Medical Coverage Policy

Effective Date **1/15/2022**
Next Review Date **1/15/2023**
Coverage Policy Number **0104**

Intervertebral Disc (IVD) Prostheses

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Overview

This Coverage Policy addresses intervertebral disc prostheses, which are prosthetic devices used to replace a degenerated intervertebral disc for the treatment of degenerative disc disease (DDD) in the lumbar or cervical spine.

Coverage Policy

Lumbar Intervertebral Disc Prosthesis

Surgical implantation of an FDA–approved lumbar intervertebral disc (IVD) prosthesis for chronic, unremitting, discogenic low back pain and disability secondary to single-level degenerative disc disease (DDD) is considered medically necessary in a skeletally mature individual when ALL of the following criteria are met:

- Unremitting low back pain and significant functional impairment is refractory to at least six consecutive months of structured*, physician supervised conservative medical management, which includes **ALL** of the following components

    - exercise, including core stabilization exercises
    - nonsteroidal and/or steroidal medication (unless contraindicated)
    - physical therapy, including passive and active treatment modalities
    - activity/lifestyle modification
  - Single-level disc degeneration has been confirmed on complex imaging studies (i.e., computerized tomography [CT] scan, magnetic resonance imaging [MRI]).
- The implant will be inserted at an FDA approved lumbar/sacral level specific to the implant being used.

  ***Note: Structured medical management consists of medical care that is delivered through regularly scheduled appointments, including follow-up evaluation, with licensed healthcare professionals.**

Revision of a lumbar intervertebral disc prosthesis is considered medically necessary when imaging confirms failure of the implanted device (e.g., loosening, dislodgement, fracture, infection).

Surgical implantation of a lumbar intervertebral disc prosthesis is considered experimental, investigational or unproven for ANY other indication, including the following:

- The planned procedure includes the combined use of a prosthesis and spinal fusion (i.e., hybrid surgery).
- The individual has a history of lumbar disc replacement at any lumbar level.
- Simultaneous multilevel implantation is planned.
- The implant will be inserted outside of the recommended lumbar/sacral level for the specific implant being used.
- The individual has osteopenia or osteoporosis (T-score < -1.0).
- The individual has a history of prior lumbar fusion at an adjacent or other level.
- There is evidence on imaging studies of ANY of the following:
  - degenerative spondylolisthesis of Grade 2 or greater
  - infection
  - multilevel degenerative disc disease
  - nerve root compression or spinal stenosis
  - pars interarticularis defect with either spondylolysis or isthmic spondylolisthesis
  - scoliosis
  - severe facet joint arthrosis
  - spinal fracture
  - tumor
- Non FDA–approved lumbar intervertebral disc

Cervical Intervertebral Disc Prosthesis

Surgical implantation of a FDA–approved cervical intervertebral disc (IVD) prosthesis for symptomatic degenerative cervical disc disease at one-level or two contiguous levels, is considered medically necessary in a skeletally mature individual when ALL of the following criteria are met:

- Single-level or two contiguous level disc degeneration, has been confirmed on complex imaging studies (i.e., CT, MRI, X-ray), demonstrating at least ONE of the following at each level:
  - Herniated nucleus pulposus
  - Spondylosis (i.e., presence of osteophytes)
  - Visible loss of disc height compared to adjacent levels
- The planned implant will be used in the reconstruction of a cervical disc at C3-C7, following single-level or two-level discectomy.
- The individual is a candidate for single-level or two-level anterior cervical decompression and interbody fusion.
- EITHER of the following:

- Unremitting cervical radiculopathy and/or myelopathy (i.e., arm pain and/or neurological impairment) resulting in disability and/or neurological deficit, that clinically and radiographically correspond to the planned level(s) of disc replacement and is refractory to at least six weeks of standard conservative, nonoperative management (e.g., reduced activities, exercise, analgesics, physical therapy)
- Demonstrated progressive signs/symptoms of nerve root and/or spinal cord compression that clinically and radiographically corresponds to the planned level(s) of disc replacement and despite nonoperative treatment prior to implantation that requires immediate/urgent surgical treatment.

Subsequent surgical implantation of an FDA–approved cervical intervertebral disc (IVD) prosthesis is considered medically necessary at a second contiguous level in a skeletally mature individual with symptomatic cervical disc disease when all of the following criteria are met:

- The above medical necessity criteria is met for cervical disc replacement
- The planned subsequent procedure is at a cervical level adjacent to a previously implanted cervical artificial disc
- The cervical disc prosthesis is FDA approved for two levels
- The combined implant level is not greater than two levels.

Revision of a cervical intervertebral disc prosthesis is considered medically necessary when imaging confirms failure of the implanted device (e.g., loosening, dislodgement, fracture, infection).

Surgical implantation of a cervical intervertebral disc (IVD) prosthesis is considered experimental, investigational or unproven for ANY other indication, including the following:

- The planned procedure includes the combined use of a prosthesis and spinal fusion (i.e., hybrid surgery)
- Simultaneous multilevel implantation is planned at more than two diseased levels or two non-contiguous levels
- The individual had prior fusion at an adjacent cervical level
- The individual had prior surgery at the treated level
- Osteopenia, osteomalacia, or osteoporosis (e.g., T-score of -3.5, or -2.5, with associated compression fracture)
- Neck or arm pain of unknown etiology
- Absence of neck and/or arm pain
- Infection, systemic or local
- Rheumatoid arthritis or other autoimmune disease
- Paget's disease, osteomalacia or any other metabolic bone disease
- There is radiological evidence of ANY of the following:
  - clinically significant cervical instability, such as kyphotic deformity or spondylolisthesis (e.g., > 3.5 mm subluxation or > 11 degrees angulation)
  - significant cervical anatomical deformity or compromised vertebral bodies at the index level (e.g., ankylosing spondylitis, rheumatoid arthritis, or compromise due to current or past trauma)
  - multilevel degenerative disc
  - spinal metastases
- Non FDA–approved cervical disc prosthesis
- FDA-approved cervical disc prosthesis used for other than the FDA approved and intended, manufacturer specific use of the device.

General Background

Replacement of the degenerated disc, (intervertebral disc replacement) has been recommended as an alternative to spinal fusion. When conservative treatment of degenerative disc disease (DDD) fails, spinal fusion is considered the standard surgical treatment, however there are associated complications. Complications are reported in approximately 10% of all cases, and include nonunion, loss of spinal curvature and loss of flexibility. In addition, spinal fusion alters the biomechanics of the spine, reducing motion of the spinal segments, and potentially leads to premature disc degeneration at adjacent levels. Intervertebral disc replacement has been recommended as a means of improving spinal flexibility, maintaining spinal curvature, providing an equalized weight-bearing surface, and reducing or possibly eliminating back pain.

Lumbar Intervertebral Disc Prosthesis

Lumbar intervertebral disc prostheses are implanted anteriorly in the lumbar spine, the approach is the same for anterior interbody fusion. Three devices have received approval by the U.S. Food and Drug Administration (FDA) for surgical implantation within the spine for single-level disc replacement (activL® Artificial Disc [Aesculap Implant Systems], Charite® [DePuy Spine], and ProDisc-L [DePuySynthes]). Following the initial approval of these devices various supplemental approvals have been granted for each device based on modifications to the initial device. For example, The Charité® was initially developed in 1984 and has been modified several times, with one prior modification being called the SB Charité III. The Charite® lumbar disc has since been pulled from the market and replaced with the INMOTION® artificial lumbar disc.

In general, these devices are proposed for use in the lumbar spine for the treatment of DDD. Although each device has specific labeling information the devices are approved for individuals who are skeletally mature with DDD at a single level, either three millimeters or less of spondylolisthesis at the involved level or Grade 1 spondylolisthesis, and failure of at least six months of conservative nonsurgical treatment prior to implantation of the device.

The FDA defined DDD as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies (i.e., patient selection criteria for these studies included magnetic resonance imaging [MRI] or computerized tomography [CT] in conjunction with a discogram that mapped the specific anatomic location of the DDD as well as demonstrated concordant pain reproduction).

Each device has specific contraindications; however in general these include the following:

- active systemic infection or infection localized to the site of implantation
- osteoporosis
- osteopenia
- bony lumbar stenosis
- allergy or sensitivity to implant materials
- isolated radicular compression syndromes, especially due to disc herniation
- pars defect

Long-term efficacy and safety of TDR compared with fusion in patients with functionally disabling chronic low back pain due to single-level lumbar DDD at 5 years has been evaluated (Zigler, et al 2018); evidence suggests clinical results at five years are at least as good as or better than fusion in patients who have failed conservative care and suffer from single-level lumbar DDD.

U.S. Food and Drug Administration (FDA): According to the FDA lumbar intervertebral disc devices are regulated as Class III devices and require premarket approval (PMA). As part of the approval process, in order to determine long term safety and effectiveness the FDA has mandated post approval studies for each device and has provided guidance for acceptable success and radiological parameters. All adverse events are to be reported, including those that occur within the continued access subjects who participated in the investigational device exemption (IDE) studies.

There are several artificial disc replacement (ADR) devices that are being studied for use in the lumbar spine. Until approval can be obtained through the FDA, and clinical trials are conducted that provide guidance on specific patient selection, or patient net health outcomes, the use of these devices for the treatment of lumbar degenerative disc disease remains investigational.

Charité Artificial Disc: Early evidence supporting the use of the SB Charité III device was in the form of case series, retrospective case reviews and observational studies (Griffith, et al., 1994; Cinotti, et al., 1996; LeMarie, et al., 1997; Zeegers, et al., 1999; Van Ooij, et al., 2003, 2007; DeKleuver, et al., 2003). The studies were generally small in sample size, evaluated the use of various models of the device and included heterogeneous patient populations. Throughout the early published studies the device was implanted for both single and multilevel disease. Improvements in radicular and back pain were reported; however there was concern regarding rates of implant migration and other complications, in addition to the need for reoperation. Overall, the reported clinical outcomes of these initial studies are short-term (2 to 4 years).

Randomized controlled trials that were performed as part of the investigational device exemption (IDE) studies for the Charité device (Geisler, et al., 2004; Blumenthal, et al., 2005; McAfee, et al., 2005) demonstrated promising results favoring lumbar disc replacement compared to anterior lumbar interbody fusion. Authors continued to evaluate and report on the safety and clinical utility of intervertebral disc replacement devices. Subsequent studies published in peer-reviewed scientific literature continue to support safety and improved health outcomes such as reduction of pain and improved motion.

Initial FDA approval of the Charité device was based on two-year safety and effectiveness data from a multicenter, prospective, randomized investigational device exemption (IDE) study, the CHARITE IDE trial (N=304), which was conducted by the manufacturer at six medical centers (Geisler, et al., 2004). The purpose of the study was to demonstrate the non-inferiority of the Charite Artificial Disc to an interbody fusion system. Patients were followed and evaluated at three, six, 12, and 24 months using patient response questionnaires, radiographic films of the spine, Oswestry Disability Scores, (ODI) and visual analogue scale (VAS) scoring for pain reduction. At two year follow-up the study showed that patients treated with the artificial disc did no worse than patients treated with intervertebral body fusion. Rates of adverse events from the use of the artificial disc were similar to those from treatment with fusion; furthermore there was no statistically significant difference in the range of motion noted at the level of disc replacement or in the relief of the patients' pain.

Upon approval of the device the FDA required the manufacturer to conduct a post-approval study to determine the long-term safety and effectiveness of the IVD device; the FDA identified endpoints for determining overall success, patients were required to be evaluated for a total of five years post-implantation.

After two years of the five-year mandated patient follow-up required by the FDA, McAfee and colleagues (2006) conducted an analysis of the reasons for and the success rate of revising the Charité prosthesis within this entire study population. Of the 589 patients (71 nonrandomized, 205 randomized and 313 continued access) who underwent TDR, 52 (8.8%) required secondary revisions at the index level. Within the control group of 99 BAK procedures, 10 (9.9%) required revisions. According to the authors there was no significant difference between the two groups with respect to the rate of revisions (p=0.7041). McAfee and colleagues concluded that lumbar TDR did not preclude additional surgery at the primary site with replacements being revisable to a new motion-preserving prosthesis, ALIF and/or posterior instrumentation.

Five year prospective follow-up results to the multicenter Charité IDE randomized controlled trial comparing arthroplasty to arthrodesis was published in September 2008 (Guyer, et al. 2008a). A total of 160 patients completed the five year study (27 nonrandomized training cases and 133 randomized cases [90 Charité and 43 BAK cases]). Clinical evaluations were completed preoperatively, and at six weeks, three, six, 12, 24, and 60 months after surgery utilizing ODI, VAS scores, SF-36, neurological status and work status evaluations. Results were presented on an "intent-to-treat" basis rather than "as treated"; patients who crossed over to a different treatment group were maintained in the "intended-to-treat" group. The results included an improvement in ODI scores, a decrease in VAS scores, and improvements in SF-36 scores. Device success rates favored the Charité group as well as return to work status. Mean ROM at the index level also favored the Charité group. Overall, the results of the five year study are consistent with the two year reports of noninferiority of the Charité device versus ALIF with BAK cages and iliac autograft.

