Artificial Intervertebral Disc

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DESCRIPTION

Artificial intervertebral disc insertion is an emerging technology intended for use in the cervical or lumbar spine to treat back or neck pain due to degenerative disc disease (DDD). DDD is a common cause of neck and/or low back pain. DDD is often defined as discogenic back pain with degeneration of the disc confirmed by individual history and radiographic studies. When conservative treatment for the disease (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], physical therapy) fails to relieve pain, a common surgical approach is spinal fusion. However, by surgically altering the biomechanics of the back, spinal fusion may also cause premature disc degeneration at adjacent levels, which results in increased pain and decreased range of motion (ROM). This is a notable concern for younger individuals. The artificial disc was designed to restore normal disc height, to preserve the spinal flexibility and decrease degeneration of adjacent discs, which can occur as a result of DDD with the goal of avoiding the problems associated with spinal fusion surgery, which include a decreased ROM.

Artificial intervertebral disc insertion is intended to preserve ROM at the operative level once the diseased spinal disc is surgically removed, and an artificial disc is inserted

between the adjoining vertebrae. The artificial disc generally consists of two metal endplates and a central, free component that moves within the disc space during spinal motion. Theoretically, the artificial intervertebral disc insertion procedure is designed to reduce or eliminate back pain and restore disc height while maintaining spinal curvature, flexibility, and load bearing. However, there are concerns that the use of an artificial disc increases the potential for implant failure due to device fracture, dislocation or wear, bone implant interface failure due to subsidence (i.e., sinking or settling in a bone), dislocation migration, or vertebral body fracture, and host response to the implant, which may include adverse events such as osteolysis, heterotopic ossification, and pseudotumor formation.

Cervical Degenerative Disc Disease Treatment

Anterior cervical discectomy and fusion has historically been considered the definitive surgical treatment for symptomatic degenerative disc disease of the cervical spine. The goals of anterior cervical discectomy and fusion are to relieve pressure on the spinal nerves (decompression) and to restore spinal column alignment and stability. Resolution of pain and neurologic symptoms may be expected in 80% to 100% of anterior cervical discectomy and fusion individuals.

Cervical disc arthroplasty is proposed as an alternative to anterior cervical discectomy and fusion for individuals with symptomatic cervical degenerative disc disease. Cervical artificial disc replacement (CADR), also known as cervical total disc replacement or cervical arthroplasty may be indicated for the following conditions:

- Myelopathy or myeloradiculopathy related to central spinal stenosis from one-or two-level(s) of degenerative disease (either herniated disc or spondylotic osteophyte)
- Radiculopathy related to nerve root compression from one-or two-level(s) of degenerative disease (either herniated disc or spondylotic osteophyte) refractory to medical or nonoperative management.

In cervical disc arthroplasty, an artificial disc device is secured in the prepared intervertebral space rather than an interbody cage and/or bone. An anterior plate is not used to stabilize the adjacent vertebrae, and postsurgical external orthosis is usually not required. The cervical disc arthroplasty was designed to maintain anatomic disc space height, normal segmental lordosis, and physiological motion patterns at the index and adjacent cervical levels. The potential to reduce the risk of adjacent-level degenerative disc disease above or below a fusion site has been the major reason driving device development and use. Disc arthroplasty and anterior cervical discectomy and fusion have very similar surgical indications, primarily unremitting pain due to radiculopathy or myelopathy, weakness in the extremities, or paresthesia. However, the chief complaint in cervical disc arthroplasty candidates should be radicular or myelopathic symptoms in the absence of significant spondylosis or spondylolisthesis.

Lumbar Artificial Disc Replacement
Potential candidates for artificial disc replacement have chronic low back pain attributed to DDD, lack of improvement with non-operative treatment, and they do not have any of the contraindications for the procedure, which include multilevel disease, spinal stenosis or spondylolisthesis, scoliosis, previous major spine surgery, neurologic symptoms, and other minor contraindications. These contraindications make artificial disc replacement suitable for a subset of individuals in which fusion is indicated. Individuals who require procedures in addition to fusion such as laminectomy and/or decompression are not candidates for the artificial disc.

Populations
The relevant population of interest is individuals with symptomatic cervical or lumbar degenerative disc disease (DDD).

- Degenerative disc disease (DDD) is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographs.

Interventions
The therapy being considered is artificial intervertebral disc arthroplasty of the cervical or lumbar spine.

- Multiple artificial intervertebral discs are currently marketed in the U.S.

Comparators
The following therapies are currently being used to make decisions about lumbar artificial intervertebral disc.

Relevant comparators are conservative therapy and cervical or lumbar spinal fusion.

Conservative treatment may include physical therapy, pharmacotherapy, epidural steroid injections, and many other modalities. The terms “nonsurgical” and “nonoperative” have also been used to describe conservative treatment. For example, professional societies recommend that surgery for cervical or lumbar spinal stenosis should be considered only after a patient fails to respond to conservative treatment, but there is no consensus about what constitutes an adequate treatment course or duration.

Outcomes
The general outcomes of interest are symptoms, morbid events, functional outcomes (pain scale), quality of life, and treatment-related morbidity.

Cervical Artificial Intervertebral Disc: Systematic Reviews
A number of systematic reviews and meta-analyses have been published.

(2020) Deng et al. completed in a meta-analysis of 9 studies with 48 to 120 months of follow-up. The results revealed that the overall rate of symptomatic adjacent-level disease requiring surgery in the cervical disc replacement group was significantly lower than that of the anterior cervical fusion group at 48–120 months’ follow-up. The subgroup analysis

of different follow-up periods also yielded the same results. The rate of symptomatic adjacent-level disease requiring surgery in the cervical disc replacement group using unrestricted prosthesis was significantly lower than that of the anterior cervical fusion group ($p < 0.001$); however, the cervical disc replacement group using semi-restricted prosthesis showed no statistical difference compared with the fusion group. The current study also has some limitations influencing its validity. Firstly, only 9 articles were included in this meta-analysis. Since most RCTs comparing TDR and ACDF were designed as non-inferiority studies, the number of RCTs focusing on SALDRS was limited. In the future, more relevant RCTs are needed. Secondly, although the included articles were considered to have a low risk of bias, most studies showed a high risk of bias in incomplete outcome data, and a follow-up rate of over 80% in both groups was observed in only two studies. A review of the literature demonstrated that RCTs investigating the SALDRS rates were insufficient. Therefore, more RCTs focusing on SALDRS with longer-term follow-up are warranted. In conclusion: The study showed that the SALDRS rates of the TDR group were significantly lower than those of the ACDF group at 48–120 months' follow-up and at different follow-up periods, and the SALDRS rate of the TDR group with unrestricted prosthesis was significantly lower than that of the ACDF group. However, the SALDRS rate of the TDR group with semi-restricted prosthesis was lower than that of the ACDF group, without statistical difference, which may be attributed to the small number of included studies and patients. Hence, more high-quality RCTs with longer-term follow-up are required to achieve a better comparative analysis of the SALDRS rate after TDR and ACDF.

(2020) Wang et al. examined the long-term safety and efficiency of CDA and ACDF for cervical disc disease. These researchers carried out this trial according to the Cochrane methodology. An extensive search was performed in PubMed, Embase, and Cochrane databases up to June 1, 2019 using the following key words: "anterior cervical fusion", "arthroplasty", "replacement" and "artificial disc". RevMan 5.3 (Cochrane, London, U.K.) was used to analyze data. Safety and efficiency outcome measures included the success rate, functional outcome measures, AEs, ASD, secondary surgery, and patients' satisfaction and recommendation rates. The OR and MD with 95 % CI were used to examine discontinuous and continuous variables, respectively. The statistically significant level was set at $p < 0.05$. A total of 11 RCTs with 3,505 patients (CDA/ACDF: 1,913/1,592) were included in this meta-analysis. Compared with ACDF, CDA achieved significantly higher overall success (2.10, 95 % CI: 1.70 to 2.59), NDI success (1.73, 95 % CI: 1.37 to 2.18), neurological success (1.65, 95 % CI: 1.24 to 2.20), patients' satisfaction (2.14, 95 % CI: 1.50 to 3.05), and patients' recommendation rates (3.23, 95 % CI: 1.79 to 5.80). Functional outcome measures such as VAS neck pain (-5.50, 95 % CI: -8.49 to -2.52) and arm pain (-3.78, 95 % CI: -7.04 to -0.53), the SF-36 physical component score (SF-36 PCS) (1.93, 95 % CI: 0.53 to 3.32), and the SF-36 mental component score (SF-36 MCS) (2.62, 95 % CI: 0.95 to 4.29), revealed superiority in the CDA group. CDA also achieved a significantly lower rate of symptomatic ASD (0.46, 95 % CI: 0.34 to 0.63), total secondary surgery (0.50, 95 % CI: 0.29 to 0.87), secondary surgery at the index level (0.46, 95 % CI: 0.29 to 0.74), and secondary surgery at the adjacent level (0.37, 95 % CI: 0.28 to 0.49). However, no significant difference

was found in radiological success (1.35, 95 % CI: 0.88 to 2.08), NDI score (-2.88, 95 % CI: -5.93 to 0.17), total reported AE (1.14, 95 % CI: 0.92 to 1.42), serious AE (0.89, 95 % CI: 0.71 to 1.11), device/surgery-related AE (0.90, 95 % CI: 0.68 to 1.18), radiological superior ASD (0.63, 95 % CI: 0.28 to 1.43), inferior ASD (0.45, 95 % CI: 0.19 to 1.11]), and work status (1.33, 95 % CI: 0.78 to 2.25). Furthermore, subgroup analysis showed different results between US and non-US groups. The authors concluded that the findings of this study provided further evidence that compared to ACDF, CDA had a higher long-term clinical success rate and better functional outcome measurements; and resulted in less symptomatic ASD and fewer secondary surgeries.

(2020) Zhai et al. conducted a systematic review of overlapping meta-analyses on a total disc replacement compared with fusion for cervical degenerative disc disease. Multiple databases were comprehensively searched for meta-analyses comparing TDR with fusion for treating CDDD. The meta-analyses that comprised only randomized controlled trials (RCTs) were included. Two authors independently assessed the meta-analysis study quality and extracted the data. The Jadad decision algorithm was used to ascertain which meta-analysis studies represented the best evidence. A total of 14 meta-analysis studies were included. All these studies only included RCTs and were determined as Level-II evidence. The authors concluded cervical disc arthroplasty was superior compared to anterior discectomy and fusion for the treatment of symptomatic cervical disc disease.

(2019) Latka et al. conducted a meta-analysis of RCTs on cervical disc arthroplasty to evaluate the safety and long-term efficacy for reducing adjacent segment degeneration. They included 20 publications from 13 RCTs (N=3,656) that reported 24 to 60-month results of 1 or 2-level cervical disc arthroplasty versus anterior cervical discectomy and fusion. visual analog scale for neck pain was lower in patients who had cervical disc arthroplasty (mean difference, -2.30; 95% CI,- 3.72 to -0.87, p=0.002) along with the frequency of dysphagia/dysphonia (odds ratio [OR], 0.69; 95% CI, 0.49 to 0.98; p=0.04). Adjacent segment degeneration was lower with cervical disc arthroplasty compared to anterior cervical discectomy and fusion (OR, 0.33; 95% CI, 0.21 to 0.50; p=0.0001). They concluded a significantly lower probability of ASD reoperations in the CDA cohort after a 60-month or longer follow-up was the most important finding of this study. Despite the moderate quality of this evidence, the pooled data corroborated for the very first time that CDA was efficacious in preventing ASD.

(2016) Hu et al. published a systematic review and meta-analysis of 8 RCTs (l nN=2368) reporting mid-term outcomes (at least 48 months) comparing artificial intervertebral disc arthroplasty with anterior cervical discectomy and fusion. This meta-analysis had the highest AMSTAR rating out of 14 meta-analyses published between 2011 and 2017. All 8 trials included in Hu et al were rated as low risk of bias, despite lack of blinding. Only 2 trials reported on overall success, and 3 reported on Neck Disability Index success. Six trials reported neurologic success data; pooled data favored the cervical disc arthroplasty group to a small degree (relative risk [RR], 1.04; 95% confidence interval (CI), 1.01 to 1.08; p=0.01). Pooled data also showed a significant benefit of cervical disc arthroplasty for secondary procedures at the index level (6 studies) RR, 0.40; 95% CI,

0.28 to 0.58; p<0.001) and at the adjacent level (5 studies) r RR, 0.42; 95% CI, 0.26 to 0.70; p<0.002). These trials and outcome measures are detailed below. In conclusion, this meta-analysis showed that cervical disc arthroplasty was superior over anterior discectomy and fusion for the treatment of symptomatic cervical disc disease in terms of overall success, NDI success, neurological success.

Cervical Artificial Intervertebral Disc: Single-Level Cervical Disc Arthroplasty
There are nine pivotal trials of artificial cervical discs. All of the trials utilized a non-inferiority design that compared cervical disc arthroplasty to the standard of anterior cervical discectomy and fusion with a Food and Drug Administration (FDA)-mandated composite clinical outcome. The studied populations included patients with cervical radiculopathy or myelopathy, and the composite outcome included improvements in disability and neurologic symptoms with an absence of serious adverse events or secondary surgery at the index level. At the 24-month follow-up, all of the trials met non-inferiority and 4 of the 8 trials achieved superiority compared to anterior cervical discectomy and fusion (Table 3). Five of the trials (Prestige ST, ProDisc-C, Bryan, Mobi-C, PCM) have reported follow-up at 3 to 10 years. At 3 to 7 years, trial results are consistent with the continued non-inferiority of cervical disc arthroplasty for clinical outcomes and/or lower cumulative reoperation rates. The pivotal study of the Bryan cervical disc has the longest follow-up at 10 years, with 100 patients per group planned for the post-approval study. Overall success was 81.3% for cervical disc arthroplasty compared to 66.3% for anterior cervical discectomy and fusion (p=0.005) There was a statistically significant difference in the improvement of the neck disability index between the groups (cervical disc arthroplasty: -38.3, anterior cervical discectomy and fusion: -31.1, p=0.01), but there was no significant difference in arm pain or neurologic success between the cervical disc arthroplasty and anterior cervical discectomy and fusion groups. There was not a statistical difference in secondary surgeries, with 9.7% of cervical disc arthroplasty patients and 15.8% of anterior cervical discectomy and fusion patients requiring secondary surgery at either the index or adjacent level (p=0.146). implant/surgery-related serious adverse events, secondary procedure, functional outcomes, patient satisfaction and recommendation, and superior adjacent segment degeneration.

