provided favourable clinical and radiological outcomes. However, we should understand the different biomechanical backgrounds resulting in common advantages	Larger studies are included in table 2.
Yoon DH, Yi S, Shin HC et al. (2006) Clinical and radiological results following cervical arthroplasty. Acta Neurochirurgica 148(9):943–50	n = 46 FU = 12 months	Arthroplasty using the Bryan disc appears to be safe and provided a favourable preliminary clinical and radiological outcome. Postoperative kyphosis can be prevented by understanding the biomechanical properties of the Bryan disc.	Larger studies included in table 2

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

Guidance	Recommendations
Interventional procedures	**Percutaneous endoscopic laser cervical discectomy. NICE interventional procedures guidance 303 (2009)** 1.1 Current evidence on the safety and efficacy of percutaneous endoscopic laser cervical discectomy is inadequate in quantity and quality. Therefore this procedure should only be used with special arrangements for clinical governance, consent, and audit or research. 1.2 Clinicians wishing to undertake percutaneous endoscopic laser cervical discectomy should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having percutaneous endoscopic laser cervical discectomy (see section 3.1). 1.3 Clinicians undertaking this procedure should have specific training in the use of lasers and in endoscopy of the spinal canal. 1.4 NICE may review the procedure on publication of further evidence.

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

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	15/04/2009	Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease 2004 Rehabilitation after lumbar disc surgery 2006 Surgery for cervical radiculomyelopathy 2006	3
Database of Abstracts of Reviews of Effects – DARE (CRD website)	15/04/2009	-	10
HTA database (CRD website)	15/04/2009	-	10
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	15/04/2009	Issue 2, 2009	54
MEDLINE (Ovid)	14/04/2009	1950 to April Week 1 2009	329
MEDLINE In-Process (Ovid)	15/04/2009	April 14, 2009	35
EMBASE (Ovid)	15/04/2009	1980 to 2009 Week 15	232
CINAHL (NLH Search 2.0 or EBSCOhost)	15/04/2009	1981-present	75
BLIC (Dialog DataStar)	15/04/2009	-	4

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

1	Intervertebral Disk/ (7990)
2	Cervical Vertebrae/ (21033)
3	or/1-2 (27970)
4	"Prostheses and Implants"/ (30473)
5	Joint Prosthesis/ (7379)

6	Arthroplasty, Replacement/ (2394)
7	or/4-6 (39075)
8	3 and 7 (602)
9	(intervertebral* adj3 disk* adj3 (prosthe* or implant* or replac* or arthroplast*)).tw. (14)
10	(intervertebral* adj3 disc* adj3 (prosthe* or implant* or replac* or arthroplast*)).tw. (97)
11	(Cervical adj3 vertebrae* adj3 (prosthe* or implant* or replac* or arthroplas*)).tw. (6)
12	Spinal Diseases/ (14650)
13	Spinal Cord Diseases/ (8940)
14	(Spinal* adj3 Diseas*).tw. (2122)
15	Intervertebral Disk Displacement/ (12903)
16	(Intervertebra* adj3 dis* adj3 displace*).tw. (173)
17	(Degenerat* adj3 dis* adj3 diseas*).tw. (10335)
18	Radiculopathy/ (2483)
19	Radiculopath*.tw. (2557)
20	((prolaps* or slipp* or hernia*) adj3 Dis*).tw. (1505)
21	Myelopath*.tw. (7037)
22	Spinal Osteophytosis/ (3144)
23	(Spina* adj3 Osteophytos*).tw. (17)
24	CSM.tw. (713)
25	Neck Pain/ (2549)
26	((Neck* or cervical*) adj3 (pain* or ache* or disabilit* or immobilit* or vertebra*)).tw. (8473)
27	(cervical* adj3 spondylo*).tw. (1859)
28	or/12-27 (63035)
29	or/8-11 (664)
30	28 and 29 (387)
31	(Prodisc adj3 C).tw. (21)
32	((Bryan* or Bristol* or cummins* or Prestige* or Charite* or Frenchay* or traxis* or stryker*) adj3 (dis* or prosthes* or joint* or device*)).tw. (294)
33	or/31-32 (309)
34	33 or 30 (618)

35	Animals/ not Humans/ (3263264)
36	34 not 35 (585)