Aside from the FDA-related trials which support noninferiority two to five years following implantation, safety and efficacy has been evaluated by several authors following the device approval. These studies are primarily in the form of retrospective case series with some comparative trials and few additional randomized controlled trials

(Wagner, et al., 2006; SariAli, et al., 2006; Putzier, et al., 2006; Kurtz, et al, 2007; David, et al., 2007, Guyer, et al., 2008; Punt, et al., 2008; Geisler, et al., 2008, Cunningham, et al., 2008). These additional publications support the safety and efficacy of lumbar TDR for the treatment of degenerative disc disease.

ProDisc®-L: April 2020, the FDA granted premarket approval application (PMA) supplement for the prodisc® L Total Disc Replacement (Centinel Spine, LLC, West Chester, PA) for expanding the indications to include treatment of two adjacent levels of the lumbar spine. The device is indicated for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one or two adjacent vertebral level(s) from L3-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients should have no more than Grade 1 spondylolisthesis at the involved level(s). Patients receiving the prodisc® L Total Disc Replacement should have failed at least six months of conservative treatment prior to implantation of the prodisc® L Total Disc Replacement.
Initially, the applicant for ProDisc-L performed a clinical study to determine a reasonable assurance of safety and effectiveness of the prodisc® L for patients with contiguous two-level DDD between L3 and S1 who had not previously received fusion surgery at any intervertebral level, and who had failed to improve with conservative treatment for at least six months prior to enrollment.

The original PMA (P050010) was approved on August 14, 2006 and is indicated for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one level from L3-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients should have no more than Grade 1 spondylolisthesis at the involved level. Patients receiving the prodisc® L Total Disc Replacement should have failed at least six months of conservative treatment prior to implantation of the prodisc® L Total Disc Replacement.

As part of the IDE study for ProDisc®-L , outcomes from a multicenter, prospective randomized controlled clinical trial of 292 patients (162 randomized, 50 nonrandomized, and 80 control subjects) were submitted to the FDA. The control group was treated for DDD at a single level between L3 to S1 using a circumferential fusion technique (i.e., interbody fusion with femoral ring allograft, posterolateral fusion with autogenous iliac crest bone graft, combined with pedicle screw instrumentation). The randomized patients received implantations of the ProDisc-L via an anterior surgical approach, with no additional instrumentation being used to secure the device placement.

During this study, the FDA requested that the data be analyzed and reported using the following criteria:

- improvement in the ODI score ≥ 15 points at 24 months compared to the score at baseline
- maintenance or improvement of ROM defined as (24-month flexion/extension ROM, Pre-operative flexion/extension ROM) ≥ 0 (with ± 3° measurement error applied)
- a non-inferiority margin of 10%

The outcomes from this study led to the FDA's PMA decision based on the severity and number of adverse events that were no worse than the control group, and the overall success rate of the ProDisc that was no worse than the overall success rate of the control group; a non-inferiority margin of 10% (FDA, 2006; Zigler, 2007).

Several other well-designed studies, some including patients from the FDA IDE trial, supported safety and efficacy of ProDisc-L (Delamarter et al., 2003; 2005; Leivseth, et al., 2006; Bertagnoli, et al., 2005c, 2006a, 2006b; Siepe, et al., 2006; Chung, et al., 2006). Delamarter et al. (2003) reported results at 18-24 months indicating fusion patients reported a decrease in pain and functional status within the first six months, which was comparable to the scores obtained from the ProDisc implant group. At 24 months follow-up, Leivseth et al. (2006) documented the rotational and translational ROM at the level of implant versus adjacent levels of the spine. The ROMs obtained from this study group were compared to ROM norms that had been published within the literature. The authors found that sagittal plane rotational ROM of lumbar segments with ProDisc implants was low compared to the norm. When the researchers compared the ROM of the treated levels to the ROM of adjacent levels, they found these measures to be low as well. Thus, the researchers concluded that prospective studies are required to show whether the ROM of instrumented and untreated segments depends on prosthesis design, patient selection, or surgical technique and whether postoperative physical therapy could restore a normal ROM at least at the untreated levels of the spine.

Bertagnoli and colleagues evaluated ProDisc arthroplasty in several studies (2005, 2006a, 2006b). In 2005 the authors reported the results of prospective data collected from 104 subjects who underwent single-level ARD for DDD. By three months post-surgery there was a decrease in ODI scores and individual pain scores. The results of this study show a 96% rate of satisfaction as reported by the patients at two years. In 2006 Bertagnoli and associates evaluated the efficacy of ProDisc arthroplasty in patients with symptomatic adjacent-segment degeneration following remote lumbar fusion (n=20). In this group of subjects at 24 month follow-up, ODI scores significantly improved although individual pain scores did not. The authors noted long term studies were needed to determine feasibility of artificial disc replacement for adjacent segment degeneration. The results of a case series was published by this group of authors (2006b) evaluating the healing effects of smoking in subjects who received ProDisc lumbar artificial disc replacement (n=110). In this study the authors noted the intervention of disc arthroplasty was not confounded by smoking.

Three-year clinical results of ProDisc insertion for different indications were reported by Siepe et al. in 2006 (n=92). Average follow-up was 34.2 months and was subdivided into three distinct diagnostic groups in order to compare their subjective, VAS and ODI findings. Group I (n=40) was categorized as having DDD without additional pathology and served as the control group during this study. Group 2 (n=12) had DDD with nucleus pulposus prolapse (NPP); group 3 (n=17) had previously undergone discectomy procedures, and group 4 (n=23) had DDD with modic changes. The combined group analysis showed highly significant postoperative improvement for VAS and ODI in all groups; however, postoperative differences between groups 1, 3 and 4 were not statistically significant. Group 2 appeared to achieve and maintain the best subjective and objective results, at a mean follow-up of 33.1 months. Complication rate was 19.6%, requiring revision surgery at the index level in 8.7% of the patients and another 2.2% at the non-index level. These occurrences were considerably higher for bisegmental disc replacements (n=5 of 14 operations; 35.7%) compared with monosegmental interventions (n=11 of 77; 14.3%). The researchers concluded:

- monosegmental symptomatic DDD changes can be regarded as an acceptable indication for TDR
- previous discectomy did not have a negative impact on outcomes
- patients with DDD and large, contained, soft disc herniations with predominant low back pain are candidates for TDR
- bisegmental and multisegmental implantations were associated with a considerably higher complication rate
- three-dimensional CT reconstruction of the prevertebral vessels should be obtained for all TDRs planned for levels L4–L5 and above before surgery
- patient selection must be precisely determined
- longer follow-up evaluations are needed to determine the real benefits of TDR for patients

Subsequent studies published in the peer-reviewed scientific literature have continued to evaluate safety and efficacy and consist of various retrospective, prospective and comparative trials involving small populations evaluating short-term outcomes (Chung, et al, 2008; Leahy, et al., 2008; Yaszay, et al., 2008; Siepe, et al., 2008). The focus of these studies vary and include occurrence of surgical complications, comparison of clinical outcomes using ODI scores and range of motion between single-level and two-level replacement, the impact of prior discectomy on results of TDR clinical outcomes, and the effect of preoperative disc height on postoperative motion using ODI scores and VAS scores. Results of these studies supported that better clinical outcomes occurred in single-disc replacement compared to two-level (Chung, et al., 2006); prior discectomy did not compromise TDR outcomes (Leahy, et al., 2008); preoperative and postoperative disc height did influence range of motion (Yaszay, et al., 2008) and that the level of disc replacement did influence post-operative pain outcomes with L5-S1 replacement or two-level replacement resulting in a significant incidence of high pain levels.

Lumbar Total Disc Replacement and Adjacent Segment Degeneration: Authors have investigated the effect of TDR on adjacent segment degeneration (Park et al., 2008; Zigler, et al., 2012a). Park et al. (2008) reported results of a retrospective case series (n=46, 32 which completed the trial) evaluating radiologic changes in the discs at the adjacent levels and facets after disc replacement using the ProDisc II device. At an average follow-up of 32.2 months using outcome measures such as VAS scores, ODI scores, and imaging examinations facet degeneration was noted in 12 out of 41 segments; and among 47 adjacent segments, facet arthrosis was noted

in 6.4%. Degenerative changes in the discs and facets were minimal at adjacent segments; however the progression of facet arthrosis at the index level was 29.3%. In 2011 Park and colleagues reported a minimum five year follow-up in this same cohort noting that improvements in clinical outcomes were maintained (VAS, mean ODI, physical component scores, and sports activity scores) although outcome scores at last follow-up were lower when compared with one or two year scores. The authors noted clinical success for 25 subjects (71.4%). In a larger study Zigler et al. (2012a) compared adjacent level degeneration among subjects who underwent either circumferential lumbar fusion for single-level disc degeneration (n=75) or total disc replacement using ProDisc-L (n=161). Average follow-up was five years and clinical outcomes were measured using ODI, SF-36, and VAS. Degenerative disc disease was evaluated with radiograph confirmation by CT, MRI, discography, plain film x-ray, myelography, and/or flexion and extension radiography. Changes in adjacent level degeneration were demonstrated in 9.2% of TDR subjects and 28.6% of fusion subjects (p=0.0040). Clinical outcomes were improved at five years in both groups and were not correlated with adjacent level degeneration. Nevertheless additional studies are warranted to support longer term outcomes regarding the continued effect of TDR on the adjacent segments.

Comparative Device Studies: Evidence evaluating and comparing outcomes of Charité and ProDisc devices are limited to comparative trials and systematic reviews. Freeman and Davenport (2006) conducted a systematic review of the current evidence for total disc replacement using the Charité or ProDisc devices. Their search produced two randomized trials, two systematic reviews, seven prospective cohort studies, eleven retrospective cohort studies and eight case series. The authors concluded that the long-term benefits of TDR in preventing adjacent disc degeneration is unknown; the role of two- or multi-level TDR remains unproven; the role of arthroplasty adjacent to a TDR is unproven; the complications of TDR may not be known for many years; and well-designed prospective RCTs are needed.

Shim and colleagues (2007) published the results of a retrospective study evaluating and comparing radiologic outcomes of the Charité and ProDisc devices among a total of 61 patients who underwent TDR (n=57). They concluded that, while the clinical outcomes were fairly good, the facet joint of the index level and the disc at the adjacent level showed an aggravation of the degenerative process in a significant number of patients, regardless of the device used.

Multilevel versus Single-Level Studies: Increased segmental instability, increased load and altered stress distribution following total disc replacement remains a concern among authors. In 2020, the FDA approved the FDA granted premarket approval application (PMA) supplement for the prodisc® L Total Disc Replacement (Centinel Spine, LLC, West Chester, PA) for expanding the indications to include treatment of two adjacent levels of the lumbar spine. Studies comparing the clinical outcomes of single-level disc replacement with disc replacement performed at more than one level is limited (Hannibal, et al., 2007; Siepe, et al., 2007; Zindrick, et al., 2008; DiSilvestre, et al., 2009**;** Delemarter, et al., 2011; Bai, et al., 2019) and further studies are needed to support recommendations for multilevel disc replacement.