(2021) Phillips et al. completed a prospective, multicenter, concurrently and historically controlled, FDA-approved investigational device exemption clinical trial which evaluated the safety and effectiveness of the novel M6-C compressible artificial cervical disc compared with ACDF for subjects with single-level degenerative cervical radiculopathy. The subjects were with one-level symptomatic degenerative cervical radiculopathy were enrolled and assigned to receive M6-C or ACDF. The results noted both ACDF and M6-C subjects reported significant improvements in patient-reported outcomes at all time points over baseline. Overall SF-36 Physical Component Score and neck and arm pain scores were significantly improved for M6-C as compared to ACDF treatment. CCS and mean Neck Disability Index improvements were similar between M6-C and ACDF. Correspondingly, there were significantly fewer subjects that utilized pain medication or opioids following M6-C treatment at 24 months relative to baseline. Range of motion was

maintained in subjects treated with M6-C. Subsequent surgical interventions, dysphagia rates, and serious adverse events were comparable between groups. The authors concluded M6-C treatment demonstrated both safety and effectiveness for the treatment of degenerative cervical radiculopathy. Treatment with M6-C demonstrated noninferiority for the primary endpoint, indicating a similar ability to achieve CCS at 24 months. However, for the secondary endpoints, M6-C subjects demonstrated significantly improved pain and function compared to ACDF subjects, while maintaining range of motion, improving quality of life, and decreasing analgesic and opioid usage at 2 years postoperatively relative to baseline.

(2015) Gornet et al. completed a study compared the safety and efficacy of treatment with the PRESTIGE LP cervical disc versus a historical control anterior cervical discectomy and fusion (ACDF). METHODS Prospectively collected PRESTIGE LP data from 20 investigational sites were compared with data from 265 historical control ACDF patients in the initial PRESTIGE Cervical Disc IDE study. The 280 investigational patients with single-level cervical disc disease with radiculopathy and/or myelopathy underwent arthroplasty with a low-profile artificial disc. Key safety/efficacy outcome included Neck Disability Index (NDI), Neck and Arm Pain Numerical Rating Scale scores, 36-Item Short Form Health Survey (SF-36) score, work status, disc height, range of motion, adverse events (AEs), additional surgeries, and neurological status. Clinical and radiographic evaluations were completed preoperatively, intraoperatively, and at 1.5, 3, 6, 12, and 24 months postoperatively. Predefined Bayesian statistical methods with noninformative priors were used, along with the propensity score technique for controlling confounding factors. Analysis by independent statisticians confirmed initial statistical findings. The investigational and control groups were mostly similar demographically. There was no significant difference in blood loss (51.0 ml [investigational] vs 57.1 ml [control]) or hospital stay (0.98 days [investigational] vs 0.95 days [control]). The investigational group had a significantly longer operative time (1.49 hours vs 1.38 hours); 95% Bayesian credible interval of the difference was 0.01-0.21 hours. Significant improvements versus preoperative in NDI, neck/arm pain, SF-36, and neurological status were achieved by 1.5 months in both groups and were sustained at 24 months. Patient follow-up at 24 months was 97.1% for the investigational group and 84.0% for the control group. The mean NDI score improvements versus preoperative exceeded 30 points in both groups at 12 and 24 months. SF-36 Mental Component Summary superiority was established (Bayesian probability 0.993). The mean SF-36 PCS scores improved by 14.3 points in the investigational group and by 11.9 points in the control group from baseline to 24 months postoperatively. Neurological success at 24 months was 93.5% in the investigational group and 83.5% in the control group (probability of superiority ~ 1.00). At 24 months, 12.1% of investigational and 15.5% of control patients had an AE classified as device or device/surgical procedure related; 14 (5.0%) investigational and 21 (7.9%) control patients had a second surgery at the index level. The median return-to-work time for the investigational group was 40 days compared with 60 days for the control group ($p = 0.020$ after adjusting for preoperative work status and propensity score). Following implantation of the PRESTIGE LP device, the mean angular motion was maintained at 12 months (7.9°) and 24 months (7.5°). At 24

months, 90.0% of investigational and 87.7% of control patients were satisfied with the results of surgery. PRESTIGE LP superiority on overall success (without disc height success), a composite safety/efficacy end point, was strongly supported with 0.994 Bayesian probability. The authors concluded this device maintains mean postoperative segmental motion while providing the potential for biomechanical stability. Investigational patients reported significantly improved clinical outcomes compared with baseline, at least noninferior to ACDF, up to 24 months after surgery.

(2014) Hisey et al. completed a prospective, randomized comparison of cervical total disk replacement versus anterior cervical fusion with results at 48 months follow-up. Patients from 23 centers were randomized in a 2:1 ratio with 164 receiving the investigational device (Mobi-C Cervical Disc Prosthesis) and 81 receiving ACDF using an anterior plate and allograft. Patients were evaluated preoperatively and 6 weeks, 3, 6, 12, 18, 24, 36, and 48 months postoperatively. Outcome assessments included a composite success score, Neck Disability Index, visual analog scales assessing neck and arm pain, patient satisfaction, major complications, subsequent surgery, segmental range of motion, and adjacent-segment degeneration. The composite success rate was similar in the 2 groups at 48-month follow-up. Mean Neck Disability Index, visual analog scale, and SF-12 scores were significantly improved in early follow-up in both groups with improvements maintained throughout 48 months. On some measures, TDR had significantly greater improvement during early follow-up. At no follow-up were TDR scores significantly worse than ACDF scores. Subsequent surgery rate was significantly higher for ACDF compared with TDR (9.9% vs. 3.0%, $P<0.05$). Range of motion was maintained with TDR having a mean baseline value of 8 degrees compared with 10 degrees at 48 months. The incidence of adjacent-segment degeneration was significantly higher with ACDF at inferior and superior segments compared with TDR (inferior: 50% vs. 30%, $P<0.025$; superior: 53% vs. 34%, $P<0.025$). The authors concluded significant improvements were observed in pain and function. TDR patients-maintained motion and had significantly lower rates of reoperation and adjacent-segment degeneration compared with ACDF. This study supports the safety and efficacy of TDR in appropriately selected patients.

(2013) Phillips et al. completed a prospective, multicenter, randomized clinical trial on the long-term outcomes of the US FDA IDE comparing PCM cervical disc arthroplasty with anterior cervical discectomy and fusion. Patients with single-level cervical spondylosis and radiculopathy with or without myelopathy unresponsive to nonoperative treatment were enrolled. The per protocol patient sample at 5 years included 293 patients (163 PCM, 130 ACDF). Adverse events and secondary surgical procedures are reported on the cohorts through current follow-up, which include 110 patients (68 PCM, 42 ACDF) at 7 years. The results noted at 5 years postoperative, all patient-reported outcomes-neck and arm pain visual analogue scale score, neck disability index, and general health (36-Item Short Form Health Survey physical and mental component scores: physical component summary, mental component summary)-were significantly improved from baselines in both groups, and mean scores were significantly better in the PCM group for neck disability index ($P=0.001$), neck pain ($P=0.002$), general health ($P_{physical\ component\ summary}=0.014$; $P_{mental\ component\ summary}=0.004$), and

patient satisfaction (P=0.005). PCM patients trended toward fewer 2- to 7-year device-related serious adverse events (1/214, 0.5% PCM; 2/190, 1.1% ACDF) and secondary surgical procedures (7/211, 3.3% PCM; 14/290, 7.6% ACDF). Adjacent-level degeneration was radiographically more frequent after ACDF (33.1% PCM, 50.9% ACDF; P=0.006) and was the primary indication for the increase in late-term secondary surgical procedures after ACDF. The author's concluded the long-term results show good clinical outcomes after ACDF and PCM arthroplasty. PCM patients showed greater improvement in neck disability index and neck pain scores with a lower rate of radiographical adjacent-level degeneration and a trend toward fewer secondary surgical procedures. These data support PCM arthroplasty to be a viable and sustainable alternative to ACDF.

(2013) Vaccaro et al. completed a prospective, multicenter, randomized and controlled investigational device exemption (IDE) clinical trial on the clinical outcome with selectively constrained SECURE-C cervical arthroplasty, the two-year results. A total of 380 patients from 18 investigational sites were prospectively enrolled in the study. Patients were randomized, treated surgically, and evaluated postoperatively at 6 weeks, 3 months, 6 months, 12 months, and 24 months. Clinical outcomes include overall success, visual analogue scale pain (right arm, left arm, and neck), neck disability index, neurological status, Short Form 36 (SF-36) Health Status Survey questionnaires, range of motion, and adverse events. Bayesian statistical methods were used to analyze the outcomes. Overall success results demonstrated statistical superiority of the randomized SECURE-C group compared with the randomized ACDF group at 24 months, with a posterior probability of 100% using the protocol-specified criteria and 98.1% using Food and Drug Administration-defined criteria. At 24 months postoperatively, SECURE-C demonstrated clinically significant improvement in pain and function in terms of neck disability index, visual analogue scale, and 36-Item Short Form Health Survey. At 24 months, the percentage of patients experiencing secondary surgical interventions at the index level was statistically lower for the SECURE-C group (2.5%) than the ACDF group (9.7%). At 24 months, 84.6% of as-treated SECURE-C patients were range-of-motion successes. Satisfaction was high among SECURE-C patients. The authors concluded selectively constrained SECURE-C Cervical Artificial Disc is as safe and effective as the standard of care, an anterior cervical discectomy and fusion. SECURE-C is statistically superior in terms of overall success, index-level subsequent surgical procedures, and patient satisfaction, making it an attractive surgical option for patients with symptomatic cervical disc disease.

Section Summary: Single-Level Cervical Disc Arthroplasty
At 2-year follow-up, the pivotal trials of 9 artificial cervical discs met non-inferiority criteria, with 5 achieving statistical superiority compared to anterior cervical discectomy and fusion. Mid-term outcomes have been reported on 5 devices. At 3 to 7 years, trial results have been consistent with the continued non-inferiority of cervical disc arthroplasty for clinical outcomes and/or lower cumulative reoperation rates. Ten-year follow-up for the Bryan Cervical Disc continues to support the safety and efficacy of cervical disc arthroplasty. Longer-term results for other discs are expected, given the

FDA requirement for 7-year post approval studies of the safety and function of the devices, and 5-to-10-year enhanced surveillance to characterize more fully adverse events in a broader patient population. Serious adverse events appear to be uncommon. Heterotopic ossification can occur in a substantial proportion of spinal segments with artificial intervertebral discs but does not appear to lead to a decline in clinical outcomes.

Cervical Artificial Intervertebral Disc: Two-Level Cervical Disc Arthroplasty
(2017) Radcliff et al. completed a randomized, prospective, multicenter clinical trial with seven-year follow-up of a long-term evaluation of cervical disc arthroplasty with Mobi-C Cervical Disc. It was a continuation of a prospective, multicenter, randomized, US FDA IDE clinical trial comparing cervical TDR with the Mobi-C© Cervical Disc versus ACDF through 7 years follow-up. Inclusion criteria included a diagnosis of symptomatic cervical degenerative disc disease at one or two cervical levels. TDR patients were treated using a Mobi-C© artificial disc (Zimmer Biomet, Austin TX, USA). ACDF with allograft and anterior plate was used as a control treatment. Outcome measures were collected preoperatively and postoperatively at 6 weeks, at 3, 6, 12, 18 months, annually through 60 months, and at 84 months. Measured outcomes included Overall success, Neck Disability Index (NDI), VAS neck and arm pain, segmental range of motion (ROM), patient satisfaction, SF-12 MCS/PCS, major complications, and subsequent surgery rate. The primary endpoint was an FDA composite definition of success comprising clinical improvement and an absence of major complications and secondary surgery events. A total of 599 patients were enrolled and treated, with 164 treated with one-level TDR, 225 treated with two-level TDR, 81 treated with one-level ACDF, and 105 treated with two-level ACDF. At seven years, follow-up rates ranged from 73.5% to 84.4% (overall 80.2%). The overall success rates of two-level TDR and ACDF patients were 60.8% and 34.2%, respectively ($p<0.0001$). The overall success rates of one level TDR and ACDF patients were 55.2% and 50%, respectively ($p>0.05$). Both the single- and two-level TDR and ACDF groups showed significant improvement from baseline NDI scores, VAS neck and arm pain scores, and SF-12 MCS/PCS scores ($p<0.0001$). In the single level cohort, there was an increased percentage of TDR patients who reported themselves as "very satisfied" (TDR 90.9% vs ACDF 77.8%; $p= 0.028$). There was a lower rate of adjacent level secondary surgery in the single level TDR patients (3.7%) versus the ACDF patients (13.6%; $p = 0.007$). In the two-level TDR group, the NDI success rate was significantly greater in the TDR group (TDR: 79.0% vs. ACDF: 58.0%; $p=0.001$). There was significantly more improvement in NDI change score at 7 years in the TDR patients versus ACDF. The TDR group had a significantly higher rate of patients who were "very satisfied" with their treatment compared to the ACDF group (TDR: 85.9% vs. ACDF: 73.9%). The rate of subsequent surgery at the index level was significantly lower in the TDR group compared to the ACDF group (TDR: 4.4% vs. ACDF: 16.2%; $p=0.001$). The rate of adjacent level secondary surgery was significantly lower in the two-level TDR (4.4%) patients compared to the ACDF (11.3%; $p=0.03$) patients. In both single- and two-level cohorts, the percentage of patients with worse NDI (2.5%-3.8% of two-level surgeries and 1.2%-2.5% of single level surgeries) or worse neck pain (5%-6.8% of the two-level surgeries and 1.3% - 3.8% of the single level surgeries) was strikingly low in both groups but trended lower in the TDR patients. The

authors concluded at seven years, the composite success analysis demonstrated clinical superiority of two-level TDR over ACDF and non-inferiority of single level TDR versus ACDF. There were lower rates of secondary surgery and higher adjacent level disc survivorship in both groups. Both surgeries were remarkably effective in alleviating pain relative to baseline and the rate of patients with worse disability or neck pain was surprisingly low. Overall, greater than 95% of patients (from both groups) who underwent TDR and 88% of patients who underwent ACDF were "very satisfied" at seven years. The differences in clinical effectiveness of TDR versus ACDF becomes more apparent as treatment increases from one-to-two-levels, indicating a significant benefit for TDR over ACDF for two-level procedures.