Delamarter, et al. (2011) conducted a study to determine the twenty-four-month results of a clinical trial of the ProDisc-L total disc replacement as compared with spinal fusion for the treatment of degenerative disc disease at two contiguous vertebral levels from L3 to S1. The study included a total of 237 patients were treated in a randomized controlled trial designed as a non-inferiority study for regulatory application purposes. Blocked randomization was performed with use of a 2:1 ratio of total disc arthroplasty to circumferential arthrodesis. Evaluations, including patient self-assessments, physical and neurological examinations, and radiographic examinations, were performed preoperatively, six weeks postoperatively, and three, six, twelve, eighteen, and twenty-four months postoperatively. At twenty-four months, 58.8% (eighty-seven) of 148 patients in the total disc replacement group were classified as a statistical success, compared with 47.8% (thirty-two) of sixty-seven patients in the arthrodesis group; non-inferiority was demonstrated. The mean Oswestry Disability Index in both groups significantly improved from baseline (p<0.0001); the mean percentage improvement for the total disc replacement group was significantly better than that for the arthrodesis group (p=0.0282). An established clinical criterion for success, a ≥15-point improvement in the Oswestry Disability Index from baseline, occurred in 73.2% (109) of 149 patients in the total disc replacement group and 59.7% (thirty-seven) of sixty-two patients in the arthrodesis group. The Short Form-36 physical component scores were significantly better for the total disc replacement group as compared with the arthrodesis group (p=0.0141 at twenty-four months). Visual analog scale scores for satisfaction significantly favored total disc replacement from three to twenty-four months. At

twenty-four months, 78.2% (111) of 142 patients in the total disc replacement group and 62.1% (thirty-six) of fifty-eight patients in the arthrodesis group responded "yes" when asked if they would have the same surgery again. Lumbar spine range of motion on radiographs averaged 7.8° at the superior disc and 6.2° at the inferior disc in patients with total disc replacement. Reduction in narcotics usage significantly favored the total disc replacement group at twenty-four months after surgery (p=0.0020). At twenty-four months, 58.8% (eighty-seven) of 148 patients in the total disc replacement group were classified as a statistical success, compared with 47.8% (thirty-two) of sixty-seven patients in the arthrodesis group; non-inferiority was demonstrated. The mean Oswestry Disability Index in both groups significantly improved from baseline (p < 0.0001); the mean percentage improvement for the total disc replacement group was significantly better than that for the arthrodesis group (p = 0.0282). An established clinical criterion for success, a ≥15-point improvement in the Oswestry Disability Index from baseline, occurred in 73.2% (109) of 149 patients in the total disc replacement group and 59.7% (thirty-seven) of sixty-two patients in the arthrodesis group. The Short Form-36 physical component scores were significantly better for the total disc replacement group as compared with the arthrodesis group (p = 0.0141 at twenty-four months). Visual analog scale scores for satisfaction significantly favored total disc replacement from three to twenty-four months. At twenty-four months, 78.2% (111) of 142 patients in the total disc replacement group and 62.1% (thirty-six) of fifty-eight patients in the arthrodesis group responded "yes" when asked if they would have the same surgery again. Lumbar spine range of motion on radiographs averaged 7.8° at the superior disc and 6.2° at the inferior disc in patients with total disc replacement. Reduction in narcotics usage significantly favored the total disc replacement group at twenty-four months after surgery (p = 0.0020). The study is limited by the relatively short duration of follow-up and design limitations. The study concluded that although the present study suggests that two-level lumbar disc arthroplasty is an alternative to and offers clinical advantages in terms of pain relief and functional recovery in comparison with arthrodesis longer-term follow-up is needed to determine the risks for implant wear and/or degenerative segment changes.

Balderston et al. (2014) reported on a prospective clinical data analysis to determine the long-term clinical success of 2-level total disc replacement (TDR) in patients with degenerative disc disease. The study included 15 patients that underwent 2-level lumbar TDR with the ProDisc-L as part of a randomized trial, 13 of whom were available for follow-up. The patients were assessed preoperatively and at two, five years, and more than 9 years postoperatively using visual Oswestry Disability Index. At the last follow-up visit, two additional questions were asked: satisfaction with surgery and willingness to undergo the same treatment and then clinical success was assessed using a previously described definition. Mean follow-up time was 9.6 years (range, 9.2-10.3 yr). Postoperatively there was a significant improvement in Oswestry Disability Index score from baseline (70.0 vs. 15.7 at 2 yr, P=0.002) that remained unchanged during the period of follow-up (19.8 at 5 yr, P=0.003 and 12.9 at 9-10 yr, P=0.002). Ninety-two percent of patients were "satisfied" or "somewhat satisfied" with treatment and the same number would undergo treatment again. Eighty-five percent of patients achieved clinical success. This study was limited by the small number of patients and lack of a control group.

Trincat et al. (2015) reported on a continuous series of 108 patients (51 women, 57 men) surgically treated over two levels with the ProDisc-L implant and were evaluated retrospectively with an average follow-up of four years. Ninety-three of these patients were operated for L4/L5 and L5/S1 degenerative disc disease, while 15 were operated for L3/L4 and L4/L5 disease. The Oswestry score, lumbar VAS and radicular VAS were used to evaluate function. The motion of the prosthetic disc segments was evaluated using Cobb's method. The procedure led to a statistically significant improvement in the functional scores. The motion of the upper disc segment was 9° (0°-19°) in flexion/extension and 5.5° (2°-12°) in lateral bending. It was 6.2° (0°-14°) and 1.9° (0°-7°) at the lower disc segment. The range of motion was similar in L3/L4 and L4/L5, but was less in L5/S1. Lack of mobility was not correlated with alterations in the functional outcome. The complication rate was 18%. The authors noted that while two-level lumbar disc replacement improves spinal function while preserving its mobility, the procedure is fraught with risks and must be carried out by a highly-experienced team and that a longer follow-up is needed to evaluate the sustainability of the results and to detect any adjacent segment disease.

Radcliff et al. (2018) conducted a long-term analysis to determine the incidence and risk factors for secondary surgery in patients treated with lumbar total disk replacement (TDR) or circumferential fusion at two contiguous levels of the lumbar spine. The study included a total of 229 patients that were treated and randomized to receive either TDR or circumferential fusion to treat degenerative disk disease at two contiguous levels between L3 and S1 (TDR, n=161; fusion, n=68). Overall, at final 5-year follow-up, 9.6% of subjects underwent a

secondary surgery in this study. The overall rate of adjacent segment disease was 3.5% (8/229). At 5 years, the percentage of subjects undergoing secondary surgeries was significantly lower in the TDR group versus fusion (5.6% vs. 19.1%, P=0.0027).Most secondary surgeries (65%, 17/26) occurred at the index levels. Index level secondary surgeries were most common in the fusion cohort (16.2%, 11/68 subjects) versus TDR (3.1%, 5/161 subjects, P=0.0009). There were no statistically significant difference in the adjacent level reoperation rate between TDR (2.5%, 4/161) and fusion (5.9%, 4/68). The most common reason for index levels reoperation was instrumentation removal (n=9). Excluding the instrumentation removals, there was not a significant difference between the treatments in index level reoperations or in reoperations overall. The authors concluded that these results establish that, TDR is noninferior to fusion in the overall rate of secondary surgery. Further study is necessary to identify longer term (10 y) adjacent segment disease rates to determine if the trend observed at 5 years becomes statistically significant.

Technology Assessment/Guidelines: In 2009, the National Institute for Health and Clinical Excellence (NICE) published an update to their 2005 guidance (without change to position) on intervertebral lumbar disc prosthesis and considered the evidence on safety and efficacy adequate to support the use of the procedure under normal arrangements (NICE, 2009).

Hayes published a technology assessment in 2015 evaluating lumbar total disc replacement for DDD (Hayes, 2015; 2020). According to Hayes, single-level disc replacement had comparable efficacy and safety in comparison to fusion although there is insufficient evidence to support safety and efficacy of two-level disc replacement, to support whether motion preservation will prevent symptomatic adjacent segment degeneration and whether there is a correlation of improved clinical outcomes resulting from restoration of disc height and preservation of flexion-extension. Hayes published an annual review 2020 and reported that although there were some new studies regarding safety published the review of abstracts did not change the conclusions (Hayes, 2020).

International Society for the Advancement of Spine Surgery (ISASS) published a position statement on cervical and lumbar disc replacement with the conclusion that ISASS, “strongly supports both cervical and lumbar total disc replacements, including multi-level use as approved by the FDA, as safe and effective treatment alternatives to fusion in appropriately selected patients. FDA study guidelines and labelling regarding inclusion and exclusion criteria should be followed for use, as supported by a strong published database.” (Schroeder, et al., 2021)

Cervical Intervertebral Disc Prosthesis

Surgical decompression of the nerve root or spinal cord by anterior cervical discectomy and fusion, with or without plate fixation, using autologous or allogeneic bone is considered the standard surgical treatment for symptomatic cervical DDD when conservative measures have failed. Adjacent segment degeneration following cervical fusion is a concern however; Hilibrand et al. (1999) estimated that more than 25% of patients will develop adjacent segment disease during the first 10 years following cervical fusion and the risk of repeat operation after a prior fusion in half of all symptomatic patients. In hopes of restoring spinal motion and preventing adjacent segment disease, cervical intervertebral disc prostheses have been developed for use in patients with symptomatic cervical disc disease associated with DDD at a single level between C3 to C7. Cervical disc arthroplasty utilizes the same surgical approach as a fusion; however instead of using bone graft and anterior plate fixation during the arthroplasty, the surgeon secures a prosthetic disc into the intervertebral space. The device is designed to assist in maintaining vertebral height while decompressing the spinal cord or nerve root in the neck.

Cervical intervertebral disc prostheses that have been approved by the FDA for surgical implantation within the spine, for single-level cervical disc replacement include but are not limited to: The Prestige™ ST Cervical Disc and Prestige LP Cervical Disc (Medtronic Sofamor Danek, Memphis, TN), the PRODISC-C® Total Disc Replacement (Synthes, Inc., New York, NY), the BRYAN® Cervical Disc (Medtronic Sofamor Danek, Memphis, TN), Secure®-C Cervical Artificial Disc (Globus Medical, Audubon, PA), PCM® Cervical Disc System (NuVasive, Inc., San Diego, CA) and M6-C Artificial Cervical Disc (Spinal Kinetics LLC, Sunnyvale CA).

Although each device has specific labeling information, in general the devices are approved for use in a skeletally mature individual for the reconstruction of a cervical disc from C3–C7 following single-level discectomy for intractable radiculopathy and/or myelopathy. The intractable radiculopathy and/or myelopathy (i.e., herniated

disc, and/or osteophyte formation) should be severe enough to produce symptomatic nerve root and/or spinal cord compression, documented by patient history (e.g., neck and/or arm pain, functional deficit, and/or neurological deficit) and radiographic studies (e.g., CT, MRI, x-rays).

Each device has specific contraindications however these generally include, but are not limited to, active infection or an allergy to product material (e.g., stainless steel). In addition, the safety and effectiveness of these devices has not been established in patients with the following conditions:

- more than one cervical level with DDD (except those specifically FDA approved for two level disease)
- not skeletally mature
- clinically significant cervical instability
- prior fusion at an adjacent cervical level
- severe facet joint pathology or involved vertebral bodies
- prior surgery at treated level
- osteopenia, osteomalacia, or osteoporosis as defined by bone mineral density T-score of -3.5, or -2.5 with vertebral crush fracture
- spinal metastases
- chronic or acute renal failure or history of renal disease
- taking medications known to potentially interfere with bone/soft tissue healing (e.g., steroids)
- pregnant
- severe insulin-dependent diabetes
- neck or arm pain of unknown etiology
- Rheumatoid arthritis or other autoimmune disease
- significant cervical anatomical deformity or compromised vertebral bodies at the index level (e.g., ankylosing spondylitis, rheumatoid arthritis, or compromise due to current or past trauma)

The safety and effectiveness of the use of this device has also not been established in patients who have not undergone six weeks of conservative treatment or had signs of progression or spinal cord/nerve root compression with continued nonoperative care.

U.S. Food and Drug Administration (FDA): Similar to lumbar intervertebral devices cervical devices are Class III devices and require premarket approval. The FDA has granted PMA approval for several devices and as part of the approval, the FDA is requiring follow-up post-approval studies to evaluate long-term safety and effectiveness of the device. The FDA has defined outcome measures that include Neck Disability Index (NDI) scores, radiograph information and neurological status as well as detailed information regarding adverse events.

PRESTIGE ST Cervical Disc: Evidence in the peer-reviewed published scientific literature evaluating early models of the PRESTIGE cervical disc included case series with few randomized trials (Wigfield, et al.,2002; Robertson and Metcalfe, 2004; Porchet, 2004). Sample populations of these studies were small ranging from 15 to 55 subjects with follow-up that ranged from 24 to 48 months. The results of these studies supported device stability, deceased neck and arm pain, improved SF-36 quality of life scores and improved NDI scores.

Mummaneni et al. (2007) conducted a prospective, randomized controlled study under an FDA-approved IDE to assess the safety and effectiveness of the PRESTIGE ST Cervical Disc System. This study compared anterior cervical discectomy with fusion and plating to cervical discectomy with immediate arthroplasty and insertion of the PRESTIGE ST Cervical Disc System (n=541). Subjects were randomized into an investigational group (n=276) and a control group (n=265) within 32 institutions. Patients in the investigational group received a PRESTIGE ST Cervical Disc system prosthesis, and individuals in the control group underwent interbody fusion with cortical ring allograft and supplemental fixation using cervical plating. All patients entering the study had Neck Disability Index (NDI) scores of 30 or greater and numeric pain scores greater than or equal to 20. Prior to surgery, patients received six weeks of medical management (e.g., physical therapy, a reduction in activities, and anti-inflammatory medications) unless progressive neurological worsening occurred.