(2016) Radcliff et al. completed a randomized controlled trial. The purpose of this study was to report the outcome of a study of 2-level cervical total disc replacement (Mobi-C) versus anterior cervical discectomy and fusion (ACDF). Although the long-term outcome of single-level disc replacement has been extensively described, there have not been previous reports of the 5-year outcome of 2-level cervical disc replacement. METHODS This study reports the 5-year results of a prospective, randomized US FDA investigational device exemption (IDE) study conducted at 24 centers in patients with 2-level, contiguous, cervical spondylosis. Clinical outcomes at up to 60 months were evaluated, including validated outcome measures, incidence of reoperation, and adverse events. The complete study data and methodology were critically reviewed by 3 independent surgeon authors without affiliation with the IDE study or financial or institutional bias toward the study sponsor. A total of 225 patients received the Mobi-C cervical total disc replacement device and 105 patients received ACDF. The Mobi-C and ACDF follow-up rates were 90.7% and 86.7%, respectively ($p = 0.39$), at 60 months. There was significant improvement in all outcome scores relative to baseline at all time points. The Mobi-C patients had significantly more improvement than ACDF patients in terms of Neck Disability Index score, SF-12 Physical Component Summary, and overall satisfaction with treatment at 60 months. The reoperation rate was significantly lower with Mobi-C (4%) versus ACDF (16%). There were no significant differences in the adverse event rate between groups. The authors concluded both cervical total disc replacement and ACDF significantly improved general and disease-specific measures compared with baseline. However, there was significantly greater improvement in general and disease-specific outcome measures and a lower rate of reoperation in the 2-level disc replacement patients versus ACDF control patients. Clinical trial registration no. NCT00389597 (clinicaltrials.gov).

(2016) The Prestige LP™ received FDA approval for implantation at 2 levels after a multicenter, non-inferiority trial. Overall success was achieved in 81.4% of Prestige LP patients and 69.4% of anterior cervical discectomy and fusion controls, meeting both non-inferiority and superiority margin, with a posterior probability of near 100% and 99.3%. The difference in success rates between the Prestige LP™ and anterior cervical discectomy and fusion patients achieved at 24 months was maintained through 10 years.

(2015) Bae et al. completed a prospective, randomized, post hoc analysis of data from the pivotal 1- and 2-level Mobi-C. and fusion [ACDF]) at 24 sites. Ultimately, 164 patients received TDR at 1 level and 225 patients received TDR at 2 contiguous levels. An additional 24 patients (15 one-level, 9 two-level) were treated with TDR as training cases. Outcome measures included neck disability index, visual analogue scale neck and arm pain, Short Form 12-item Health Survey (SF-12) Mental Composite Score (MCS) and Physical Composite Score (PCS), range of motion, major complication rates, and secondary surgery rates. Patients received follow-up examinations at regular intervals through 4 years after surgery. Preoperative characteristics were statistically similar for the 1- and 2-level patient groups. Four-year follow-up rates were 83.1% (1-level) and 89.0% (2-level). There was no statistically significant difference between 1- and 2-level TDR groups for all clinical outcome measures. Both TDR groups experienced significant improvement at each follow-up when compared with preoperative scores. One case of migration was reported in the 2-level TDR group. The authors concluded a 4-year post hoc comparison of 1- and 2-level TDR patients concurrently enrolled in a 24-center, Food and Drug Administration Investigation Device Exemption clinical trial indicated no statistical differences between groups in clinical outcomes, overall complication rates, and subsequent surgery rates.

(2013) Davis et al. completed a randomized controlled trial with two and 4-year results from the 2-level Mobi-C investigational device exemption trial. A total of 225 patients received the Mobi-C TDR device and 105 patients received ACDF. At 24 months only 3.0% of patients were lost to follow-up. On average, patients in both groups showed significant improvements in Neck Disability Index (NDI) score, visual analog scale (VAS) neck pain score, and VAS arm pain score from preoperative baseline to each time point. However, the TDR patients experienced significantly greater improvement than ACDF patients in NDI score at all time points and significantly greater improvement in VAS neck pain score at 6 weeks, and at 3, 6, and 12 months postoperatively. On average, patients in the TDR group also maintained preoperative segmental range of motion at both treated segments immediately postoperatively and throughout the study period of 24 months. The reoperation rate was significantly higher in the ACDF group at 11.4% compared with 3.1% for the TDR group. Furthermore, at 24 months TDR demonstrated statistical superiority over ACDF based on overall study success rates.
In conclusion, the results of this study represent the first available Level I clinical evidence in support of cervical arthroplasty at 2 contiguous levels of the cervical spine using the Mobi-C cervical artificial disc. These results continue to support the use of cervical arthroplasty in general, but specifically demonstrate the advantages of 2-level arthroplasty over 2-level ACDF. Clinical trial registration no.: NCT00389597 (ClinicalTrials.gov).

(2011) Huppert et al. compared outcomes between single-level (n=175) and multilevel (2-4 levels, n=56) cervical disc arthroplasty with the Mobi-C device in a prospective multicenter study from Europe. At 2 years, there were no significant differences between groups for overall success, radicular and cervical visual analog scale scores, Neck Disability Index scores, and range of motion There was a trend for more patients in the

single-level group than in the 2-level group to return to work (70% vs 46%) and for the return to work to occur sooner (4.8 months vs 7.5 months), respectively. The authors concluded multi-level DDD with radiculopathy and/or myelopathy is a challenging indication to treat surgically in the cervical spine. The extensive use of fusion and the documented outcomes have shown the limitations of fusion treatment option, including revision surgeries, major complications, and the effects on the adjacent segment degeneration. Leaning on the increasing accumulation of favorable results with CDR all over the world, this alternative treatment modality continues to be validated through clinical studies. The results of the second study in time comparing the clinical and radiological outcomes of single- versus multi-level disc replacement. No significant difference was observed between the two groups regarding the major clinical outcomes. The number of revision surgery at the index levels was very low in the multi-level group. Further studies are needed to know more about the impact of multi-level CDR, especially on the adjacent segments, but these results are encouraging and lend credibility to the technique in selected indications of multi-level cervical DDD.

Cervical Artificial Intervertebral Disc: Section Summary: Two-Level Cervical Disc Arthroplasty

The FDA approval for the Prestige LP™ disc at 2 levels was based on superiority to 2-level ACDF at 2-year follow-up. At present, over 80% of patients have reached 3-year follow-up, and 85% of expected patients have reached 10-year follow-up. The difference in overall success rates at 2 years has been maintained at 10 years. Secondary outcome measures showed the superiority of cervical disc arthroplasty over anterior cervical discectomy and fusion.

The first artificial cervical disc approved for 2 levels (Mobi-C) was found to be noninferior to anterior cervical discectomy and fusion in the investigational device exemption trial. Superiority to anterior cervical discectomy and fusion was achieved for Neck Disability Index scores, Neck Disability Index success rates, and overall success composite outcome. Reoperation rates were significantly lower in the Mobi-C group. At 5, and 7 years, trial results were consistent with the continued superiority of 2-level cervical disc arthroplasty for clinical outcomes and lower cumulative reoperation rates. Although a third of patients who received the Mobi-C had clinically significant heterotopic ossification, adjacent-segment degeneration with Mobi-C was found in a lower percentage of patients than in anterior cervical discectomy and fusion patients.

Cervical Artificial Intervertebral Disc: Hybrid Surgery for Multi-Level Cervical Degenerative Disc Disease

(2020) Zhang et al. examined the outcomes and reliability of HS versus ACDF for the treatment of multi-level cervical spondylosis and disc diseases. Hybrid surgery, combining CDA with fusion, is a novel treatment to MLCDDD in recent years. However, the effect and reliability of HS are still unclear compared with ACDF. These investigators examined the studies of HS versus ACDF in patients with multi-level cervical disease -- electronic databases (Medline, Embase, PubMed, Cochrane library, and Cochrane Central Register of Controlled Trials) were searched. Studies were

included when they compared HS with ACDF and reported at least one of the following outcomes: functionality, neck pain, arm pain, cervical ROM, QOL, and incidence of complications. No language restrictions were used. Two authors independently assessed the methodological quality of included studies and extracted the relevant data. A total of 7 clinical controlled trials were included in this study; 2 were prospective and the remaining 5 were retrospective. The results of the meta-analysis indicated that HS achieved better recovery of NDI score ($p = 0.038$) and similar recovery of VAS score ($p = 0.058$) compared with ACDF at 2 years follow-up. Moreover, the total cervical ROM (C2 to C7) following HS was preserved significantly more than the cervical ROM after ACDF ($p = 0.000$) at 2 years follow-up. Notably, the compensatory increase of the ROM of superior and inferior adjacent segments was significant in ACDF groups at 2-year follow-up ($p < 0.01$), compared with HS. The results demonstrated that HS provided equivalent outcomes and functional recovery for cervical disc diseases, and significantly better preservation of cervical ROM compared with ACDF in 2-year follow-up, suggesting that the HS is an effective alternative invention for the treatment of multi-level cervical spondylosis to preserve cervical ROM and reduce the risk of adjacent disc degeneration.

(2019) Xu et al. compared the cervical sagittal balance and surgical outcomes between ACDF and hybrid decompression and fusion (HDF; 1-level corpectomy combined with 1-level discectomy) for consecutive 3-level cervical spondylotic myelopathy (CSM). From January 2013 to June 2016, a total of 82 patients with 3-level CSM who underwent ACDF ($n = 40$) and HDF ($n = 42$) were retrospectively reviewed. Peri-operative parameters, clinical outcomes, and radiologic sagittal alignment were analyzed and compared. Patients were followed-up for 35.5 ± 6.5 months (range of 25 to 53 months). All patients had achieved significant improvement in NDI and JOA scores following operation, with similar clinical outcomes between both groups ($p > 0.05$). In the ACDF group, 2 patients were found with axial symptoms, and 1 with hoarseness. In the HDF group, 5 patients were found with axial symptoms, 1 with hoarseness, 1 with dysphagia, and 1 with pseudarthrosis. The ACDF group had less operation time and bleeding compared with the HDF group ($p < 0.05$). The restoration of segmental and C2 to C7 lordosis were significantly greater in the ACDF group than the HDF group ($p < 0.05$). The C2 to C7 sagittal vertical axis and T1 slope minus C2 to C7 lordosis decreased in the ACDF group at final follow-up ($p < 0.05$); however, there was no obvious change in those of the HDF group ($p > 0.05$). The authors concluded that both ACDF and HDF were safe and effective for the treatment of 3-level CSM; ACDF showed superiority to HDF in terms of less blood loss, shorter operation time, and better post-operative sagittal balance.

(2018) Laratta et al. noted DDD and spondylosis resulting in radiculopathy and retrodiscal myelopathy are among the most frequently encountered cervical spinal disorders. Traditionally, ACDF has successfully achieved neural decompression and restored intradiscal height in these conditions. Unfortunately, non-union and iatrogenic adjacent segment pathology associated with fusion procedures in the cervical spine has led to an interest in motion-preserving procedures; CDA was developed in hopes of

preserving cervical biomechanics while mitigating the complications associated with ACDF. Through a systematic review of both published and ongoing studies on single- and multi-level CDA, and HS, these investigators provided evidence on their safety and efficacy in the treatment of various cervical pathologies. A systematic search of several large databases, including Cochrane Central, PubMed, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry was conducted to identify published studies and ongoing clinical trials on CDA and HS. Among the relevant studies reviewed, 3 were RCTs, 2 systematic reviews, as well as multiple prospective case series, biomechanical studies, and meta-analyses. The authors concluded that over the past 10 years, multiple high-quality studies had shown that single-level CDA can offer equivalent clinical outcomes with a reduction in secondary procedures and total cost when compared to ACDF. However, more recently there has been an increasing prevalence of 2-level CDA and HS. Although the data regarding these multi-level procedures is less robust, it appeared that they may be as effective as their single-level counterparts.