Mummaneni reported that the 24-month overall follow-up rate was 80% (223 of 276) in the investigational group and 75% (198 of 265) in the control group. Patients were counted as treatment failures if data could not be

obtained during this 24-month period. Secondary surgery occurred within both groups. No revisions occurred in the investigational group, while five revisions occurred within the control group. Implant removal was required in both groups (1.8%—investigational versus 3.4%—control), although not statistically significant. Reoperations were required for adjacent-segment disease in both groups, with a statistically significant lower rate occurring in the investigational group ($p=0.0492$) versus the control group. During the perioperative period, 17 adverse events (6.2%) occurred in the investigational group and 11 (4.2%) occurred in the control group. These events included hematoma formation, dysphagia, and dysphonia. Neck Disability Index (NDI) scores in both groups improved significantly over preoperative scores ($p<0.001$), with statistical significance noted at six weeks and at three months for the investigational group. Neck pain scores improved significantly throughout the study in both groups, with no statistical difference noted in arm pain improvement between the groups.

At 24 months, neurological success was 92.8% in the investigational group versus 84.3% in the control group, the incidences of employment were 75.4% and 74.7% (investigational versus control group), there were no implant failures, migrations, or subsidence found; and only one case of ectopic ossification was in the investigational group. Radiographic angulation was increased in the investigational group. Evidence of fusion in the control group was high at 12 (98.7%) and 24 (97.5%) months. Overall success for the investigational group was 77.6% at 12 months and 79.3% at 24 months. Overall success for the control group was 66.4% at 12 months and 67.8% at 24 months. The researchers determined that the outcomes proved the device was noninferior to anterior cervical discectomy with fusion (ACDF) ($p<0.0001$) at both 12 and 24 months. They also determined that neurological functioning outcomes were statistically superior ($p=0.0040$, 12 months; $p=0.0053$, 24 months).

Burkus et al. (2010) published five-year results of a prospective randomized multicenter RCT (32 centers, n=541), comparing cervical disk replacement using the Prestige disc (n=276), to anterior instrumented interbody fusion (n=265). The study was a continuation of 36 month data which is used in this study as a point of comparison. All surgeries were performed at a single disc space level between C3-C4 and C6-C7. All patients had neck and arm pain which continued despite nonoperative treatment for at least six weeks prior to surgery. One center did not participate in the long term follow-up study leaving 533 subjects eligible for the post-approval study. Of those patients, 271 have completed the 60-month follow-up. A total of 197 patients of the investigational group and 160 of the control group were included in the results evaluated at 36 months. Clinical outcome measures included NDI, SF-36 PCS, neck and arm pain scores, return to work status range of motion and secondary surgical procedures. The latter were classified as revision, removals, supplemental fixations or reoperations. Adjacent segment ossification was not a specific data point in the study. Reported results favored the cervical implant for the following end points which was statistically significant:

- NDI scores at 35 and 60 months
- Rates of revision (5 versus 0) and supplemental fixation (3.4% versus 0%)
- Sagittal motion retention (averaging 7.3° at 36 months and 6.5° at 60 months

Non- statistical results were identified for the following end points:

- Subsistence rates
- Neck and arm pain scores as well as SF-36 scores, which improved in both groups
- Neurological success rates which were high in both groups
- Subjects returning to work, each exceeding 70%
- Complaints of dysphagia and dysphonia were similar among both groups

The authors concluded the Prestige disc maintains improvement of clinical outcomes at five year follow-up.

Burkus et al. published seven year clinical and radiographic results comparing cervical disk replacement using the Prestige disc (n=276), to anterior instrumented interbody fusion (n=265) (Burkus, et al. 2014). A total of 395 subjects completed seven years of follow-up (76.8% investigational group, 69.1% control group); the authors noted improved clinical outcomes and segmental motion were sustained in both groups with confirmation of continued non-inferiority in overall success at the seven year follow-up.

PRODISC-C®: Nabhan and colleagues (2007) reported on the results of a prospective randomized controlled study evaluating segmental motion following artificial disc replacement with the ProDisc-C device over one year.

The authors compared segmental motion and clinical results of disc replacement (n=25) to the “gold standard” anterior cervical discectomy and fusion (n=24). Eight patients were excluded due to ineligibility for roentgen stereometric analysis, leaving 41 for the RCT, one patient died during the trial period. Clinical symptoms of neck and arm pain were evaluated at baseline and at one, three, six, 12, 24 and 52 weeks after surgery. VAS was used for grading neck and arm pain. At one year there was no sign of adjacent level degeneration in either group, pain relief was comparable in both groups and mean VAS scores for neck and arm pain decreased significantly in both groups from preoperative. The authors reported that cervical spine motion decreased over time in both the prosthesis and fusion group although the loss was significantly higher in the fusion group at one year postoperatively. The authors noted further studies are warranted with long-term follow-up to ascertain whether or not cervical motion is preserved following disc replacement**.**

Murrey et al. (2008) conducted a prospective, randomized controlled study under an FDA-approved IDE study (noninferiority design) to assess safety and effectiveness of the ProDisc-C Total Disc Replacement. The study population involved 209 patients with symptomatic cervical degenerative disc disease causing intractable debilitating radiculopathy from one vertebral segment (between C3 and C7) who were unresponsive to nonoperative treatment for at least six weeks and had neck disability index scores of 15/50 (30%) or more. The study compared ProDisc-C (n=103) to a control group who received anterior cervical discectomy and fusion (n=106). Overall success was determined by four-component endpoints: NDI success (defined as a 15 point improvement from baseline value), neurological success (defined as the maintenance of improvement of each neurologic evaluation [sensory, motor, reflex functions], device success and absence of adverse events related to the device or its implantation with ratings defined as the percentage of individual patients achieving success in all four-component endpoints. The clinical status of each patient was evaluated pre and postoperatively at six weeks, three, six, 12, 18 and 24 months and included self-assessment, physical and neurological examination and radiograph evaluation.

The follow-up rate at 24 months for the entire group was 96.5% and the authors noted there were no statistically significant differences between ProDisc-C patients (98.0%) and control patients (94.8%) returning at 24-months. Both operative time and blood loss were lower for the fusion group compared to the ProDisc-C group and were statistically significant. Other statistically significant outcomes favored the disc group and included neurological success at 6 months, NDI scores at three and 24 months and device success. Other reported outcomes that favored the disc group but were not statistically significant included secondary surgical procedures, adverse event success, VAS scores and return to work.

There was no evidence of migration, subsidence, change in disc height, or visible gaps found on radiograph assessment in either group at 24 month follow-up. The fusion rate for patients who did not require a secondary surgery at 24 months was 90.2%. A total of 84.4% or ProDisc-C patients achieved a more than or equal to 4º of motion or maintained motion relative to preoperative baseline at the operative level.

Based on FDA criteria for success, 72.3% of ProDisc-C patients and 68.3% of fusion patients were successful at 24 months. The additional minimally clinically important difference (MCID) found 73.5% of ProDisc-C patients and 60.5% of fusions patients successful at 24 months. The authors concluded that the ProDisc-C is proven as safe and effective compared to standard treatment of anterior cervical discectomy and fusion.

In 2010 Delamarter et al. published the four year follow-up results of the 24-month IDE trial of ProDisc-C versus anterior cervical discectomy and fusion. In total, 63% of the subjects who underwent disc replacement were available for 48 month follow-up and 46.2% of subjects who underwent cervical fusion were available at 48 months. The measured outcomes were the same as for the initial FDA trial and included NDI scores, VAS scores for pain and satisfaction, radiographic, and neurological and physical examinations. The results remained superior for neurological success, and sustained improvement for NDI and VAS scores, and SF 36 scores. Range of motion was maintained for the disc replacement group who reached 48 month follow-up. A total of 2.9% of disc patients and 11.3% required secondary surgery at 48 month follow-up. In the authors opinion although the cervical fusion group had higher risk for secondary surgical intervention, both groups demonstrated good clinical results at 48 month follow-up. The authors noted the subjects were continuing to be followed up for seven years (Delamarter, et al., 2010).

Kelly et al. (2011) compared adjacent segment motion following disc arthroplasty using the ProDisc-C device versus ACDF in 209 patients in a prospective randomized controlled trial. Changes in motion were compared, and flexion and extension radiographs were obtained at an average 24 month follow-up. At 24 months the ACDF group had a significant decrease in ROM while the disc replacement group did not ($p<0.0001$, $p=0.275$). Linear regression analysis revealed that treatment and time from surgery were significantly associated with changes in postoperative motion, the effect of time differed between the ACDF group and the disc group ($p<0.0001$). In the ACDF group only, there was a significant increase in motion at the cranial and caudal adjacent segments, time from surgery was a significant predictor of postoperative ROM. ROM decreased over time with fusion whereas disc replacement results in immediate motion sustained throughout the follow-up period.

Nabhan et al. (2011) conducted a prospective randomized controlled trial comparing segmental motion following cervical disc replacement (n=10) versus cervical fusion (n=10) and correlation to clinical outcome. Results were evaluated using the VAS and NDI scales, roentgen stereometric analysis (RSA) was performed immediately postoperative and after six weeks and 12 months. In the authors opinion the precision of RSA is high making it suitable for small study samples compared to functional X-ray. At an average of 12 months there was no change in the average segmental motion immediately cranial to the disc prosthesis; there was an increase in the average segmental motion immediately cranial to the fusion but without significant difference ($p>0.05$) when compared with the prosthesis. Both procedures resulted in significant reduction in arm and neck pain; statistical significance however was lacking between groups ($p>0.05$). The authors concluded here was no significant difference in segmental motion of the adjacent level, with either prosthesis or fusion, one year post surgery.

Zigler and colleagues (2012) published interim five year clinical outcomes of the patient cohorts in the original noninferiority FDA IDE trial comparing cervical arthroplasty using ProDisc-C to anterior cervical discectomy and fusion (ACDF). This study is an interim report to the seven year post-approval study. The FDA IDE study involved 209 subjects from 13 sites. NDI scores, VAS neck and arm pain scores, SF-36, neurological exam, devices success, adverse events, and patient satisfaction were evaluated. At five years follow-up, 13 subjects withdrew from the study and five were deceased (n=195). An additional 52 subjects were lost to follow-up. The authors accounted for those who dropped out and were lost to follow-up by using a “last observation carried forward” sensitivity analysis, reporting that the results with this method were consistent with results obtained with the missing data. All clinical outcomes improved at both two and five years compared to baseline with a statistically significant difference in NDI scores ($p=0.0001$), neck and arm pain scores ($p=0.0001$), and SF-36 scores ($p=0.0001$). There were no differences between groups at two and five years for NDI scores, SF-36 scores, patient satisfaction or neurological assessments. There was no percent change between groups for neck pain intensity and frequency at two years but there was a difference at five years. Though both groups had statistically significant reduction of neck pain intensity and frequency at five years compared to baseline, the reduction was more significant in the Pro-Disc group. A between groups analysis did reveal a statistical difference between the intervention groups at five years on both neck pain intensity and frequency, at $p=0.0122$, and $p =0.0263$, respectively. The fusion group demonstrated significantly reduced ROM at the index level at two and five years compared to preoperative values; the ProDisc-C group maintained ROM at the index level compared to preoperative values. A statistical assessment was not reported. Device migration was not detected in either group. Rates of adverse events related to implants were not statistically different though Pro-Disc trended lower at 1% compared to 2.8% for fusion patients. No p value was reported. Surgical adverse events were statistically comparable between groups with an overall incidence of 12 in the ProDisc-C group versus 22 in the fusion group ($p=0.09$). For all subjects included in the analysis, the ProDisc-C patients were reported to have had statistically significantly less secondary spinal surgery compared to the ACDF group (2.9% versus 11.3% respectively, $p =0.0292$). The data reported in this interim study are promising regarding the authors’ conclusion of non inferiority however there are limitations of the study. More than 25% of subjects were lost to follow-up; 27 in the Pro-Disc group and 25 in the ACDF group and the statistical inclusion of last data point as part of the outcomes for those lost to follow-up is a concern, and introduces treatment bias favoring reduced adversity, reoperation rates, and diminishing validity of reduced symptom severity over time. Both groups had statistical improvement in nearly all areas and both groups were very satisfied with their outcomes. Additional follow-up of this cohort is needed to determine long-term outcomes supporting safety and clinical utility for this group of subjects, and results that can be generalized to a larger population.

Mehren and colleagues (2017) published 10 year results of a prospective nonrandomized trial evaluating 50 subjects who underwent cervical disc replacement using the ProDisc-C device. Subjects were followed by

radiological and clinical exam at one, five and ten years post procedure. The authors reported significant clinical improvements were maintained at 10 year follow-up (e.g., VAS arm, VAS neck, and NDI scores) with low implant-related reoperation rates (2%) and low symptomatic adjacent segment degeneration rates. High grade ossification was noted and associated with a significant reduction in range of motion. Segmental motion at the index level declined from 9.1° at one year to 7.7° and 7.6° at five and ten years, respectively. Adjacent segment disease was detected in 35.7% of subjects; 7.9% of these subjects had symptoms that required conservative management. In the authors opinion the high grade ossification did not have a detrimental effect on the subject's clinical symptomatology. Limitations of the trial included lack of a control group and small sample population.