(2018) Xiong et al. compared the mid-term outcomes of HS and ACDF for the treatment of contiguous 2-segment CDDD. From 2009 to 2012, a total of 42 patients who underwent HS (n = 20) or ACDF (n = 22) surgery for symptomatic contiguous 2-level CDDD were included. Clinical and radiological records, including JOA, NDI, VAS, local cervical lordosis, and ROM, were reviewed retrospectively. Complications were recorded and evaluated. Mean follow-up was 77.25 and 79.68 months in HS group and ACDF group, respectively ($p > 0.05$). Both in HS group and ACDF group, significant improvement for the mean JOA, NDI, and VAS scores was found at 2-week post-operation and at the last follow-up ($p < 0.05$). However, there were no significant differences between the 2 groups ($p > 0.05$). At the last follow-up, the ROM of superior adjacent segments in ACDF group was significantly larger than HS group ($p < 0.05$), while the ROM of C2 to C7 was significantly smaller ($p < 0.05$). In the HS group, 2 (10 %) sagittal wedge deformities, 1 (5 %) heterotopic ossification, and 1 (5 %) anterior migration of the Bryan disc prosthesis were found. No symptomatic ASD occurred in the 2 groups. The authors concluded that HS appeared to be an acceptable option in the management of contiguous 2-segment CDDD. It yielded similar mid-term clinical improvement to ACDF, and demonstrated better preservation of cervical ROM. The incidence of post-operative sagittal wedge deformity was low; however, it could significantly reduce the cervical lordosis.

(2017) Lu et al. stated the traditional surgical approach to treat MLCDDD has been ACDF. There has been recent development of other surgical approaches to further improve clinical outcomes. Collectively, when elements of these different approaches are combined in surgery, it is known as HS that remains a novel therapeutic option. These investigators carried out a systematic review and meta-analysis to compare the outcomes of HS versus ACDF for the treatment of MLCDDD. Relevant articles were identified from 6 electronic data-bases from their inception to January 2016. From 8 relevant studies identified, 169 patients undergoing HS were compared with 193 ACDF procedures. Operative time was greater after HS by 42 mins ($p < 0.00001$), with less

intra-operative blood loss by 26 ml ($p < 0.00001$) and shorter return-to-work by 32 days ($p < 0.00001$). In terms of clinical outcomes, HS was associated with greater C2 to C7 ROM preservation ($p < 0.00001$) and less functional impairment ($p = 0.008$) after surgery compared to ACDF. There was no significant difference between HS and ACDF with respect to post-operative pain ($p = 0.12$). The post-operative course following HS was not significantly different to ACDF in terms of length of stay ($p = 0.24$) and post-operative complication rates ($p = 0.18$). The authors concluded that HS is a novel surgical approach to treat MLCDDD, associated with a greater operative time, less intra-operative blood loss and comparable if not superior clinical outcomes compared to ACDF.

(2015) Grasso stated that although several studies have established the safety and efficacy of CDA as compared to ACDF, few studies have examined the role of HS that incorporates ACDF and CDA techniques in multi-level cervical DDD (MLCDDD). This prospective study enrolled patients with MLCDDD who underwent HS. A total of 20 consecutive patients who underwent HS were compared with patients who underwent ACDF and CDA at the same level of surgery. Patients were followed-up for more than 2 years. Intra-operative parameters, clinical features and outcome scores were recorded. Radiological assessments included overall ROM, disc height (DHI), and changes in adjacent disc spaces. Duration of surgery was significantly shorter for ACDF compared with HS and CDA ($p < 0.05$). The VAS, SF-36, JOA, and NDI scores improved significantly after surgery in all the patients without significant differences among the groups. Cervical ROM increased significantly in CDA and HS groups as compared with ACDF-treated patients ($p < 0.05$). The mean DHI at the treated level was significantly restored after surgery in all the groups. The HS group returned to work faster (30 days) when compared with both ACDF (62 days) and CDA (65 days) ($p < 0.05$). The authors concluded that HS was an effective, reliable, and safe procedure for the treatment MLCDDD. Such a surgical construct was comparable to ACDF and CDA in terms of safety and feasibility.

(2015) Tian et al. completed a meta-analysis, compared HS and ACDF for MLCDDD. Systematic searches of all published studies through March 2015 were identified from Cochrane Library, Medline, PubMed, Embase, ScienceDirect, CNKI, WanFang DATA and CQVIP; RCTs and non-RCTs involving HS and ACDF for MLCDDD were included. All literature was searched and evaluated by 2 independent reviewers according to the standard of Cochrane systematic review. Data of functional and radiological outcomes in the 2 groups were pooled, which was then analyzed by RevMan 5.2 software; 1 RCT and 4 non-RCTs entailing 160 patients met the inclusion criteria. Meta-analysis revealed significant differences in blood loss ($p = 0.005$), post-operative C2 to C7 ROM ($p = 0.002$), ROM of superior adjacent segment ($p < 0.00001$) and ROM of inferior adjacent segment ($p = 0.0007$) between the HS group and the ACDF group. No significant differences were found regarding operation time ($p = 0.75$), post-operative VAS ($p = 0.18$) and complications ($p = 0.73$) between the 2 groups. The authors concluded that HS demonstrated excellent clinical efficacy and radiological results; post-

operative C2 to C7 ROM was closer to the physiological status. No decrease in the ROM of the adjacent segment was noted in the HS group.

(2014) Jia et al. noted that the optimal surgical technique for multi-level cervical DDD remains controversial. Hybrid surgery (HS) incorporating ACDF and CDR is increasingly performed for cervical DDD. These researchers examined the biomechanical and clinical evidence available for HS and provided a systematic review of current understanding of HS. This systematic review was undertaken by following the PRISMA Statement. Multiple databases and online registers of clinical trials were searched up to February 2014. The biomechanical and clinical studies on HS for cervical DDD written in English were included; 2 authors independently assessed methodological quality and extracted data. A total of 15 studies including 8 biomechanical studies and 7 clinical studies were identified. The biomechanical studies showed that HS was beneficial to motion preservation of the operative levels and revealed less adverse effect on adjacent segments. All clinical studies demonstrated improvement in validated functional scores after HS. Segment motion and immobilization were achieved at the arthroplasty level and arthrodesis level, respectively. Post-operative assessments and complication rate were similar or in favor of HS when comparing with ACDF or CDR. The authors concluded that there is a paucity of high-quality evidence for HS. These researchers stated that HS may be a safe and effective technique to benefit a select group of multi-level cervical DDD.

Summary of Evidence: Cervical Artificial Intervertebral Disc: Hybrid Surgery for Multi-Level Cervical Degenerative Disc Disease
Artificial disc replacement at one level combined with spinal fusion surgery at another level (adjacent or non-adjacent) is referred to as hybrid surgery. Based on the current peer reviewed medical literature there are few clinical trials to support improved net health outcomes and patient selection criteria has not been firmly established. Further randomized clinical trials are needed to determine the safety and efficacy to include patient selection criteria. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Cervical Artificial Intervertebral Disc: Registry Data
(2018) MacDowall et al. compared 5- year outcomes of cervical disc arthroplasty and anterior cervical discectomy and fusion from the Swedish Spine Registry. Using propensity matching, the investigators identified 185 patients in each group who had cervical degenerative disc disease and radiculopathy. The primary outcome was the Neck Disability Index, with a minimum clinically important difference of > 15%. Scores on the Neck Disability Index were halved in both groups, but there was no significant difference (3.0%; 95% CI, -8.4 to 2.4; p=0.28) between the groups. There were also no differences between the groups in EuroQol-5 Dimensions or in pain scores for the neck and arm.

(2016) Staub et al. evaluated the clinical effectiveness of cervical disc arthroplasty for 987 patients in the Spine Tango registry.44, The primary outcome measures were the neck and arm pain relief and the Core Outcome Measures Index. One analysis evaluated

outcomes from a matched pair of patients (190 pairs) who met the selection criteria of published RCTs. With an average follow-up of 17 months, there were small but statistically significant differences in outcomes between cervical disc arthroplasty and anterior cervical discectomy and fusion. The mean group differences on a 10-point scale for both pain measures were 0.6 points in postoperative neck pain (p=0.04) and 0.7 points in arm pain (p=0.02); mean Core Outcome Measures Index score difference was 0.8 points (p=0.01). Change scores did not differ significantly. The probability of being a responder (2-point change) was significantly better in the cervical disc arthroplasty group than in the anterior cervical discectomy and fusion group for arm pain relief (78.4% vs 67.4%, p=0.02) and Core Outcome Measures Index score (81.6% vs 67.9%, p<0.01) but not neck pain relief (62.1% vs 57.9%, p-value not significant), respectively.

For patients who would have been excluded from the RCTs, most commonly due to an age greater than 60 years or spondylosis, there were no significant differences in clinical outcomes between cervical disc arthroplasty and anterior cervical discectomy and fusion. A third analysis compared outcomes of cervical disc arthroplasty with anterior cervical discectomy and fusion in patients who had a follow-up of more than 2 years (mean, 55.0 months; range, 27.0-76.5 months). After controlling for patient age, patients treated with cervical disc arthroplasty had significantly higher responder rates for arm pain relief (80.0%) compared with patients treated with anterior cervical discectomy and fusion (64.9%; p=0.05), with no significant difference in responder rates between groups for neck pain relief or Core Outcome Measures Index. Rates of adjacent-level degeneration and secondary surgeries were not assessed.

Limitations of registry studies include the possibility of selection bias, which can be reduced by propensity matching.

Cervical Artificial Intervertebral Disc: Adverse Events

Heterotopic ossification appears to be common with cervical disc arthroplasty but there is no evidence of a large impact on clinical outcomes. A meta-analysis by Chen et al (2012) evaluating rates of heterotopic ossification (McAfee grade 3-4) after cervical disc arthroplasty included 8 studies (total n=617 patients). The pooled prevalence of any heterotopic ossification was 58.2% at 24 months after cervical disc arthroplasty and the pooled prevalence of advanced heterotopic ossification was 16.7% after 24 months.

(2018) Nunley et al. evaluated the effect of heterotopic ossification on clinical outcomes. Heterotopic ossification was radiographically graded for 164 1-level and 225 2-level cervical disc arthroplasty patients from the Mobi-C pivotal trials and correlated with clinical outcomes. At 7 years, clinically relevant (grade 3 or 4) heterotopic ossification that affects range of motion was present in 28.7% of 1-level patients and 37.4% of 2-level patients. Patients were divided into non-clinically relevant heterotopic ossification and clinically relevant (motion restricting) heterotopic ossification. Arm pain and 12-Item Short Form Health Survey scores were not significantly different between the groups. There was an interaction between heterotopic ossification and time for the Neck Disability Index (p=0.04), with a statistically significant difference between groups of 4.0

beginning at 48 months. There was also a statistical interaction between heterotopic ossification and visual analog scale neck pain, with a difference of 5 to 8 mm out of 100. The clinical significance of these differences is uncertain.

Summary of Evidence: Cervical Artificial Disc Replacement
For individuals who have cervical radicular pain or myelopathy who receive single-level cervical disc arthroplasty, the evidence includes RCTs and meta-analyses of RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity. At 2-year follow-up, trials of all artificial cervical discs met non-inferiority criteria compared to anterior cervical discectomy and fusion. Mid-term outcomes have been reported on 5 devices (Prestige ST, ProDisc-C, Bryan, Mobi-C, PCM [Porous Coated Motion]). At 4 to 5 years, the trial results have been consistent with the continued non-inferiority of cervical disc arthroplasty for clinical outcomes and lower cumulative reoperation rates. Seven-year follow-up of the Prestige, ProDisc-C, and Mobi-C pivotal trials continue to show lower secondary surgery rates, although this is not a consistent finding in other reports. Serious adverse events appear to be uncommon. Heterotopic ossification can occur in a substantial proportion of spinal segments with artificial intervertebral discs but does not appear to lead to a decline in clinical outcomes. The evidence to date shows outcomes that are at least as good as the standard treatment of anterior cervical discectomy and fusion. There have been no safety signals with discs approved by the FDA for single-level cervical disc arthroplasty. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cervical radicular pain or myelopathy who receive 2-level cervical disc arthroplasty of the cervical spine, the evidence includes RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity. FDA approval for the Prestige LP™ was based on superiority to 2-level anterior cervical discectomy and fusion in overall success at 2 years. The increase in overall success rates at 2 years has been maintained for those patients who have reached the 10-year follow-up. At 2- and 4-year follow-ups, the first artificial cervical disc approved for 2 levels (Mobi-C) was found to be superior to anterior cervical discectomy and fusion for Neck Disability Index scores, Neck Disability Index success rates, reoperation rates, and overall success composite outcome. At 5 years, trial results were consistent with the continued superiority of 2-level cervical disc arthroplasty for clinical outcomes and lower cumulative reoperation rates. Adjacent-segment degeneration with Mobi-C was found in a significantly lower percentage of patients compared with 2-level anterior cervical discectomy and fusion patients. Based on this evidence, it can be concluded that 2-level cervical disc arthroplasty with either of these FDA-approved discs is at least as beneficial as the established alternative. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Lumbar Artificial Intervertebral Disc

Lumbar Artificial Intervertebral Disc: Randomized Controlled Trials
Three RCTs have compared the treatment of degenerative disc disease using lumbar fusion with artificial lumbar intervertebral discs currently available in the United States. They include the pivGotal trials for the ProDisc-L and activL discs, and a U.S. Food and Drug Administration (FDA) regulated trial of the ProDisc-L for 2-level degenerative disc disease. A fourth trial compared ProDisc-L with multidisciplinary rehabilitation. The composite success endpoint included improvements in Oswestry Disability Index scores (typically 15 points), improvement or maintenance in neurologic status, radiologic measures of range of motion, freedom from additional surgery, and freedom from serious device-related adverse events. Five-year outcomes have been reported from the pivotal trials for both ProDisc-L and activL. Eight-year data have been reported from a comparison of ProDisc II with multidisciplinary rehabilitation.

A key feature all of these trials is the recruitment of patients specifically with degenerative disease of the intervertebral disc. Degenerative disc disease is partly a diagnosis of exclusion where the degenerated disc is believed to be the pain generator. Radiographic evidence of degenerative disc disease may include a reduction of disc height and Modic changes, a posterior high-intensity zone, or a dark/black nucleus pulposus on T2-weighted images. Patients with common indications for spinal fusion such as scoliosis, spondylolisthesis, instability, or radiculopathy were excluded. Characteristics of these trials are summarized in Table 3, results in Table 4, and study relevance, design, and conduct limitations are summarized in Tables 5 and 6.

Lumbar Artificial Intervertebral Disc: activL Artificial Disc
There are no RCTs of activL® compared to fusion or conservative treatment.

(2019) Yue et al. completed the five-year results from outcomes from the multicenter investigational device exemption trial of the activL artificial intervertebral disc and reported in of 341 patients enrolled, 261 contributed data at 5 years (76.5%). The primary composite endpoint results were reported graphically only and demonstrated noninferiority at 5 years for activL versus control artificial discs. Sensitivity analyses using various imputation methods for missing data also showed noninferiority of activL, with the exception of the worst-case scenario (missing data counted as failure for activL and success for control). Freedom from serious adverse events through 5 years was 64% with activL and 47% with control artificial discs (P=0.0068). Because this study compared activL to other fusion devices, it provides only indirect evidence of effectiveness compared to fusion or conservative care. The study was not powered to detect differences by different control devices, and the control group includes patients who received a device that is no longer available in the United States. Additional limitations were a high loss to follow-up at 5 years, unblinded outcome assessment, and no blinding of patients at the 5-year assessment.

(2015) Garcia et al. completed the two-year outcomes from the multicenter investigational device exemption trial of the activL artificial intervertebral disc were reported in this patient-blinded noninferiority trial, patients with degenerative disc

disease were randomized to treatment with activL or an FDA approved disc (ProDisc-L or Charité). At 2 years, activL was both noninferior and superior to the control group of patients treated with ProDisc-L or Charité. Intention-to-treat analysis of secondary outcome measures showed similar improvements between activL and controls. Range of motion at the index level, measured by an independent core radiographic laboratory, was higher in the activL group than in the controls. The authors stated that this study had several limitations. First, the long-term durability of the activL TDR is unknown and requires further investigation (this study provided only short-term follow-up -- 2 years). Recent studies with the ProDisc-L and Charite TDR devices have reported excellent patient outcomes through 5 years. Second, a TDR should only be used in patients with confirmed lumbar DDD refractory to non-surgical treatment. Third, although patients, the Clinical Events Committee (CEC) and statisticians were blinded to treatment allocation and imaging was independently reviewed by a core laboratory, surgeons and clinical outcome assessors were not blinded, which may have influenced study results. Finally, this study was under-powered to evaluate activL in comparison to each control device separately. This limitation was partially mitigated by the fact that patient characteristics and main outcomes with the ProDisc-L and Charite´ devices were comparable.

Lumbar Artificial Intervertebral Disc: Charite

(2004) Geisler et al. completed a multi-center, prospective, randomized investigational device exemption study of the Charite intervertebral disc compared the Charite artificial disc with lumbar fusion using the BAK cages in patients with lumbar degenerative disc disease (n = 304). The authors found that the neurological status was equivalent between the two groups at 6, 12, and 24 months, post-operatively. They concluded that the Charite intervertebral disc is safe and effective for the treatment of single-level degenerative disc disease, resulting in no higher incidence of neurological complications compared with BAK-assisted fusion, and leading to equivalent or better outcomes (as indicated by visual analog scale and Oswestry Disability Index scores) compared with fusion with those obtained in the control group and those reported in the lumbar fusion literature. The authors concluded that the findings of this study are promising, but longer follow-up is needed to determine the durability of the Charite artificial disc and its long-term safety and effectiveness.

(2003) Caspi et al. reported results of lumbar disk prosthesis (Charite) after a follow-up period of 48 months. These investigators found that 80% of patients reported satisfactory to very good results. Poor results were reported by four patients, one of whom underwent postero-lateral fusion, and another is waiting for the same operation. There were two dislocations of the prosthesis followed by immediate revision surgery. The authors concluded that contraindications for surgery appear to be the principal cause of failure rather than the prosthesis itself.

(2003) Van Ooij et al. reported a series of 27 patients who presented with unsatisfactory results or complications after Charite disc replacement. Most patients were operated on at the L4 - L5 and/or the L5 - S1 vertebral levels. The patients were evaluated with plain

radiography, some with flexion-extension x-rays, and most of them with computed tomography scans. The group consisted of 15 women and 12 men. Their mean age was 40 years (range, 30 - 67 years) at the time of operation. The patients presented to the investigators a mean of 53 months (range 11 - 127 months) following disc replacement surgery. In two patients, an early removal of a prosthesis was required and in two patients a late removal. In 11 patients, a second spinal reconstructive salvage procedure was performed. Mean follow-up for 26 patients with mid- and long-term evaluation was 91 months (range 15 - 157 months). Early complications were the following: In one patient, an anterior luxation of the prosthesis after 1-week necessitated removal and cage insertion, which failed to unite. In another patient with prostheses at L4 - L5 and L5 - S1, the prosthesis at L5 - S1 dislocated anteriorly after 3 months and was removed after 12 months. Abdominal wall hematoma occurred in four cases. Retrograde ejaculation with loss of libido was seen in one case and erection weakness in another case. A temporary benefit was experienced by 12 patients, while 14 patients reported no benefit at all. Main causes of persistent complaints were degeneration at another level in 14, subsidence of the prosthesis in 16, and facet joint arthrosis in 11. A combination of pathologies was often present. Slow anterior migration was present in two cases, with compression on the iliac vessels in one case. Polyethylene wear was obvious in one patient 12 years after operation. In eight cases, posterior fusion with pedicle screws was required. In two cases, the prosthesis was removed and the segment was circumferentially fused. These procedures resulted in suboptimal long-term results. In this relatively small group of patients operated on with a Charite disc prosthesis, most problems arose from degeneration of other lumbar discs, facet joint arthrosis at the same or other levels, and subsidence of the prosthesis.

The Charite Artificial Disc was approved by the FDA based on a clinical trial comparing the device to anterior lumbar interbody fusion (ALIF) with BAK cages filled with iliac crest autograft in subjects with symptomatic single level degenerative disc disease from L4 to S1 who had failed at least 6 months of conservative management. The purpose of the study was to demonstrate the non-inferiority of the Charite Artificial Disc to an interbody fusion system. A total of 304 patients were enrolled in the study using a 2:1 (Charite to BAK) randomization scheme. 184 subjects receiving the Charite Artificial Disc and 81 subjects receiving interbody fusion (controls) completed 24 months follow up. Safety of the Charite Artificial Disc was assessed by monitoring the intraoperative and postoperative complications, including infection, thrombosis, disc migration, and disc subsidence, as well as reoperation and other adverse events. Efficacy of the Charite Artificial Disc was assessed primarily by a success criteria comprised of level of disability (Oswestry Low Back Disability Index (ODI)), neurological assessment (functional status) and information from adverse event data. To be considered an overall success, a subject must have had: 1) an improvement of at least 25% in the ODI score at 24 months compared to baseline; 2) no device failures requiring revision, reoperation, or removal; 3) absence of major complications, defined as major blood vessel injury, neurological damage, or nerve root injury; and 4) maintenance or improvement in neurological status at 24 months, with no new permanent neurological deficits compared to baseline. Based on these criteria, the overall success rate was 64% for subjects

receiving the Charite Artificial Disc and 57% for control subjects receiving interbody fusion. The FDA requested that the data be analyzed and reported using an improvement in the Oswestry Disability Index of greater than 15 points at 24 months compared to the score at baseline. Based on these alternate criteria, the overall success rate for subjects receiving the Charite Artificial Disc was 58%, and the success rate for control subjects was 54%. The study sponsor considered the study a success if the overall success rates of the two treatment groups were non-inferior, i.e., the difference in overall success rates (i.e., non-inferiority margin) is no greater than 15 %. However, the FDA requested that the data also be analyzed and reported using a non-inferiority margin of 10 %. The study demonstrated non-inferiority of the Charite Artificial Disc (within the 90 % 1-sided confidence interval) to interbody fusion for secondary endpoints, including pain (using a visual analog scale (VAS)), quality of life (Shoft Form-36 Questionnaire), disc height, and device migration. At 24 months follow-up, subjects receiving the Charite Artificial Disc had 7.5 degrees vertebral range of motion (ROM) at the operative level, compared to 1.1 degrees vertebral ROM for subjects receiving interbody fusion. The FDA analyzed ROM data versus Overall Success Outcome for all Charite artificial disc subjects with available ROM data at 24 months. No statistically significant association was found between ROM and success/failure at 24 months.

Because the long-term safety and effectiveness of the Charite Artificial Disc are unknown, the FDA has required the manufacturer to conduct a post-approval study using a maximum of 366 subjects (201 randomized investigational subjects; 67 training investigational subjects; and 98 control subjects). The manufacturer will be required evaluate subjects on Overall Success and secondary endpoints and submit annual reports for a total of 5 years post-implantation.

According to the FDA-approved labeling, the Charite Artificial Disc:

- Should not be implanted in patients with the following conditions: osteoporosis; osteopenia; pars defect; bony lumbar stenosis; active systemic infection or infection localized to the site of implantation; allergy or sensitivity to implant materials; and isolated radicular compression syndromes, especially due to disc herniation.
- The safety and effectiveness of the device have not been established in patients with the following conditions: pregnancy; morbid obesity; two or more degenerative discs; spondylolisthesis greater than 3 mm; or two or more unstable segments.

Data on the long-term outcomes of the Charite Artificial Disc comes from France, where the artificial disc has been in use for more than a decade. David (2000) reported in abstract form on a retrospective review of the outcome of 92 patients with chronic low back pain who were implanted with the artificial disc. The investigators reported "excellent or good" results in 75% of patients after a minimum of 5 years follow up, with no disc space height loss and no loosening or expulsion of the core. Lemaire, et al., described their 5-year and 10-year results with the Charite Artificial Disc. In the paper reporting on 10-year results, Lemaire, et al. (2002) reported an excellent or good outcome

in 90% of 100 patients with a return-to-work rate of 91.6%. In addition, the investigators reported no subluxations or core expulsions, a reoperation rate of 5% and a 2% rate of adjacent-level disc disease. The mean flexion/extension range of motion was 10.3 degrees, with a mean lateral bending motion of 5.4 degrees.

Lumbar Artificial Intervertebral Disc: ProDisc -L at a Single Level Compared to Fusion

(2018) Mu et al. completed a systematic review and meta-analysis, compared the safety and efficacy of lumbar TDR with the safety and efficacy of anterior lumbar interbody fusion (ALIF) for the treatment of lumbar DDD (LDDD). The electronic databases PubMed, Web of Science and the Cochrane Library were searched for the period from the establishment of the databases to March 2018. The peer-reviewed articles that examined the safety and efficacy of TDR and ALIF were retrieved under the given search terms. Quality assessment must be done independently by 2 authors according to each item of criterion. The statistical analyses were performed using RevMan (version 5.3) and Stata (version 14.0). The random-effect model was carried out to pool the data. The I2 statistic was used to evaluate heterogeneity. The sensitivity analysis was carried out to assess the robustness of the results of meta-analyses by omitting the articles one by one. A total of 6 studies (5 RCTs and 1 observational study) involving 1,093 patients were included in this meta-analysis. The risk of bias of the studies could be considered as low-to-moderate. Operative time (MD = 4.95; 95 % CI: -18.91 to 28.81; p = 0.68), intra-operative blood loss (MD = 4.95; 95 % CI: -18.91 to 28.81; p = 0.68), hospital stay (MD = -0.33; 95 % CI: -0.67 to 0.01; p = 0.05), complications (RR = 0.96; 95 % CI: 0.91 to 1.02; p = 0.18) and re-operation rate (RR = 0.54; 95 % CI: 0.14 to 2.12; p = 0.38) were without significant clinical difference between groups. Patients in the TDR group had higher post-operative satisfaction (RR = 1.19; 95 % CI: 1.07 to 1.32; P = 0.001) and, better improvements in ODI (MD = -10.99; 95 % CI: -21.50 to -0.48; p = 0.04), VAS (MD = -10.56; 95 % CI: -19.99 to -1.13; p = 0.03) and post-operative lumbar mobility than did patients in the ALIF group. The follow-up time in the investigative and control groups ranged from 12 months to 60 months. The authors concluded that this meta-analysis based on the current available studies showed that the efficacy of TDR was superior to that of ALIF in the short-term; TDR may be an ideal alternative for selected patients with LDDD in the short term. However, the results of this study could not suggest the use of TDR above the use of ALIF for lumbar spinal treatments only on the basis of short-term results. Furthermore, these researchers thought that this study still has a certain clinical significance, although the limitations of this meta-analysis led them to be cautious about the present conclusions. They stated that multi-center, well-designed, high-quality, large sample and long-term follow-up studies are needed to further evaluate the short- and long-term safety and efficacy of TDR comparison of ALIF or other fusion approaches in the treatment of LDDD.