BRYAN® Cervical Disc: The BRYAN cervical disc is composed of a plastic (polyurethane) center with titanium endplates. It is designed as a one-piece device that allows unconstrained motion and is unique in that there is a flexible membrane that surrounds the nucleus (the inner portion of the disc) that is filled with a lubricant. This membrane is designed for two purposes: to contain any wear debris that forms and to prevent any soft tissue in-growth. The articulating surfaces of this device are polyurethane on titanium. It has beaded porous coated endplates intended for biological fixation instead of fixation using screws into the vertebrae or fixation by use of stabilizing keels.

Results from preliminary prospective trials evaluating this device supported range of motion of ≥ 2 degrees, improved activities of daily living scores and neurological improvement at follow-up periods of six months, 12 months, and 24. Nonetheless the authors acknowledged five year data was needed to evaluate long term device functionality and impact on adjacent segments (Goffin et al., 2002; 2003).

Sasso et al. (2007a, 2007b) reported a subset of data from 115 patients who participated in the FDA IDE study of the BRYAN® cervical disc. At 12 months, data from 109 patients were available; data from 71 patients were available at 24 months in the initial publication, however in the second publication 99 subjects were available for 24 month follow-up. Outcomes from these both groups were determined by comparing preoperative PCS, NDI and VAS pain scores to those recorded at each follow-up time. Sasso reported that both groups had significant improvement from baseline NDI scores and neck pain at 24 months. The disc replacement group retained an average ROM of 7.3 degrees at 12 months and 7.0 degrees at 24 months. By 24 months, there was no statistically significant change noted over preoperative measurements. Three patients in the investigational group required ACDF due to adjacent level disease during the 24 months of follow-up. No spontaneous fusions or heterotopic ossification (HO) were noted in the BRYAN group.

Some studies evaluating the BRYAN artificial disc included a subset of subjects involved in the FDA IDE trial (Garrido, et al., 2010; Anderson, et al., 2008; Sasso, et al., 2008a, Sasso, et al., 2008 b). Other clinical trials published in the peer-reviewed scientific literature consisted of randomized controlled trials (Anderson, et al., 2008; Heller, et al., 2009), prospective comparative trials (Yang, et al., 2008), prospective case series (Zhang, et al., 2014; Heidecke, et al., 2008), and retrospective case series (Yang, et al, 2009). The type of outcomes evaluated in all of these trials varied by author group and included outcomes such as occurrence of adverse events of disc replacement compared with cervical anterior fusion, the ability of the disc to maintain motion at the implanted level, range of motion, clinical outcomes such as improvement of neck and arm pain, changes in functional activity, radiographic outcomes such as migration or subsidence, and overall quality of life improvements. Sample populations and outcome follow-up varied among trials but ranged from 15 to 98 subjects with the FDA IDE trial consisting of 463. On average follow-up time ranged from 12 to 48 months; Garrido et al. (2010) reported 48 month results and Goffin et al. (2010) reported follow-up at four and six years. Although study design, sample size, outcomes measured and follow-up time varied these studies support safety and efficacy of the implanted BRYAN Disc. Results of the studies demonstrated improvements postoperatively in neck and arm pain, NDI, VAS , SF-36, cervical motion, and improved quality of life.

In 2010 the Swiss federal office of health conducted a prospective multicenter observational study to evaluate safety and efficacy various cervical discs. As part of a mandatory Health Technology Assessment registry 808 interventions with implantation of 925 discs from five different suppliers were evaluated. Data was recorded preoperatively, at three months, one year and annually thereafter and included patient self-reported measures (EQ-5D, COSS, comorbidity questionnaire) as well as surgeon reported outcome instruments which included intervention, implant and follow-up forms. Evaluation of results extending to two years was published. Disc replacement resulted in significant and clinically relevant reductions of neck pain and arm pain (using VAS scale)

and decreased use of analgesics. Quality of life improved from preoperatively to postoperatively on the EQ-5D scale. The authors reported four intraoperative complications and 23 revisions during the same hospitalization for 691 monosegments, and two complications and six revisions for 117 two-level replacements. Cervical total disc arthroplasty was determined to be safe and effective for relief of pain, reduction of analgesic use and improved quality of life in the short-term (Schluessman, et al., 2010).

Some authors have reported on clinical outcomes for the Bryan disc that range intermediate to long-term (Ren, et al., 2011; Quan, et al., 2011; Yan-bin, et al., 2010; Walraevens, et al., 2010). Although not in the form of randomized controlled trials and often involving small sample populations, the reported intermediate to long-term outcomes suggest preservation of motion, reduction in adjacent level degeneration, and improvement in neurological symptoms. In 2010 Walraevens et al. published preliminary results of a prospective case series involving 89 subjects who received the Bryan disc. Eight-year results were available for 26 (radiographic assessment) out of 89 patients at the time of publication, although 82 completed four year follow-up. At four years 85% of the devices were mobile, at six years 87% were mobile, and of those available at eight years 88% were mobile. Improvements in ROM stabilized around the preoperative value at the four year time period. A total of 66% were free from heterotopic ossification at four years, at six years 62% were free and at eight years 61% were free. At all follow-ups there were no cases of anteroposterior migration >3 mm or of subsidence >2mm. Good to excellent clinical outcomes were reported for 87% at four years, and 85% and 82% respectively for six and eight year follow-up.

Zhao et al (2010) reported from a case series the radiograph and MRI results of 22 patients who underwent cervical disc replacement using the Bryan disc. Mean follow-up was five years. Range of motion on radiograph at the operated level improved at baseline from final follow-up 7.2° to 7.8°. Eight levels developed heterotopic ossification and two had lost motion. Upper adjacent segment worsened by a grade in 2 of 22 subjects and lower adjacent segment worsened by a grade for 3 of 22 patients; 22 of 24 levels showed preserved motion at five years while 8 of 24 developed heterotopic ossification and two levels lost motion. In the authors opinion by preserving motion the Bryan disc may reduce adjacent segment degeneration.

Ren at al. (2011) reported the results of a prospective case series involving 45 subjects who received 51 Bryan cervical discs, 39 received single-level replacement and six subjects received two-level replacements. Follow-up evaluation ranged from 24 to 70 months, with an average of 35 months. The authors noted all patients had improvement in neurological symptoms. Japanese Orthopedic Association Scale (JOA) scores increased from 10.2 preoperatively to 15.4 at final follow-up. NDI scores were reduced from 43.6 to 28.4 at final follow-up and Odom's Criteria also improved and was rated as excellent in 23 subjects, good in 11 subjects, fair in 6 subjects, poor in 5 subjects. Overall clinical success rates were 88.8%. The average ROM improved, stabilization was achieved for all discs and migration of the disc greater than 2mm was not seen.

Quan et al. (2011) reported the results of a prospective cohort of 21 subjects who underwent single-or two-level disc replacement using the Bryan cervical disc. Although initially there were 30 subjects, nine subjects were either lost to follow-up or had incomplete data and were not included. The authors reported no patient required further spinal surgery on either the arthroplasty or adjacent segment at final follow-up. Fourteen of the 21 patients were working and the remaining seven were either retired or not working due to poor health. Twelve subjects reported no occupational or recreational limitations when compared to preoperative activity levels; seven retired patients also reported no limitations. Based on Odom criteria 18 of 21 subjects had excellent outcomes. VAS scores for neck and arm pain both improved postoperatively, mobility was maintained in 21 of 27 segments and there was no significant difference in range of motion between functional prostheses and upper or lower adjacent segments. A total of 13 of 27 subjects had heterotopic ossification and those patients had slightly higher VAS scores for neck and arm pain. One case of posterior migration was reported which consolidated and did not result in additional surgery. Radiograph evidence of adjacent segment degeneration was noted in four subjects, and in three of those the prosthesis had fused. These patients did have pre-existing degenerative disc disease.

Sasso and colleagues (2011) reported 48 month follow-up data to the pivotal FDA clinical trial published by Heller et al (2009). Of the original 463 subjects who were enrolled in the FDA trial, 24 month results for 424 subjects in total have been previously reported. A condition for approval of the device from the FDA was an extension of the original trial to 10 years post-surgery. The results reported by Sasso et al. (2011) reflect a total

of 319 subjects (181 arthroplasty, 138 fusions) who were available for follow-up at 48 months (68%). The measured clinical outcomes were similar to the original trial and included NDI scores, SF-36 scores, determination of neurological success, radiograph assessment and adverse events. The primary endpoint was overall success for which patients had to achieve all of the following: > 15 point improvement in NDI, neurological improvement, no serious (WHO grade-3 or 4) adverse events, and no subsequent surgery or intervention that would be classified as a treatment failure. The authors reported that at 48 months greater improvement in NDI scores, arm pain scores, SF-36 results, and overall success (p=0.004) continued to favor the experimental group. Neurological success rates at 48 months were similar to those reported at 24 month and were not significantly different. At 48 months more TDR subjects returned to work compared to the fusion group, although not significantly different. Mean cervical spine motion increased for the disc group at all time points whereas the fusion group showed a decrease of motion at 48 months. Forty-four subjects in the arthroplasty group had 63 adverse events while 36 of the subjects in the fusion group had 64 adverse events; the difference was not significant. The authors noted most of the events were unrelated to the index surgery or cervical spine. Nine patients of TDR group and ten of the fusion had secondary surgical procedures involving the index cervical spine level. One patient in each group had the device removed. Despite the limitation of a low rate of follow-up, which the authors attribute to the original design of the study (set for 24 months), the authors concluded significantly superior outcomes were sustained for cervical spinal arthroplasty with the Bryan disc compared to fusion at 48 month follow-up.

The results of two separate FDA IDE trials were combined to evaluate long term outcomes of cervical TDR (n=41) with ACDF (n=33) (Coric, et al., 2013). Sixty-three subjects were available for a minimum of 48 month follow-up, although average follow-up was six years. Both groups demonstrated significant improvement of NDI scores and VAS scores (p<0.0001) that continued through the 48 month follow-up with no significant differences between groups. ROM in the cervical group was significantly greater compared with the ACDF group. There was no statistically significant difference in overall reoperation rate or adjacent–level reoperation rate between groups. The authors concluded both treatments appeared to be safe and effective at a minimum of 48 months follow-up. The study is limited by small sample population.

A meta-analysis published by Gao and colleagues (2013) of 27 RCTs indicated as expected ACDF subjects had less range of motion at the operated level compared with TDR. The arthroplasty subjects had significantly better neurological success (p=0.000) and significantly lower neck and arm pain scores (p=0.01, p=0.02) while maintaining a comparable NDI score. Data for adverse events were not consistent, some studies supported less adverse events in the TDR group compared with the ACDF group and some did not. Overall, outcomes were either equivalent or superior in favor of the disc replacement group.

Simplify® Cervical Artificial Disc (Simplify Medical, Inc., Sunnyvale, CA): Simplify® Cervical Artificial Disc received PMA approval (P200022) 9/2020. The device is indicated for use in skeletally mature patients for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and manifested by at least one of the following conditions confirmed by radiographic imaging (e.g., X-rays, computed tomography (CT), magnetic resonance imaging (MRI)): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels. Patients receiving Simplify® Cervical Artificial Disc should have failed at least six weeks of non-operative treatment or have the presence of progressive symptoms (e.g., numbness or tingling) prior to implantation. Simplify® Cervical Artificial Disc is implanted via an open anterior approach.

In April 2021, the FDA approved a PMA supplement for the Simplify® Cervical Artificial Disc to expand the indication for use to include use at two contiguous levels. This device is indicated for use in skeletally mature patients for reconstruction of the disc at one or two contiguous levels from C3-C7 following discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to abnormality localized to the disc space and manifested by at least one of the following conditions confirmed by radiographic imaging (e.g., X-rays, computed tomography (CT), magnetic resonance imaging (MRI)): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels. Patients receiving Simplify® Cervical Artificial Disc should have failed at least six weeks of non-operative treatment or demonstrated progressive signs or symptoms despite non-operative treatment prior to implantation. Simplify® Cervical Artificial Disc is implanted via an open anterior approach.

The Simplify Cervical Artificial Disc is a cervical artificial intervertebral device manufactured from PEEK endplates and a mobile, zirconia-toughened alumina ceramic core. The PEEK endplates have a plasma-sprayed titanium coating per ISO 5832-2 and ASTM F1580. The articulating surfaces on the endplates have a concave surface and the core has two convex surfaces.