(2018) Zigler et al. completed a meta-analysis, examined the long-term safety and efficacy of TDR compared with fusion in patients with functionally disabling chronic low back pain (LBP) due to single-level lumbar degenerative disc disease (DDD) at 5 years. PubMed and Cochrane Central Register of Controlled Trials databases were searched for

RCTs reporting outcomes at 5 years for TDR compared with fusion in patients with single-level lumbar DDD. Outcomes included ODI success, back pain scores, re-operations, and patient satisfaction. All analyses were conducted using a random-effects model; analyses were reported as relative risk (RR) ratios and mean differences (MDs). Sensitivity analyses were conducted for different outcome definitions, high loss to follow-up, and high heterogeneity. The meta-analysis included 4 studies; TDR patients had a significantly greater likelihood of ODI success (RR 1.0912; 95 % CI: 1.0004 to 1.1903) and patient satisfaction (RR 1.13; 95 % CI: 1.03 to 1.24) and a significantly lower risk of re-operation (RR 0.52; 95 % CI: 0.35 to 0.77) than fusion patients. There was no association with improvement in back pain scores whether patients received TDR or fusion (MD -2.79; 95 % CI: -8.09 to 2.51). Most results were robust to sensitivity analyses. Results for ODI success and patient satisfaction were sensitive to different outcome definitions but remained in favor of TDR. The authors concluded that TDR was an effective alternative to fusion for lumbar DDD. It offered several clinical advantages over the longer term that could benefit the patient and reduce health care burden, without additional safety consequences. Again, this study provided only mid-term (5 years) follow-up data. The authors stated that this meta-analysis had several drawbacks. A challenge of long-term lumbar TDR studies is loss of participants to follow-up. Included studies varied in the proportion of participants lost to follow-up at 5 years, ranging from 1 % to 43 %. Despite the risk high participant loss poses to a study's validity, results of sensitivity analyses excluding studies with substantial loss to follow-up (i.e., greater than 30 %) were similar to those of the primary analysis. Because few RCTs comparing TDR with fusion have reported long-term data, these researchers opted for an inclusive approach to each outcome definition. Sensitivity analyses conducted to account for differences in the definitions and measures used for ODI success, back pain, and patient satisfaction consistently favored TDR over fusion despite the loss of statistical significance for some outcomes. Similarly, the analysis could not control for heterogeneity, a typical issue when addressing surgical outcomes. Nuances such as surgical technique and post-operative compliance could not be addressed by this study design. However, given the magnitude of centers involved in the 4 RCTs incorporated in this analysis, it appeared reasonable that many variations in technique were accounted for. The analysis incorporated the most recent literature available, but data from newer TDR devices such as the activL Artificial Disc was not included, since findings at 5 years have yet to be reported. Two-year follow-up results from the activL investigational device exemption (IDE) study aligned with the findings of the current analysis. Analyses including the long-term data for activL are expected to demonstrate similar or better findings favoring TDR than those shown in the current 5-year meta-analysis.

The pivotal study for the ProDisc-L was an unblinded noninferiority trial that originally followed patients for 24 months. In the per-protocol analysis reported to FDA, ProDisc-L had a success rate of 53.4% and fusion had a success rate of 40.8%, which achieved both non-inferiority and superiority. Two-year results from this trial were published in 2007, and 5-year follow-up was reported in 2012. The definition of success was changed from the analysis requested by FDA and was reported to be higher at 63.5% at 2 years and 53.7% at 5 years. Noninferiority, but not superiority, of artificial disc replacement was

achieved at 5 years. This change in overall success in ProDisc-L patients indicates a possible decrement in response over time with the artificial disc. This decline in response rate was not observed in the standard fusion group and resulted in a between-group convergence of the primary outcome measure over time. Several individual components of the primary outcome measure and secondary outcome measures (Oswestry Disability Index, 36-Item Short-Form Health Survey Physical Component Summary, neurologic success, device success) were also statistically better in the ProDisc-L group than in the fusion group at 2 years, but not at 5 years. Post hoc analysis of radiographs found fewer patients with adjacent-level degeneration in the ProDisc-L group than in the control group. However, the adjacent-level reoperations did not differ significantly between groups (1.9% ProDisc-L vs 4% controls).

(2013) An updated TEC Assessment evaluated 5-year follow-up from the ProDisc pivotal trial. The Assessment concluded the following:

- Additional study of ProDisc in an appropriately powered clinical trial with minimum 5-year follow-up is needed to confirm the results of the investigational device exemption trial in patients with single-level chronic symptomatic degenerative disc disease unresponsive to conservative management.
- Questions remain about the durability of the disc, in particular, the long-term effects on patient health of polyethylene wear debris. Surgical revision of a failed or dysfunctional disc may be complicated and dangerous to the patient, so the lifespan of a prosthetic device is a key issue.
- The main claim of the artificial disc-that it maintains range of motion and thereby reduces the risk of adjacent-level segment degeneration better than fusion-remains subject to debate.

Lumbar Artificial Intervertebral Disc: ProDisc -L at 2 Levels Compared to Fusion
The ProDisc-L for 2-level lumbar degenerative disc disease was reported in 2011 from a multicenter, randomized, FDA regulated noninferiority trial. All patients had degenerative disc disease at 2 contiguous vertebral levels from L3 to S1 with or without leg pain, a minimum of 6 months of conservative therapy, and a minimum Oswestry Disability Index score of 40. The ProDisc-L group had faster surgeries (160.2 minutes vs 272.8 minutes), less estimated blood loss (398.1 mL vs 569.3 mL), and shorter hospital lengths of stay (3.8 days vs 5.0 days) than the arthrodesis group. The composite measure of success demonstrated noninferiority but not superiority of ProDisc-L. The ProDisc-L group showed significant benefit in the percentages of patients who achieved at least a 15-point improvement in Oswestry Disability Index scores and greater improvements in the SF-36 scores. A greater percentage of patients in the arthrodesis group required secondary surgical procedures. As noted in an accompanying commentary, the study had a number of limitations. Comparison with a procedure (open 360° fusion) that is not the criterion standard precludes decisions on the comparative efficacy of this procedure to the standard of care. Other limitations include the relatively short follow-up and lack of blinding of patients and providers.

Lumbar Artificial Intervertebral Disc: ProDisc -L Miscellaneous

(2018) Zigler et al. provided post-hoc analysis of 5-year follow-up data from a randomized, multi-center trial. These investigators examined the incidence of progression in radiographic adjacent-level degeneration (ΔALD) from pre-operative assessment to 5 years after total disc replacement (TDR) and the relationship of these changes with range of motion (ROM) and clinical adjacent-level disease. They also compared adjacent-level degeneration (ALD) outcomes between TDR and fusion. In total, 175 patients with single-level, symptomatic, lumbar disc degeneration who had received activL or ProDisc-L and had a pre-operative and 5-year post-operative radiograph available were included. Over 5-year follow-up, ΔALD was defined as an increase in ALD of greater than or equal to 1 grade and clinical ALD was defined as surgical treatment at the level adjacent to an index TDR. Matching-adjusted indirect comparisons were conducted to compare ALD outcomes after TDR (current trial) with those after fusion (published trial). At 5-year follow-up, 9.7 % (17/175) of TDR patients had ΔALD at the superior level. In patients with pre-operative ALD at the superior level, most (88 % [23/26]) showed no radiographic progression over 5 years. The rate of clinical ALD was 2.3 % (4/175) and none of these patients had ALD at baseline. For each degree of ROM gained at the TDR level, there was a consistent decrease in the percentage of patients with ΔALD. After matching and adjustment of baseline characteristics, TDR had a significantly lower likelihood of ΔALD than fusion (odds ratio [OR] 0.32; 95 % confidence interval [CI]: 0.13 to 0.76). The authors concluded that the rates of ΔALD and clinical ALD in this TDR population were similar to those previously reported in the literature for TDR at 5-year follow-up; TDR had a statistically significant lower rate of ΔALD than fusion. Level of evidence = III. It should also be noted that this study provided only mid-term (5 years) follow-up data. The authors stated that this study had several drawbacks. First, this study was a post-hoc analysis of a subset of patients from the original randomized trial. Thus, it did not represent all patients originally evaluated because not all pre-operative and 5-year radiographs were available, primarily because of loss to follow-up. Nevertheless, the sample size of 175 patients was relatively comparable to a recent study that included 161 patients with ProDisc-L and evaluated ALD outcomes. Second, caution should be exercised when comparing results of various studies because of the potential for variations in scoring methods and follow-up duration. This study was aligned with the methods published in the 2012 study, which comprehensively considered several parameters, including disc height, endplate sclerosis, osteophytes, and spondylolisthesis, in the grading scheme. Furthermore, although the indications for TDR have generally been consistently applied in randomized controlled trials, fusion data may come from less homogeneous patient cohorts, particularly in studies not involving randomized comparison to TDR. Third, a matching-adjusted indirect comparison (MAIC) was conducted because of the absence of randomized data directly comparing currently marketed TDR devices (i.e., activL and ProDisc-L) with fusion for the ALD outcomes of interest. Although MAICs involve consideration and adjustment for treatment-effect modifiers and/or prognostic factors, there was risk that treatment groups were not perfectly balanced. In the comparison of TDR with fusion, unanchored methods were used that involved more methodological assumptions. In the comparison of activL with fusion, anchored methods were used, wherein the ProDisc-L

arm from each trial acted as an anchor treatment. Results for ALD outcomes were comparable using both anchored and unanchored methods, illustrating the robustness of the methods.

(2017) Furunes et al. completed an eight-year follow-up of this trial, in both the intention-to-treat and per-protocol analysis there was a statistically significant benefit of surgery as measured by the mean Oswestry Disability Index, but these differences did not reach the clinically significant threshold of 10 points. More patients in the surgery group (43/61 [70%]) reached a clinically important difference of 15 Oswestry Disability Index points than in the rehabilitation group (26/52 [50%]; p=0.03). Twenty-one (24%) patients randomized to rehabilitation crossed over to surgery while 12 (14%) patients randomized to surgery had undergone additional back surgery. 1 serious AE after disc replacement was registered (less than 1 %). The authors concluded that substantial long-term improvement could be expected after both disc replacement and MDR. The difference between groups was statistically significant in favor of surgery, but smaller than the pre-specified clinically important difference of 10 ODI points that the study was designed to detect. These researchers stated that future research should aim to improve selection criteria for disc replacement and MDR. The authors stated that this study had several drawbacks that should be acknowledged. First, the patients could not be blinded. This may have led to a difference in placebo effect between the groups. A considerable placebo effect has been reported for vertebroplasty compared with sham surgery.

(2012) Jacobs et al. completed a Cochrane review on "Total disc replacement for chronic back pain" concluded that "Although statistically significant, the differences between disc replacement and conventional fusion surgery for degenerative disc disease were not beyond the generally accepted clinical important differences with respect to short-term pain relief, disability and Quality of Life. Moreover, these analyses only represent a highly selected population. The primary goal of prevention of adjacent level disease and facet joint degeneration by using total disc replacement, as noted by the manufacturers and distributors, was not properly assessed and not a research question at all. Unfortunately, evidence from observational studies could not be used because of the high risk of bias, while these could have improved external validity assessment of complications in less selected patient groups. Non-randomized studies should however be very clear about patient selection and should incorporate independent, blinded outcome assessment, which was not the case in the excluded studies. Therefore, because they believe that harm and complications may occur after years, they believe that the spine surgery community should be prudent about adopting this technology on a large scale, despite the fact that total disc replacement seems to be effective in treating low-back pain in selected patients, and in the short term is at least equivalent to fusion surgery".

(2012a) Zigler and Delamarter evaluated the long-term safety and effectiveness of the ProDisc-L total disc replacement (TDR) as part of an FDA-mandated post-market approval study. This report summarized the clinical findings after 5 years of follow-up. A total of 236 patients were treated and followed-up for 5 years; 161 TDRs and 75

fusions had been performed in these patients. The primary outcome was a 10-component success end-point. Secondary outcome measures included neurological status, secondary surgery, ODI, SF-36, VAS assessing pain and satisfaction, radiographic data, narcotic use, activity, and recreation status. Patients were monitored through their 5-year post-operative visits under the FDA post-market surveillance provisions in the original investigational device exemption approval. The overall follow-up rate at 5 years was 81.8 %. Study success demonstrated that TDR was non-inferior to fusion with a 12.5 % margin ($p = 0.0099$). Both TDR and fusion treatment groups maintained significant improvement on the ODI at 5 years compared with baseline ($p < 0.0001$). Secondary surgeries at the index level were performed in 12 % of fusion patients and 8 % of TDR patients. Radiographically, none of the TDRs developed spontaneous fusion. The segmental ROM following TDR remained within normal range, although it decreased by approximately 0.5° in years 3 to 5. The VAS pain scores decreased from pre-operative values by 48 % in both treatment groups at 5 years. Patient satisfaction remained high in both groups (77 %), while the percentage of patients indicating that they would have the surgery again was higher in TDR patients (82.5 %) than in fusion patients (68.0 %). The authors concluded that patients in both groups maintained significant improvement during the 5-year follow-up. The TDR group had significantly better improvement on some scales. Although TDR patients avoid the stiffness of fusion and are more satisfied than fusion patients, both fusion and TDR are reasonable surgical options in this specific patient population.

(2012b) Zigler and colleagues reported report the 5-year results for radiographically demonstrated adjacent-level degenerative changes from a prospective multi-center study in which patients were randomized to either TDR or circumferential fusion for single-level lumbar DDD. A total of 236 patients with single-level lumbar DDD were enrolled and randomly assigned to 2 treatment groups: (i) 161 patients in the TDR group were treated using the ProDisc-L, and (ii) 75 patients were treated with circumferential fusion. Radiographic follow-up data 5 years after treatment were available for 123 TDR patients and 43 fusion patients. To characterize adjacent-level degeneration (ALD), radiologists at an independent facility read the radiographic films. Adjacent-level degeneration was characterized by a composite score including disc height loss, endplate sclerosis, osteophytes, and spondylolisthesis. At 5 years, changes in ALD (ΔALDs) compared with the pre-operative assessment were reported. Changes in ALD at 5 years were observed in 9.2 % of TDR patients and 28.6 % of fusion patients ($p = 0.004$). Among the patients without adjacent-level disease pre-operatively, new findings of ALD at 5 years post-treatment were apparent in only 6.7 % of TDR patients and 23.8 % of fusion patients ($p = 0.008$). Adjacent-level surgery leading to secondary surgery was reported for 1.9 % of TDR patients and 4.0 % of fusion patients ($p = 0.6819$). The TDR patients had a mean pre-operative index-level ROM of 7.3°) that decreased slightly (to 6.0°) at 5 years after treatment ($p = 0.0198$). Neither treatment group had significant changes in either ROM or translation at the superior adjacent level at 5 years post-treatment compared with baseline. The authors concluded that at 5 years after the index surgery, ProDisc-L maintained ROM and was associated with a significantly lower rate of ΔALDs than in the patients treated with circumferential fusion. In fact, the fusion patients were greater than

3 times more likely to experience ΔALDs than were the TDR patients. These researchers stated that the findings of this post-hoc analysis of data obtained from a randomized controlled trial (RCT) provided a baseline reference point in the evolving knowledge database for lumbar TDR and should serve as a benchmark for future study.