Literature review Simplify Cervical Artificial Disc: Guyer et al. (2021) reported on 24-month follow-up of single-level cervical disc replacement using a Polyetheretherketone (PEEK)-on-Ceramic Implant (Simply cervical artificial disc). The prospective, nonrandomized, historically controlled, multicenter US Food and Drug Administration (FDA) Investigational Device Exemption (IDE) trial included 150 patients that received the PEEK-on-ceramic Simplify Cervical Artificial Disc. The historic control group included 117 propensity-matched anterior cervical discectomy and fusion (ACDF) patients from an earlier IDE trial. The primary outcome was a composite success classification at the 24-month follow-up. Outcome measures included the Neck Disability Index (NDI), neurological status, adverse events, subsequent surgery, a visual analog scale assessing neck and arm pain, and the Dysphagia Handicap Index. Radiographic assessment included flexion/extension range of motion and heterotopic ossification. Facet joints were assessed at 24 months using MRI. The success rate was significantly greater in the cervical total disc replacements (TDRs) group vs the ACDF group (93.0% vs 73.6%; P<.001). Mean NDI, neck pain, and arm pain scores improved significantly in both groups at all follow-up points. Mean NDI scores in the TDR group were significantly lower than ACDF scores at all follow-up points. No significant differences in the rates of serious adverse events were noted. Range of motion of the TDR level had increased significantly by three months and remained throughout follow-up. Facet joint assessment by MRI in the TDR group showed little change from preoperation.

Other FDA-approved Cervical Disc Devices
Other cervical artificial discs devices that have received FDA PMA approval include:
Secure®-C Cervical Artificial Disc, PCM® Cervical Disc System: The Secure-C device is an articulating intervertebral disc device that has two endplates and a central core; the endplates have multiple serrated keels and a pure titanium plasma spray coating on the bone contacting surfaces. The sliding core is composed of ultra-high molecular weight polyethylene. The PCM device is also an articulating device, is composed of two cobalt chromium molybdenum alloy endplates and an ultra-high molecular weight polyethylene spacer fixed to the caudal endplate. The contact between the spacer and cephalad component is a bone and socket articulation. The bone contacting surface of each endplate has a layer of calcium phosphate and consists of transverse ridges designed to improve postoperative bone fixation. The M6-C device is an IVD that is designed to allow six degrees of motion which mimics a normal human disc. This device is made of ultra-high molecular weight polyethylene fiber wound that interacts with two titanium alloy inner endplates. M6-C is offered in four different footprint sizes. All three devices are inserted with an anterior approach and according to FDA labeling the indications for use and contraindications for these devices are similar to those for other devices previously approved.

Mobi-C® Cervical Disc (LDR Spine USA, Inc.): According to the FDA (PMA -P110009) approval has been granted for the Mobi-C® Cervical Disc (LDR Spine USA, Inc.). This device is a cervical disc prosthesis approved for use at two adjacent levels for the treatment of intractable radiculopathy with or without neck pain, or myelopathy due to abnormality localized to the level of the disc space, and at least one of the following conditions confirmed by radiographic imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height compared to adjacent levels. According to the manufacturer the device can be used for either one or two level disc disease. The FDA required a 7-year post approval for this device, similar to other FDA approved disc prosthesis. According to the FDA the post approval study was completed in 2014, the total follow-up rate at 84-months was 82%; however, only 136 two-level Mobi-C subjects (66.3%) and 48 ACDF subjects (57.1%) had actual 'in-window' efficacy data at the final timepoint. The FDA deemed two-level Mobi-C was a safe alternative to ACDF. Non-inferiority for the two-level Mobi-C compared to ACDF with respect to individual subject success was demonstrated up to the time point of 84 months.

The Prestige LP™ Cervical Disc System (Medtronic, Sofamor Danek, Memphis, TN): The Prestige LP™ Cervical Disc System received FDA PMA (supplemental, S003: P090029) approval in 2016 for treating

degenerative disc disease at two adjacent vertebral levels (C3-C7). According to the FDA approval order this device is indicated for the same indications as the Mobi-C device noted above.

M6-C Artificial Cervical Disc: The M6-C Artificial Cervical Disc received FDA approval through the PMA process (P170036) on February 6, 2019 for reconstruction of the disc following a single level discectomy. This device is indicated in skeletally mature patients with intractable degenerative cervical radiculopathy with or without spinal cord compression at one level from C3-C7. The device is implanted via an anterior approach like other devices of this kind.

Literature Review— Other FDA Approved Devices: The Secure-C, PCM, and Mobi-C cervical devices were evaluated in investigational device exemption (IDE) studies as part of the FDA PMA approval process. These studies were prospective randomized trials involving multiple centers, used ACDF as the control, and evaluated clinical outcomes extending to at least two years ([PCM-Phillips, et al, 2013]; [Mobi-C - Davis, et al., 2013]). As per the IDE protocol outcome measures and definitions of success were similar although not identical to other cervical disc IDE trials. According to the PMA for each device the IDE trials supported safety and efficacy of the devices at two year follow-up. Five year clinical outcomes reported by Hisey et al.(2016) evaluating one level Mobi-C continue to support cervical TDR is a viable alternative to anterior cervical discectomy and fusion in a specific subset of individuals**.** Nevertheless, similar to some of the other FDA approved devices the FDA is requiring a 7 year post approval study for each device in order to evaluate the longer-term safety and effectiveness. The FDA expects at least 85% follow-up at the 7 year time period for each of these studies to provide sufficient data.

Cervical Total Disc Replacement and Adjacent Segment Disease: The effects of cervical TDR on adjacent segments are under investigation. The results of early publications did not firmly establish that maintaining motion after single-level cervical discectomy delayed or prevented symptomatic postoperative disc disease at 24 months average follow-up (Roberston, et al., 2005; Yi, et al., 2009).

Nunley et al. (2012) published the results comparing clinical success rates and occurrence of adjacent segment disease in subjects following ACDF and TDA (n=182). The control group consisted of 57 subjects who received ACDF and an experimental group who received TDA (n=113). It was noted that twelve subjects did not complete follow-up. The initial trials were conducted as part of the FDA IDE trials. The identification of adjacent segment disease was not required as part of the IDE trials; subjects documented as having adverse events such as cervical radiculopathy/myelopathy, were evaluated with MRI or CT scans in addition to plain radiographs as part of the IDE protocol. Once the presence of adjacent segment disease was established, records of subsequent surgery or medical management were maintained and are reported on within this study. The follow-up period ranged from 32 to 54months (median 42 months); 16.5% (n=28) subjects had established adjacent segment disease during the follow-up period (nine ACDF, 19 TDA). A total of seven were categorized as severe disease and underwent subsequent surgery at the adjacent level; five underwent fusion and two underwent decompression. Twenty-one who had less severe grades of disease received conservative management which included pain medications, physical therapy and at least one epidural steroid injection. The authors reported that at most recent follow-up 83.2% of the TDA group and 86% of the fusion group were free of adjacent segment disease. There was no statistical difference in the incidence of disease between the two groups. Survival analysis for the adjacent level disease-free period demonstrated a trend towards increased survival rates for subjects without osteopenia compared to those with osteopenia (82.3% ± 0.425; 54% ± 1.76%, respectively). The result was statistically significant (P=0.04). The presence of concurrent degenerative disc disease was also associated with lower disease-free survival rate compared to those without disease (55.5%± 0.12%, 74.5%± 0.6%, respectively) and was statistically significant (P=.023). The authors concluded the development of adjacent segment degeneration was equivalent at 38 month median follow-up and that the presence of osteopenia and degenerative disc disease significantly increased risk of adjacent segment degeneration.

Ding et al (2012) published the results of a retrospective case series (n=34 patients) evaluating intermediate clinical and radiograph outcomes of the Bryan cervical disc. Follow-up ranged from 32 to 69 months, average 49.4 months. Clinical outcomes, adjacent segment degeneration, complications and reoperations were evaluated. Radiograph outcomes demonstrated the Bryan discs preserved normal range of motion at the operative level as well as the adjacent segments. Degeneration scores of the upper and lower discs increased significantly to 1.5 ± 1.4 and 1.3 ± 1.2 respectively, at 24 months following surgery (P>0.05) and at 1.7±2.3 and

1.4 ± 2.1, respectively at last follow-up (48 months). While degeneration did not affect the mid-term clinical outcome, at last follow-up degeneration was noted in 25% of the upper and 22 % of the lower segments which was either new degeneration or progression of the initial degeneration. Long term follow-up is required to determine if and when degeneration will result in symptoms.

Yang et al. (2012) published a meta-analysis of randomized controlled trials evaluating the incidence of adjacent segment degeneration following TDA using guidelines of the Cochrane Collaboration. Five RCTS met the inclusion criteria. The devices evaluated included Kineflex-C, Mobi-C, Advent Cervical Disc, Bryan Cervical Disc, and Prestige disc. There was no statistical heterogeneity among any studies. The rate of adjacent segment disease was fewer in the TDA group compared with ACDF although the difference was not statistically significant (P=0.32). Three trials reported reoperations were required; the rate of adjacent segment surgery was fewer in TDA group (3.21%) compared to the fusion groups (4.84%). The authors suggest that adjacent segment degeneration is affected by patient individuality and not only by the fusion. Due to the low number of studies included the results of the analysis should be interpreted carefully.

Tian et al (2014) reported the results of a six-year prospective nonrandomized trial comparing cervical artificial disc replacement (n=45) using the Bryan disc with anterior cervical discectomy and fusion (n=48) to assess adjacent segment degeneration over time. A total of 63 subjects completed radiograph and clinical follow-up (67.7%) at an average timeframe of 77-80 months postoperatively. Both treatment groups included those who received either single or multilevel treatment. Using radiographs, tomography and MRI the authors evaluated adjacent segment degeneration and reported that the incidence of adjacent segment degeneration overall was significantly lower for the disc replacement group compared with the fusion group at the final follow-up. Limitations of this clinical study include the amount of subjects lost to follow-up, a small sample population and lack of randomization.

In a prospective randomized controlled, multicenter trial conducted by Hisey, et al (2014), one of the clinical outcomes the authors evaluated and reported on included adjacent segment degeneration. Within this trial subjects were randomized to receive either cervical disc replacement using the Mobi-C disc (n=164) or anterior cervical discectomy and fusion (n=81) using a 2:1 randomization ratio. Follow-up occurred at various time points from six weeks to 48 months postoperatively. Adjacent segment degeneration was determined radiographically using the Kellgren-Lawrence scale and was defined as having had at least one grade of increased degeneration at the inferior or superior adjacent segment. The authors reported that at 48-month follow-up adjacent segment degeneration occurred significantly more often in the fusion group when compared to the disc replacement group, 60.7% versus 44.3%, respectively ($p<0.05$). Furthermore it was reported that the occurrence rates degeneration were greater in the fusion group at both areas, inferior and superior adjacent segments.

Chang et al. (2016) reported the results of a systematic review evaluating adjacent segment disease requiring reoperation in cervical total disc replacement. Nine studies met inclusion criteria. The data was not pooled due to significant variation in level of evidence and length of follow-up although eight of the studies were FDA/IDE trials involving eight separate artificial discs. The authors concluded the average reoperation rate was 3.1% for total cervical disc replacement and 6.0% for anterior cervical discectomy and fusion subjects with follow-up between 24 and 80 months.

Wu et al. (2017) evaluated the four year subsequent surgery rates of cervical disc replacement versus fusion as a meta-analysis of prospective randomized clinical trials. Eight studies met inclusion criteria involving 2497 subjects (1390 received anterior cervical disc replacement [ACDR]; 1107 received anterior cervical discectomy and fusion [ACDF]). The implanted disc prostheses included the Byran, Prestige ST, Mobi-C, and PCM discs. The pooled overall rate of subsequent surgery at the adjacent level and operated level was less in the ACDR group (7.4%) than in the ACDF group (16.8%) ($P<0.0001$). Neck pain and radiculopathy were the most common reasons for subsequent surgery at the index level in both groups. Subsequent surgery for adjacent segment disease occurred in both groups but was much lower in the ACDR group than in the ACDF group ($P<0.0001$).

Multilevel versus Single-Level Studies: Pimenta et al. (2007) compared single-level cervical disc replacement utilizing the Porous Coated Motion (PCM) Device to multilevel disc replacement in a consecutive series of 140 patients. A total of 71 patients had single-level replacement and 69 patients had multilevel replacement (53 double, 12 three-level, four four–level). A total of 19 cases were complex revision cases and 21 had adjacent

segment disease following cervical fusion. Estimated blood loss, length of hospital stay and length of surgery were greater for the multilevel group. Self-assessment outcome instruments (i.e., NDI, VAS scores) demonstrated more improvement for multilevel cases. The mean improvement in the NDI for single cases was 37.6% compared to 52.6% for the multilevel cases; the difference was statistically significant (p=0.021).The mean improvement in VAS score was similar, 58.4% for single-level cases versus 65.9% for multilevel cases. The Treatment Intensity Score and Odom's criteria were also more improved for multilevel cases when compared to single-level. Reoperation and adverse events were similar between groups. Using Kaplan –Meier analysis implant survivorship for the overall group was 94.5% at three years. The results of this study suggest a greater clinical outcome improvement for multilevel disc replacement, although the authors note further analysis is necessary.