(2011) Hellum et al. reported an RCT that compared the use of the ProDisc-L with a multidisciplinary rehabilitation program. Patients (N=173) were ages 25 to 55 years, had low back pain for a least a year, received physical therapy or chiropractic treatment for at least 6 months without sufficient effect, had an Oswestry Disability Index score of at least 30, and showed degenerative intervertebral changes that included at least 40% reduction of disc height, Modic changes, a high-intensity zone in the disc, and morphologic changes identified as changes in the signal intensity in the disc of grade 3 or 4. The multidisciplinary rehabilitation included a cognitive approach and supervised physical exercise. The primary outcome was Oswestry Disability Index score, and the trial was powered to detect a 10-point difference in Oswestry Disability Index score. The analysis was intention-to-treat with the last observation carried forward. There were 13 (15%) dropouts in the surgical arm and 21 (24%) in the rehabilitation arm. Also, 5 (6%) patients crossed over from rehabilitation to surgery. Of the 34 patients lost to follow-up, 26 answered a questionnaire between 2.5 and 5 years after treatment. In the intention-to-treat analysis, there was a statistically significant benefit of surgery, but the mean difference did not achieve the 10-point difference in Oswestry Disability Index score considered clinically significant. There were significantly more patients who achieved a 15-point improvement in Oswestry Disability Index score in the ProDisc group, with a number needed to treat of 4.4. The radiographic assessment identified a similar level of adjacent segment degeneration in both groups, but an increase in facet arthropathy in the ProDisc II group.

(2006a) Bertagnoli and colleagues conducted a prospective, longitudinal study (n = 20) to evaluate the effectiveness of ProDisc arthroplasty in patients in whom symptomatic adjacent-segment degeneration has developed after remote lumbar fusion. The follow-up period was a minimum of 2 years. Subjects in this study ranged in age from 18 to 67 years. They presented with disabling adjacent-level discogenic LBP with or without L1 - S1 radicular pain. Individuals with radiographic evidence of circumferential spinal stenosis or facet joint degeneration were excluded. Patients were assessed pre-operatively and post-operatively at 3, 6, 12, and 24 months. Eighteen patients (90%) fulfilled all follow-up criteria. The median age of all patients was 50 years. Statistical improvements in VAS, Oswestry Disability Index, and patient satisfaction scores were documented 3 months after arthroplasty. These improvements remained at the 24-month follow-up examinations. Patient satisfaction rates were 86% at 24 months. Radicular pain was also significantly decreased. No additional surgeries were needed at affected or unaffected levels. The authors concluded that analysis of early results indicates that ProDisc lumbar total disc arthroplasty is an effective treatment for symptomatic adjacent-segment lumbar discogenic LBP following remote fusion. Significant improvements in patient satisfaction and disability scores were observed by 3 months post-operatively and were maintained at the 2-year follow-up examination. No device-related complications occurred. Patients

should be screened carefully for evidence of facet joint impingement/degeneration, hardware-induced pain, and/or non-union at prior fusion levels before undergoing disc replacement surgery.

(2006b) Bertagnoli et al. completed a review regarding the safety and effectiveness of single-level lumbar disc replacement in patients 60 years of age or older (also carried out a prospective, longitudinal study to obtain outcome (minimum follow-up period 2 years). This analysis involved 22 patients in whom the ProDisc was used for total disc arthroplasty. All patients presented with disabling discogenic LBP with or without radicular pain. The involved segments ranged from L2 to S1. Patients in whom there was no evidence of radiographic circumferential spinal stenosis and with minimal or no facet joint degeneration were included. Patients were assessed pre-operatively and outcome was evaluated post-operatively at 3, 6, 12, and 24 months by administration of standardized tests (VAS, ODI, and patient satisfaction). Secondary parameters included analysis of pre- and post-operative radiographic results of disc height at the affected level, adjacent-level disc height and motion, and complications. Twenty-two subjects (100%) fulfilled all follow-up criteria. The median age of all patients was 63 years (range of 61 to 71 years). There were 17 single-level cases, 4 two-level cases, and 1 three-level case. Statistical improvements in VAS, ODI, and patient satisfaction scores were observed at 3 months post-operatively. These improvements were maintained at 24-month follow-up examination. Patient satisfaction rates were 94% at 24 months (compared with 95% reported in a previously reported ProDisc study). Radicular pain also decreased significantly. Patients in whom bone mineral density was decreased underwent same-session vertebroplasty following implantation of the ProDisc device(s). There were 2 cases involving neurological deterioration: unilateral foot drop and loss of proprioception and vibration in 1 patient and unilateral foot drop in another patient. Both deficits occurred in patients in whom there was evidence pre-operatively of circumferential spinal stenosis. There were 2 cases of implant subsidence and no thrombo-embolic phenomena. These researchers concluded that significant improvements in patient satisfaction and ODI scores were observed by 3 months post-operatively and these improvements were maintained at the 2-year follow-up examination. Although the authors' early results indicate that the use of ProDisc lumbar total disc arthroplasty in patients older than 60 years of age reduces chronic LBP and improves clinical functional outcomes, they recommend the judicious use of artificial disc replacement in this age group. Until further findings are reported, the authors cautiously recommend the use of artificial disc replacement in the treatment of chronic discogenic LBP in patients older than age 60 years in whom bone quality is adequate in the absence of circumferential spinal stenosis.

(2006c) Bertagnoli et al. reported that lumbar total disc arthroplasty utilizing the ProDisc prosthesis is equally effective in smokers and non-smokers. These investigators performed a prospective analysis on 104 patients with disabling discogenic LBP treated with single-level lumbar ProDisc total disc arthroplasty. Smokers and non-smokers were evaluated before surgery and after surgery using patient satisfaction, Oswestry, and VAS. Additionally, pre-operative and post-operative neurological, radiographical, and pain

medication assessments were performed at similar post-operative intervals. Oswestry, VAS, and patient satisfaction scores revealed statistical improvement beginning 3 months after surgery and were maintained at minimum 2-year follow-up. Patient satisfaction scores were higher in smokers (94%) than in non-smokers (87%) at 2-year follow-up ($p = 0.07$). Radiographical analysis revealed an affected disc height increase from 4 to 13 mm ($p < 0.05$) and an affected disc motion from 3 to 7 degrees ($p < 0.05$). No cases of loosening, dislodgment, mechanical failure, infection, or fusion of the affected segment occurred. The authors concluded that the findings of this study indicate that smokers do equally well as non-smokers when ProDisc artificial disc replacement is used in the treatment of debilitating lumbar spondylosis. Patient outcome and radiographical scores showed significant improvement compared with pre-operative levels.

(2006) Leivseth et al. presented their findings of a longitudinal prospective study on the use of the ProDisc II prosthesis in 41 consecutive disc prosthesis patients, covering a post-operative time period of at least 2 years. They stated that disc replacement in the lumbar spine by a ProDisc II implant failed to restore normal segmental rotational motion in the sagittal plane, specifically at levels L4 - L5 and L5 - S1. As segmental motion of the untreated segments was lower than normal as well, though not quite as conspicuous as that of instrumented segments, adaptation of soft tissue taken place during the pre-operative symptomatic time period is conjectured to cause the observed motion deficit. On the other hand, it's important to note findings from other studies indicated that the ProDisc is safe and effective in treating patients with low back pain (LBP).

(2006) Schroven and Dorofey conducted a prospective, non-randomized study on the ProDisc IVD (n = 14) versus anterior lumbar interbody fusion (ALIF, n = 10). In the ProDisc group, the Oswestry Disability Index improved from +/- 38.42 pre-operatively (60 being the worst possible condition) to +/- 15.21 after 6 months, and to +/- 12.5 after 12 months. This was markedly better than the ALIF group, where the corresponding figures were +/- 38, +/- 25 and +/- 21.4. The ProDisc patients also scored better with respect to duration of hospitalization, blood loss and operation time. The complications were comparable in both groups.

(2006) Siepe et al. presented their 3-year results with total lumbar disc replacement (TLDR) by means of the ProDisc II with a minimum follow-up of 24 months. They concluded that available data suggest beneficial clinical results of TLDR for the treatment of DDD in a highly selected group of patients. Better functional outcome was obtained in younger patients under 40 years of age and patients with DDD in association with disc herniation. Multi-level disc replacement had significantly higher complication rate and inferior outcome at mid-term follow-up compared with mono-segmental interventions. Thus, only longer follow-up evaluations will demonstrate the real benefit for patients. Results are significantly dependent on pre-operative diagnosis and patient selection, number of replaced segments, and age of patient at the time of operation. The authors stated that because of significantly varying outcomes, indications for disc replacement must be defined precisely.

(2006) Tropiano et al. presented the clinical and radiographical results assessed 7 to 11 years following a ProDisc TLDR. A total of 64 patients had single- or multiple-level implantation of a TLDR between 1990 and 1993. The mean duration of follow-up was 8.7 years. Clinical results were evaluated by assessing pre-operative and post-operative lumbar pain, radiculopathy, disability, and modified Stauffer-Coventry scores. Pre-operative and post-operative radiographs were evaluated as well. Subgroup analysis was performed to determine if gender, an age of less than 45 years, previous surgery, or multi-level surgery had an effect on outcome. At an average of 8.7 years post-operatively, there were significant improvements in the back pain, radiculopathy, disability, and modified Stauffer-Coventry scores. Thirty-three of the 55 patients with sufficient follow-up had an excellent result, 8 had a good result, and 14 had a poor result. Neither gender nor multi-level surgery affected outcome. An age of less than 45 years and prior lumbar surgery had small but significant negative effects on outcome. Radiographs did not demonstrate loosening, migration, or mechanical failure in any patient. Five patients had approach-related complications. These investigators concluded that the ProDisc TLDR appears to be effective and safe for the treatment of symptomatic DDD. Gender and multi-level surgery did not affect the outcomes, whereas prior lumbar surgery or an age of less than 45 years was associated with slightly worse outcomes. The authors noted that longer follow-up of this cohort of patients and randomized studies comparing disc replacement with arthrodesis are needed.

(2005) Bertagnoli et al. completed a prospective, longitudinal minimum 2-year follow-up study (n = 118), which evaluated the safety and effectiveness of the ProDisc implant in patients with disabling single-level discogenic LBP. Patients 18 to 60 years of age with disabling and recalcitrant discogenic LBP with or without radicular pain secondary to single level discogenic LBP from L3 to S1 were included. Patients were assessed before surgery, and outcome measurements were assessed after surgery at 3, 6, 12, and 24 months. A total of 104 patients (88%) fulfilled all follow-up criteria. The median age of all patients was 47 years (range of 36 to 60 years). Statistical improvements in VAS, Oswestry, and patient satisfaction scores occurred 3 months post-operatively. These improvements were maintained at the 24-month follow-up. Radicular pain also decreased significantly. Full-time and part-time work rates increased from 10 to 35% and 3 to 24%, respectively. No additional fusion surgeries were needed either at the affected or unaffected levels. Radiographical analysis revealed an affected disc height increase from 4 to 13 mm ($p < 0.001$) and an affected disc motion from 3 to 7 degrees ($p < 0.004$). The authors concluded that single-level ProDisc lumbar total disc arthroplasty is a safe and effective treatment for debilitating lumbar discogenic LBP. Significant improvements in patient satisfaction as well as disability scores occurred after surgery by 3 months and were maintained at the 2-year follow-up. No device-related complications occurred. Patients with severe to moderate disc height loss as well as those with symptomatic posterior annular defects with minimal disc height loss achieve functional gains and significant pain relief. Careful and appropriate patient selection is essential in ensuring optimal surgical outcomes.

Lumbar Artificial Disc Replacement: Miscellaneous

(2020) Chou et al. on UpToDate has a review on "Subacute and chronic low back pain: Surgical treatment" stated, "Artificial disc replacement is a newer alternative to fusion. A theoretic advantage of lumbar disc replacement compared with fusion is that a prosthetic disc could help preserve normal range of motion and spine mechanics. This could reduce the long-term degenerative changes in adjacent vertebral segments that have been observed following spinal fusion. However, the evidence suggests that the efficacy of this approach is similar to that of spinal fusion. A 2012 systematic review of seven randomized trials evaluated the use of disc replacement for chronic low back pain. Five trials (n = 1301) specifically compared disc replacement versus fusion for improvement of pain (VAS) and function (ODI) outcomes at 2 years. All studies had risk of bias due to lack of blinding and industry sponsorship; in addition, two of the trials evaluated an artificial disc that has not been approved by the FDA. Pooled results demonstrated no significant difference in pain scores between the two groups. There was a statistically, but not clinically, significant difference in improvement in function in the disc replacement group compared with the fusion group (4.3 points, 95 % CI 1.9-6.7). Only one trial has compared lumbar disc replacement versus a multidisciplinary rehabilitation program. This study included 173 patients with chronic pain, disability, and L4-5 and/or L5-S1 degenerative disc disease. Those randomly assigned to disc replacement had a statistically, but not clinically, significant improvement in disability score (difference of 8 points on a 100-point scale) at two-year follow-up and lower pain scores (difference 12 points on a 100-point scale) compared with the rehabilitation arm. Six patients in the surgery group had complications resulting in physical impairment, with one patient requiring a lower leg amputation following revision surgery. No major complications were reported for the rehabilitation arm … A key limitation of existing evidence for the role of lumbar disc replacement is the lack of longer-term follow-up to assess efficacy and failure rates necessitating device removal and potential conversion to a fusion procedure. Regardless of treatment (disc replacement, fusion, or nonsurgical), few patients report complete symptom resolution. Disc replacement is approved by the FDA for patients who are in good health and ≤ 60 years old, with disease limited to one disc between L3 and S1 and no associated deformity, spondylolisthesis, or neurologic deficit. Patients should be treated by surgeons experienced in performing disc replacement to minimize complications and length of hospitalization. Guidelines from the American Pain Society found insufficient evidence regarding long-term benefits and harms of disc replacement to support recommendations … More research with longer follow-up is needed to determine the appropriate role of artificial disc replacement versus fusion. We suggest that vertebral fusion be performed for patients who undergo surgical intervention for chronic low back pain (Grade 2B)".