Cheng and associates (2009) published the results of prospective randomized controlled clinical trial comparing the functional results and radiographic outcomes of fusion (n=34) and BRYAN cervical disc replacement (n=31) as treatment for two-level cervical disc disease. Evaluation was conducted using the VAS scale, SF-36 and NDI during a two-year follow-up period. Three patients were lost to follow-up. The results demonstrated significant improvement in outcome measures at 24 moths, including arm pain VAS, neck pain VAS, NDI, and SF-36 physical scores. While both groups showed statistically significant improvement at two years compared to preoperative scores, the BRYAN group showed better clinical outcomes in comparison to the fusion group. The results to this study are limited by a small sample population and short term outcomes and long-term outcome data is needed to support improvement in health outcomes when used for treatment of two-level disease.

Barbagallo et al. (2009) reported the early results of a surgical technique that combined cervical fusion and disc replacement for treating multilevel DDD (n=24). Disc prostheses were implanted at either the level above or below the one receiving a cage as part of the fusion. In some cases two prostheses were implanted and in others two cages were implanted. Average follow-up was 23.8 months. In all but one patient clinical follow-up demonstrated significant improvement; radiological evaluation demonstrated functioning disc prostheses and fusion through cages. While the surgical approach seemed a safe and valid option for patients with multilevel symptomatic cervical DDD, long-term follow-up with larger patient populations are needed to support the clinical effectiveness of this approach.

In a prospective multicenter study, Huppert et al. (2011) compared clinical and radiological outcomes of cervical disc replacement using the Mobi-C disc (non FDA-approved device) between single- and multilevel subjects. A total of 231 subjects were treated with disc replacement and completed 24 month follow-up; 175 subjects received a single-level replacement and 56 received replacement of two levels or more. Measured outcomes included NDI scores, VAS scores, ROM, and satisfaction. Improvement in NDI and VAS scores for neck and arm pain were similar among groups (p=0.713, p=0.790 respectively). However in the multilevel group there was significantly more use of analgesics (p=0.029). Occurrence of heterotopic ossification was significantly lower in the single-level group. Satisfaction was comparable among subjects in both groups. Absolute range of motion improvement between pre-op and 24 months was not significantly different.

Wu and associates reported the results of a prospective case series (n=102) evaluating the differences between single and multilevel (2 or 3 levels) DDD treated with the Bryan cervical disc device. At 24 months follow-up 86 subjects completed clinical/ radiographical follow-up; 16 subjects were either lost to follow-up or had inadequate evaluations. The authors noted the multilevel group demonstrated a high rate of heterotopic ossification compared to the single level group (66.0% versus 25.0%, P<0.001) at an average follow-up of 38.3 ± 8.7 months. Most of the artificial discs remained mobile despite the heterotopic ossification (97.7%) and there were no significant differences in the mobility between single level and multilevel groups. Both groups demonstrated significant improvements postoperatively in clinical outcomes such as VAS neck and arm scores, and VAS disability scores. In the authors opinion results of multilevel surgery were similar to single level surgery at three years.

As part of the FDA IDE prospective, randomized trial, Davis et al. (2013) reported on the use of the Mobi-C cervical disc. The entire study involved two experimental groups and a control group and was designed as a noninferiority trial (n=600). Within this publication the authors reported the 24 month follow-up of one arm of the study to compare clinical outcomes of two-level disc replacement (n=225) to two-level ACDF (n=105) for subjects with two-level DDD disease of the cervical spine. Measured outcomes included NDI scores, VAS

scores, reoperation at the index level, complications, neurological function and radiological success. Overall study success was defined similar to other cervical disc IDE trials. Follow-up occurred at 6 weeks, 3, 6, 12 and 24 months post-operatively. Follow-up rates were 98.2% (disc group) and 94.3% (ACDF) at 24 months. Both groups had improvement in VAS neck and arm pain scores, had high patient satisfaction, and quality of life scores from baseline to postoperative. Physical component scores (PCS) scores were statistically significant and favored the disc group ($p=0.03$) at all time periods. NDI scores improved from baseline to postoperative for both groups although it was significantly greater in the disc group at every time period ($p<0.05$). The disc group had less neurological deterioration ($p<0.0001$), less reoperations, less device related events, and less serious adverse events that were either possibly or definitely related to the device when compared to the ACDF group. In addition in the experimental group segmental motion was maintained at both segments. According to the authors, based on all scores, the experimental group demonstrated statistical superiority at 24 months follow-up compared to two-level ACDF.

Subsequent to the 2013 publication Davis and colleagues (2014) reported 48 month outcomes for this same cohort of subjects. The 48 month follow-up rate was 89% for the disc group and 81.2% for the fusion group. Statistical significance for two level disc replacement reported at 24 months was maintained at 48 months for NDI scores, SF-12 PCS scores, patient satisfaction, and overall success. The authors reported the overall success at 48 months for the disc group was statistically superior ($p<0.0001$) compared with the fusion group; success rates of 66% versus 36% respectively, resulting primarily from the NDI scores and subsequent surgery scores significantly in favor of disc replacement. It was noted that NDI scores were the primary cause of failure in the fusion group with criteria not being met in 46.6% of the subjects versus 20.7% in the disc group. Regarding subsequent surgery rates, at 48 months 4% of the disc and 15.2% of the fusion group required at least one subsequent surgery, compared to 24 month results of 3.1% and 11.4%, respectively. The fusion group also demonstrated a higher rate of adjacent segment degeneration, while the disc group maintained segmental range of motion with no device failure.

Clinical outcomes from multilevel disc replacement continued to be investigated and reported in the medical literature (Li, et al., 2018; Zhao, et al, 2015; Bae, et al, 2015; Alvin and Mroz, 2014). Zhao et al. (2015) published the results of a meta-analysis evaluating multilevel TDA versus single-level TDA. All studies included at least one year follow-up with some reporting two–year follow-up. A total of eight publications met inclusion criteria and were reviewed; four prospective and four retrospective studies. The authors analysis of the eight cohort trials demonstrated no significant difference in NDI scores, neck VAS, arm VAS, morbidity of reoperation, heterotopic ossification and quality of living scores at one and two years post procedure ($p> 0.05$). The authors concluded that multi-level TDA is as safe and effective as single-level TDA for cervical spondylosis, however it was noted more well-designed trials involving large groups of subjects are needed to provide further evidence of benefit and reliability. Limitations of this meta-analysis include lack of randomized controlled trials and inclusion of only 8 cohorts. More recently, Bae et al. (2015) reported four year clinical outcomes as part of a post hoc analysis of the prospective randomized IDE trial involving 164 subjects who underwent single-level TDA and 225 subjects who underwent two-level TDA. The authors reported all scores (NDI, VAS neck and arm pain, SF-12 Mental and Physical Composite Scores, ROM, complication rates and secondary surgery rates) improved when compared to pre-operative scores, and there were no statistically significant differences between one and two-level outcomes for any clinical measure. Complication and secondary surgery rates were similar between TDA groups. The authors acknowledged long term studies are needed to further evaluate heterotopic ossification and effects on clinical outcomes, as well as adjacent segment pathology and how it relates to pain and function.

Radcliffe et al. (2016) reported five year outcomes of TDR using the Mobi-C cervical disc at two contiguous levels compared to ACDF. This study involved the same cohort of subjects as the second arm of the FDA IDE trial (n=225 TDR, n=105 ACDF) and is the same study cohort reported on by Davis et al. 2014 with four year outcomes. Outcome measures included NDI, VAS scores for neck and arm pain, patient satisfaction and patient recommendation for treatment, SF-12 quality of life scores, and dysphagia. Additional outcomes included neurological assessment of strength, reflex, and motor testing, radiographic fusion status and subsequent surgery, defined as revision, removal, reoperation or supplemental fixation at the index level. Overall success was defined using the FDA Post Approval study protocol, which included five metrics: NDI improvement of at least 15 points from baseline, no subsequent surgical intervention at the index level, no potential device-related adverse event, maintenance or improvement in all components of neurological status, and no Mobi-C intraoperative changes in treatment. Subjects were evaluated at various time points from baseline, up to and

including 60 months postoperatively. The follow-up rates at five years were 90.7% for the TDR group and 86.7% for the ACDF group. It was noted that subjects not eligible for five year follow-up are still considered active in the study and will continue to be followed. Regarding outcomes, the authors reported the following:

- there was significant improvement of NDI scores, SF 12 Physical Component scores, and patient satisfaction for the TDR group compared to the ACDF group
- the ACDF group had a symptomatic nonunion rate of 8.6%; a higher index level reoperation rate (16.2% vs 4.3%), and higher adjacent level reoperation rate (11.4% vs 3.1%) compared to the TDR group, respectively
- there was no significant increase in dysphagia in the ACDF group
- the TDR group had significantly less adjacent segment degeneration at either superior or inferior level compared to ACDF, 50.7% vs 90.5%
- the five year adverse event rate was higher in the ACDF group compared to TDR group, 8.6% vs 4.4%

Based on overall success rate, 61% TDR vs 31% ACDF, the authors concluded the results supported superiority and noninferiority criteria in favor of TDR. Study limitations were acknowledged by the authors. One noted limitation included unblinding of the subjects after surgery due to postoperative protocols, which varied between treatment groups. Unblinding of subjects could lead to bias regarding patient satisfaction and recommendation scores. Additional limitations included subjectivity of the decision to reoperate; it was determined by the treating surgeon and patients' personal decision and lacked specific indications; a largely Caucasian subject group (94%), which may limit the generalization of results; and the use of allograft in the ACDF group, autograft reoperation rates may have been different.

Jackson et al. (2016) evaluated five year subsequent surgery rates in subjects treated with ACDF or TDR at one or two contiguous levels, between C3-C7 (n=599). TDR was performed using the Mobi-C device, the control ACDF group underwent fusion using one of three plate systems with allograft material. Subsequent surgery was defined as any operation at the initial treatment level or at adjacent levels. For index level surgeries leading to study failure, subsequent surgical interventions were considered as any secondary surgery at any level that was a removal, revision, supplemental fixation or reoperation. The five year one-level follow-up rate was 85.5% for the TDR group versus 78.9% for the ACDF group; the two-level follow-up rate was 90.7% TDR and 86.7 ACDF, respectively. At five years follow-up, both single and two-level ACDF subjects had significantly higher subsequent surgery rates (17.3%, 21.0%) compared to the TDR subject groups (4.5%, 7.3%). The TDR group had significantly less index and adjacent-level subsequent surgeries in both the one and two level cohorts. It was noted that some subjects required multiple subsequent surgeries; however, only the initial surgery was used to determine the subsequent surgery rate. The authors acknowledged limitations of the study included lack of blinding, the use of anterior plate and allograft for ACDF precluding generalizability of results, and the use of various types of cervical plate systems.

Other Studies: MacDowall et al. (2019) conducted a randomized controlled trial of patients being treated surgically for cervical radiculopathy. The objective of the study was to determine if artificial disc replacement (ADR) prevented immobilization side effects such as adjacent-segment pathology (ASP). The randomized controlled study consisted of 153 patients (mean age n=47; n=83 ADR, n=70 fusion). Patients were included in the study when they displayed radiating arm pain with duration of three months, correlating findings on MRI at one or two cervical levels and eligible for both treatments (ADR and fusion). Exclusion criteria were: previous cervical spine surgery, more than two cervical levels, severe facet arthropathy, symptoms or marked radiological signs of myelopathy, drug abuse, dementia, or expected low compliance, cervical malformation or instability, history of cervical trauma, pregnancy, rheumatoid arthritis, malignancy, active infections and known allergy to implant material or to non-steroidal anti-inflammatory drugs (NSAIDs). The primary outcome was measured as the NDI score. The NDI is a ten item self-administered questionnaire measuring daily activities and concentration abilities. The minimum score is 0 which indicates no disability; conversely the highest score is 50 which indicates severe disability. Secondary outcomes were the EQ-5D, visual analog scales for neck and arm pain, the dysphagia short questionnaire and hospital anxiety and depression scale. Follow ups were completed at one, two and five years. Results noted that the ADR group improved in NDI from a score of 64 to 36 at the five year follow up. In the same timeframe, the fusion group improved from 61 to 32; with a mean difference between the two groups of 205 (p=0.48). The secondary outcomes of EQ-5D and the VAS showed no mean difference between groups. Adverse events included seventeen patients in the ADR group and seven in the fusion group required secondary surgery primarily attributed to loosening and subsidence. The author concludes that there is

no statistically significant outcomes between ADR and fusion at a five year follow-up. Larger RCTs are needed to determine long-term follow ups between interventions.

Cervical Technology Assessments/Guidelines: NICE published guidance on prosthetic intervertebral disc replacement in the cervical spine (NICE, 2010). The guidance includes:

- Current evidence on the efficacy of prosthetic intervertebral disc replacement in the cervical spine shows that this procedure is as least as efficacious as fusion in the short term and may result in a reduced need for revision surgery in the long term. The evidence raises no particular safety issues that are not already known in relation to fusion procedures. Therefore this procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit.
- This procedure should only be carried out in specialist units where surgery of the cervical spine is undertaken regularly.
- NICE encourages further research into prosthetic intervertebral disc replacement in the cervical spine. Research outcomes should include long-term data on preservation of mobility, occurrence of adjacent segment disease and the avoidance of revision surgery.

Although it is not an official position statement, in 2010 the American Academy of Orthopaedic Surgeons (AAOS) published a technology overview of cervical disc arthroplasty. The overview was based on the findings of studies published prior to September 2009. Regarding patient characteristics, the data was inconclusive, most studies did not report a statistical analysis, and only one level II study reported no statistically significant difference. For clinical outcomes, five level II studies were included. There was a trend for better NDI scores and NDI success rate at early follow-up, data for long term follow-up was inconclusive. While one study reported arthroplasty had significantly higher neurologic success rates, two level II studies reported no statistically significant differences. A majority of the studies reported no statistically significant difference in either neck or arm pain scores at short term follow-up (six months to 24 months), long term data was inconclusive. The result reported by three level II studies was inconclusive regarding SF-36 scores and there were no differences in the number of patients who returned to work at 24 months. The results of four level II studies were included, three did not report secondary surgery results similarly, and therefore the results could not be compared. The results for adverse events were also inconclusive in these same studies. Patients who underwent arthroplasty returned to work in significantly fewer days although the length of hospital stay did not vary between groups.

Cochrane conducted and published a review evaluating arthroplasty versus fusion in single-level cervical degenerative disc disease (Boselie, et al., 2012). The evidence reviewed included RCTs that directly compared any type of cervical disc arthroplasty to any type of cervical fusion with outcomes extending at least one year. A total of nine RCTs (n=2400) met inclusion criteria, eight were industry sponsored; five had high methodological quality and low risk of bias. With regards to relief of arm pain at one to two years, low-quality evidence favored arthroplasty as having a small but significant difference (i.e., between 1 and 5 points on a 100 point scale). The authors noted a small study effect could not be ruled out. Moderate quality evidence demonstrated a small difference in neck related functional status and neurological outcome at one to two years, in favor of arthroplasty. A clinically relevant difference was not seen in any of the primary outcomes (arm pain, neck pain, neck related functional status, patient satisfaction, neurological outcome, global health status). Mobility was preserved after disc replacement in the short-term (1-2 years). Long term effectiveness has yet to be determined and Cochrane concluded use of the devices should be limited to clinical trials.

BCBSA TEC continues to update published reports regarding artificial cervical disc replacement as a proposed treatment for DDD of the cervical spine. The most recent assessment includes data from six randomized IDE clinical trials for the FDA-approved devices up to October 2013 (Prestige ST, ProDisc-C, Bryan, PCM, Mobi-C, Secure-C); non-FDA approved and precursor devices were excluded. At two year follow-up all trials met noninferiority criteria as measured by NDI and overall success. According to the report, long-term outcomes (4 and 5 year) have been reported for three devices and are consistent with non-inferiority. However BCBSA TEC noted the quality of the original trials is not high, and raises concern regarding validity of results. Advantages such as improved ROM, lower incidence of adjacent segment disease and lower short-term morbidity have not been proven. Consistent with prior reports, BCBSA TEC concluded artificial cervical intervertebral disc arthroplasty does not meet BCBSA TEC criteria (BCBSA, 2014).

Hybrid Surgery

Artificial disc replacement at one level combined with spinal fusion surgery at another level (adjacent or non-adjacent) is referred to as hybrid surgery. Biomechanical studies lend some support that combined lumbar fusion and disc replacement function similar to single level fusion; however there are few clinical trials to support improved health outcomes and patient selection criteria has not been firmly established. While some authors have investigated this method of treatment for multilevel cervical DDD (Xiong, et al., 2020; Wang, et al., 2018; Xiong, et al., 2018; Ji, et al., 2017; Grasso, 2015; Jia, et al., 2014; Kang, et al, 2013; Lee, et al., 2012, Cardosa, et al., 2010) the evidence in the published peer-reviewed scientific literature demonstrating the safety and efficacy of combining cervical disc replacement and cervical arthrodesis procedures at multiple adjacent or non-adjacent levels is insufficient to support safety, efficacy and improved net health outcomes. Some of the authors evaluated and compared outcomes between subjects who underwent hybrid surgery or multilevel arthroplasty, the evidence is limited however by retrospective design, lack of controls, small sample populations and short-to mid-term outcomes.

The authors of one meta-analysis (Lu, et al., 2017) reviewed eight studies comparing hybrid surgery (n=169) with ACDF (n=193). Of the eight studies included only one was a RCT, the remaining studies were prospective or retrospective observational studies. The hybrid surgery group required increased operative time ($p < 0.00001$), had less intraoperative blood loss ($p < 0.00001$), shorter return to work ($p < 0.00001$), C2-C7 range of motion preservation ($p < 0.00001$), and less functional impairment ($p=0.008$) compared to ACDF. Limitations as reported by the authors include low quality of evidence available for review, small sample size and number of studies included, and retrospective and ambispective design (both prospective [HS] and retrospective [ACDF]). In the authors opinion HS is a safe alternative to ACDF, although there is lack of robust clinical evidence and additional large prospective studies are needed to firmly establish safety and efficacy. Additional research in the form of randomized controlled trials is needed to clearly establish a role for hybrid technologies.

Hollyer et al. (2020) conducted a systematic review and meta-analysis was performed to compare the clinical and radiographical outcomes of hybrid surgery (HS) against with anterior cervical discectomy and fusion (ACDF) or cervical disc arthroplasty (CDA) alone. The review included eight papers (N=424), one randomized controlled trial, prospective and retrospective studies. Post-operative C2-C7 range of motion (ROM) was significantly greater after HS than ACDF ($p = 0.004$; mean difference (MD) 6.14°). The ROM of the superior adjacent segment was significantly lower after HS than ACDF ($p < 0.0001$; MD - 2.87°) as was the ROM of the inferior adjacent segment ($p = 0.0005$; MD - 3.11°). HS patients' return to work was shorter than those who underwent ACDF ($p < 0.00001$; MD - 32.01 days) and CDA ($p < 0.00001$; MD - 32.92 days). There were no statistically significant differences in functional outcomes following CDA compared with HS. There was no significant difference in operation time, intra-operative blood loss, or post-operative complications between any of the procedures. The authors concluded that, “The number of included studies was small, the heterogeneity between them was substantial, and the quality of evidence was very low. Large randomized controlled trials are required to provide strong evidence that would enable recommendation of one intervention over another.”

Partial Disc Replacements
As an alternative to the complete replacement of both an injured or diseased disc, researchers are also exploring the possibility of performing a partial disc replacement, also referred to as a nucleus arthroplasty. With this procedure only the nucleus of the disc is replaced; theoretically the annulus and endplates function properly. Nucleus arthroplasty devices are in the earliest stages of development and study. Examples include, but are not limited to: NUBAC™ Disc Arthroplasty System (Pioneer Surgical Technology, Marquette, Michigan) Prosthetic Disc Nucleus PDN (Raymedica, Inc., Bloomington, MN); NeuDisc (Replication Medical, Inc., New Brunswick, NJ); and the Newcleus (Zimmer Spine, Warsaw, IN) (Bertagnoli, 2005b). The devices may be classified as hydrogel, polymer/synthetic or mechanical technologies. Until approval can be obtained through the FDA, and clinical trials are conducted that provide guidance on specific patient selection, or patient net health outcomes, the use of these devices for the treatment of DDD remains investigational.

Professional Societies/Organizations
At the present time, few professional societies or organizations have published a position statement or evidence-based clinical practice guidelines regarding the use of intervertebral lumbar disc prostheses.

The North American Spine Society recently published coverage policy recommendations for cervical artificial disc replacement (NASS, 2015). Within these recommendations NASS acknowledges using evidence based

approach to spine care, in the absence of evidence NASS policies reflect coverage recommendations based on multidisciplinary experience and the expertise of NASS authors. According to the recommended policy cervical disc replacement is indicated for the treatment of radiculopathy related one or two level DDD from C3-C4 to C6-C7 with or without neck pain, unresponsive to medical or nonoperative treatment, and for myelopathy or myeloradiculopathy related to one or two level DDD from C3-C4 to C6-C7 with or without neck pain which is severe enough to warrant surgical intervention. NASS policy does not support artificial disc replacement for three or more levels or in the case of adjacent segment disease. In addition, according to NASS disc replacement adjacent to a previous fusion is a common but off label procedure, and although there is some evidence to lend support to efficacy, hybrid surgery has not yet been rigorously studied and strong evidence based conclusions cannot be made. Regarding lumbar disc replacement, NASS does support lumbar intervertebral disc replacement for a specific subset of individuals as an alternative to lumbar fusion for patients with discogenic low back pain (NASS, 2014).

International Society for the Advancement of Spine Surgery (ISASS) published a position statement on cervical and lumbar disc replacement with the conclusion that ISASS, "strongly supports both cervical and lumbar total disc replacements, including multi-level use as approved by the FDA, as safe and effective treatment alternatives to fusion in appropriately selected patients. FDA study guidelines and labelling regarding inclusion and exclusion criteria should be followed for use, as supported by a strong published database." (Schroeder, et al., 2021)

Use Outside of the US: Companies are continuing to develop new cervical and lumbar artificial disc replacements. Several of these devices are available for use in markets outside of the United States and are being used for single and multi-level disc replacement surgeries. These markets include but are not limited to countries such as Australia, Brazil, China, Europe, and the United Kingdom.

Medicare Coverage Determinations

	Contractor	Policy Name/Number	Revision Effective Date
NCD	National	Lumbar Artificial Disc Replacement (LADR) (150.10).	10/2007
LCD	Palmetto	Cervical Disc Replacement (L38033)	10/2019
LCD	Palmetto	Lumbar Artificial Disc Replacement (L37826)	10/2019

Note: Please review the current Medicare Policy for the most up-to-date information.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

Single-Level Lumbar Disc Arthroplasty

Covered as medically necessary:

CPT®* Codes	Description
22857	Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression), single interspace, lumbar
22862	Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, single interspace; lumbar
22865	Removal of total disc arthroplasty (artificial disc), anterior approach, single interspace; lumbar

Multi-Level Lumbar Total Disc Arthroplasty

Experimental/Investigational/Unproven/Not Covered:

CPT®* Codes	Description
0163T	Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression), each additional interspace, lumbar (List separately in addition to code for primary procedure)
0164T	Removal of total disc arthroplasty, (artificial disc), anterior approach, each additional interspace, lumbar (List separately in addition to code for primary procedure)
0165T	Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, each additional interspace, lumbar (List separately in addition to code for primary procedure)

Single-Level or Two Contiguous Level Cervical Disc Arthroplasty

Covered when medically necessary:

CPT®* Codes	Description
22856	Total disc arthroplasty (artificial disc), anterior approach, including discectomy with end plate preparation (includes osteophytectomy for nerve root or spinal cord decompression and microdissection); single interspace, cervical
22858	Total disc arthroplasty (artificial disc), anterior approach, including discectomy with end plate preparation (includes osteophytectomy for nerve root or spinal cord decompression and microdissection); second level, cervical (List separately in addition to code for primary procedure)
22861	Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, single interspace; cervical
22864	Removal of total disc arthroplasty (artificial disc), anterior approach, single interspace; cervical
0095T	Removal of total disc arthroplasty (artificial disc), anterior approach, each additional interspace, cervical (List separately in addition to code for primary procedure)
0098T	Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, each additional interspace, cervical (List separately in addition to code for primary procedure)

Multi-Level Cervical Total Disc Arthroplasty (i.e., > 2 levels)

Experimental/Investigational/Unproven/Not Covered when used to report total disc arthroplasty (artificial disc), anterior approach, including discectomy with end plate preparation (includes osteophytectomy for nerve root or spinal cord decompression and microdissection), cervical, three or more levels:

CPT®* Codes	Description
22899	Unlisted procedure, spine

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