(2020) Sandhu et al. completed a review on lumbar arthroplasty, noted that lumbar DDD is a pathologic process that affects a large portion of the aging population. In the recent past, surgical treatment has involved fusion procedures. However, lumbar disc arthroplasty and replacement provides an alternative for carefully selected patients. It provides the major advantage of motion preservation and thus keeps adjacent segments from significantly progressive degeneration. The history of lumbar disc replacement has

roots that start in the 1960s with the implantation of stainless-steel balls. Decades later, multiple implants with different material design and biomechanical properties were introduced to the market. New 3rd-generation implants have made great strides in improved biomechanics and clinical outcomes. Although there is room for further advancement and studies are needed to evaluate the long-term durability and sustainability of lumbar disc arthroplasty, it has certainly proven to be a very acceptable alternative within the surgical armamentarium that should be offered to patients who meet indications. Moreover, these researchers stated that intervertebral disc replacements for the lumbar spine have been under constant design improvements for over 4 decades and the latest design offers safe and effective motion preservation for carefully selected patients suffering from DDD. Maintaining motion clearly reduces the development of adjacent segment disease and need for additional surgical intervention on long-term follow-up. Questions regarding lifelong durability and consequences of the devices remain and will be only gleaned over time, but experience with current discs is promising.

Summary of Evidence: Lumbar Artificial Disc Replacement
When conservative treatment of degenerative disc disease fails, a common surgical approach is spinal fusion. The outcomes of spinal fusion have been controversial over the years, in part due to the difficulty in determining whether a patient's back pain is related to degenerative disc disease (DDD) and in part due to the success of the procedure itself. In addition, spinal fusion alters the biomechanics of the back, potentially leading to premature disc degeneration at adjacent levels, a particular concern for younger individuals.

As an alternative, a variety of artificial intervertebral discs have been investigated over the past 30 years as an alternative to fusion. This approach, also referred to as total disc replacement or spinal arthroplasty, is intended to maintain motion at the operative level once the damaged disc has been removed, and to maintain the normal biomechanics of the adjacent vertebrae. It is hypothesized that artificial disc will maintain anatomical disk space height, normal segmental lordosis, and physiological motion patterns at the index and adjacent cervical levels. For individuals who have lumbar degenerative disc disease who receive a lumbar artificial intervertebral disc, the evidence includes randomized controlled trials with 5-year outcomes and case series with longer term outcomes. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The potential to reduce the risk of adjacent-level degenerative disc disease above or below a fusion site has been the major rationale driving device development and use. To help ensure a good outcome, the patient has to have motion in their bending zone. If not, placing an artificial disc in a severely degenerative disc space is not going to help. Overall, a theoretic advantage of lumbar disc replacement compared with fusion is that a prosthetic disc could help preserve normal range of motion and spine mechanics. This could reduce the long-term degenerative changes in adjacent vertebral segments that have been observed following spinal fusion. However, the evidence currently suggests that the efficacy of this approach is likely similar to that of spinal fusion. Therefore, for initial lumbar artificial disc replacement the evidence would be

sufficient to determine that the technology results in an improvement in the net health outcome.

While the evidence on the efficacy of an artificial lumbar disc revision may be limited on long-term data, the evidence currently suggests the efficacy of an artificial lumbar disc revision would be similar to a revision related to a spinal fusion and, the medical necessity would be warranted for an individual who requires a revision due to a comorbid condition (e.g., loosening, dislodgement, fracture, discitis infection) when the initial surgery was considered medically necessary. The evidence would be sufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American Academy of Orthopaedic Surgeons (AAOS)
(2010) Although it is not an official position statement, the 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.

American Pain Society (APS)
(2009) The American Pain Society's practice guidelines concluded the following:

- There was "insufficient evidence" to adequately evaluate the long-term benefits and harms of vertebral disc replacement. The guidelines were based on a systematic review commissioned by the Society and conducted by the Oregon Evidence-Based Practice Center.
- The rationale for the recommendation was that, although artificial disc replacement has been associated with outcomes similar to fusion, the trial results were only applicable to a narrowly defined subset of patients with single-level degenerative disease, and the type of fusion surgery in the trials is no longer widely used due to frequent poor outcomes. Also, all trials had been industry-

funded, and data on long-term (>2 years) benefits and harms following artificial disc replacement were limited.
(*Accessed March 2022*)

International Society for the Advancement of Spine Surgery (IASS)
(2015) The IASS published a policy statement on the *lumbar artificial disc*. The goal of the policy statement was "to educate patients, physicians, medical providers, reviewers, adjustors, case managers, and all others involved or affected by insurance coverage decisions regarding lumbar disc replacement surgery.

- " The authors of the policy statement were selected for their expertise and experience with the artificial lumbar disc and included one of the investigators for the Prodisc-L IDE trial and another for the ActivL IDE trial. RCT and long-term results that were favorable to the LADR were discussed. postoperative pain patterns in 58 (33%) patients of 175 implanted with the ProDisc II showed facet joint pain in 22 (13%) and sacroiliac joint pain in 21 (12%). Another report describes late complications in 75 patients who had received an earlier generation SB Charité prosthesis. As all of the patients had been originally treated by other surgeons, the percentage of implant failure cannot be determined from this report. The mean interval between insertion and retrieval of the prosthesis was 8 years and 11 months (range, 3-16 years). The most frequent complications included subsidence (n=39), disc prosthesis too small (n=24), adjacent disc degeneration (n=36), degenerative scoliosis (n=11), facet joint degeneration (n=25), and metal wire breakage (n=10). The report indicated that good placement and good sizing of the disc prosthesis appeared problematic for many of the patients, adjacent-disc degeneration was seen in many patients, and polyethylene wear with inflammatory fibrous tissue containing wear debris was observed. The report concluded that wear mechanisms of artificial discs may be similar to artificial hips and knees and that, due to nearby vascular structures and scar tissue from the original surgery, retrieval of an artificial disc prosthesis can be difficult and dangerous. Therefore, long-term health outcomes following disc implantation in young active patients may become a clinically significant issue. (*Accessed March 2022*)

National Institute for Health and Care Excellence (NICE)
(2010) NICE issued guidance on the artificial *cervical* disc, concluding:

- "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….
- 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."
(*Accessed March 2022*)

(2009) NICE issued guidance on the safety and efficacy of prosthetic intervertebral disc replacement in the *lumbar* spine stating,

- Current evidence on the safety and efficacy of prosthetic intervertebral disc replacement in the lumbar spine is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit.
- A multidisciplinary team with specialist expertise in the treatment of degenerative spine disease should be involved in patient selection for prosthetic intervertebral disc replacement in the lumbar spine. The procedure should only be carried out in patients for whom conservative treatment options have failed or are contraindicated.
- The current evidence includes studies with a maximum follow-up of 13 years, but the majority of evidence is from studies with shorter durations of follow-up. NICE encourages clinicians to continue to collect and publish data on longer-term outcomes, which should include information about patient selection and the need for further surgery.
(*Accessed March 2022*)

The Ontario Health Technology Advisory Committee of the Ontario Ministry of Health and Long-Term Care

(2019) The Ontario Health Technology Advisory Committee of the Ontario Ministry of Health and Long-Term Care completed a health technology assessment cervical artificial disc replacement versus fusion for *cervical degenerative disc disease which stated the following:* Conclusions In carefully selected patients with cervical degenerative disc disease undergoing C-ADR or fusion, there is evidence that:

- C-ADR is an alternative to fusion for cervical degenerative disc disease given outcomes that are statistically noninferior to fusion: perioperative outcomes (GRADE high), health related quality of life (GRADE high), patient satisfaction (GRADE high), and overall treatment success for one-level cervical degenerative disc disease (GRADE moderate)
- C-ADR might be preferable to fusion for cervical degenerative disc disease given outcomes that are statistically superior to fusion: quicker recovery and return to work (GRADE moderate), higher technical success and lower rate of re-operation at the index site (GRADE moderate), maintenance of more normal spinal segment kinetics (GRADE moderate), and higher overall treatment success for two-level cervical degenerative disc disease (GRADE moderate)
- We are uncertain if adjacent-level surgery rates differ between C-ADR and fusion for one-level and two-level cervical degenerative disc disease (GRADE low).
- Evidence was also insufficient to determine the long-term durability of C-ADR devices.

(*Accessed March 2022*)

The North American Spine Society (NASS)
The NASS provided a Coverage Policy Recommendation for the following:

A. Cervical Artificial Disc Replacement:
(2015) Cervical artificial disc replacement (CADR, also known as cervical total disc replacement and cervical arthroplasty) may be indicated for the following diagnoses with qualifying criteria from the Cervical Fusion Coverage Recommendation, when appropriate.

1. Radiculopathy related to nerve root compression from one or 2-level degenerative disease (either herniated disc or spondylotic osteophyte) from C3-4 to C6-7 with or without neck pain that has been refractory to medical or nonoperative management.
2. Myelopathy or myeloradiculopathy related to central spinal stenosis from one or 2 level degenerative disease (either herniated disc or spondylotic osteophyte) from C3-4 to C6-7 with or without neck pain.

There is not significant evidence at this time to support its use for 3 or more levels or in the case of adjacent segment disease following an index fusion.

Cervical Artificial Disc Replacement is contraindicated in the following scenarios.

- Infection
  - active at the site of proposed implantation OR
  - systemic infection
- Osteoporosis or osteopenia
- Instability defined as:
  - translation greater than 3mm difference between lateral flexion-extension views at the symptomatic level OR
  - 11 degrees of angular difference between lateral flexion-extension views at the symptomatic level
- Sensitivity or allergy to implant materials
- Severe spondylosis defined as:
  - greater than 50% disc height loss compared to minimally or non-degenerated levels OR
  - bridging osteophytes OR
  - absence of motion on flexion-extension views at the symptomatic site
- Severe facet joint arthropathy defined as:
  - Radiographic confirmation of facet joint disease or degeneration
- Ankylosing spondylitis
- Rheumatoid arthritis
- Previous fracture with anatomical deformity
- Ossification of the posterior longitudinal ligament (OPLL)
- Malignancy active, in the cervical spine

B. Lumbar Artificial Disc Replacement

(2019) Lumbar artificial disc replacement may be indicated for individuals with discogenic low back pain who meet ALL of the following criteria from the Lumbar Fusion Coverage Recommendations:

- Symptomatic single level lumbar disc disease at L3-L4, L4-L5 or L5-S1 level
- Presence of symptoms for at least 6 months or greater and that are not responsive to multi-modal nonoperative treatment over that period that should include a physical therapy/rehabilitation program but may also include (but not limited to) pain management, injections, cognitive behavior therapy, and active exercise programs
- Any underlying psychiatric disorder, such as depression, should be diagnosed and the management optimized prior to surgical intervention
- Primary complaint of axial pain, with a possible secondary complaint of lower extremity pain

Lumbar Disc Arthroplasty is not indicated in any of the following scenarios:

1. Any case that does not fulfill ALL of the above criteria
2. Presence of symptomatic degenerative disk disease at more than one level
3. Presence of spinal instability with spondylolisthesis greater than Grade I
4. Chronic radiculopathy (unremitting pain with predominance of leg pain symptoms greater than back pain symptoms extending over a period of at least one year)
5. Osteopenia as evidenced by a DEXA bone mineral density T-score less than or equal to -1.0
6. Poorly managed psychiatric disorder
7. Significant facet arthropathy at the index level
8. Age greater than 60 years or less than 18 years
9. Presence of infection or tumor

Regulatory Status

Several prosthetic devices are currently available for cervical and lumbar disc arthroplasty. *The below lists are not intended to be comprehensive lists.*

FDA Approved Cervical Artificial Disc Device(s)

Implant & Approval Year	Approved Vertebral Level(s)	Description
Bryan® Cervical Disc (2009)	Single level C3-C7	It is indicated in skeletally mature patients for reconstruction of the disc from C3-C7 following single-level discectomy for intractable radiculopathy and/or myelopathy. The device is implanted via an open anterior approach. Intractable radiculopathy and/or myelopathy is defined as any combination of the following: disc herniation with radiculopathy, spondylotic radiculopathy, disc herniation with myelopathy or spondylotic myelopathy resulting in impaired function and at least one clinical neurological sign associated with the cervical level to be treated, and necessitating surgery as demonstrated using computed tomography (CT), myelography and CT and/or magnetic resonance imaging (MRI). Patients receiving the Bryan® Cervical Disc should have failed at least six weeks of non-operative treatment prior to implantation. (P060023)
M6-C Artificial Cervical Disc (2019)	Single level C3-C7	It is indicated for disc reconstruction following single-level discectomy in skeletally mature patients with intractable degenerative cervical radiculopathy with or without spinal cord compression at one level from C3 – C7. Degenerative cervical radiculopathy is defined as arm pain and/or a neurological deficit (numbness, weakness, deep tendon reflexes changes) with or without neck pain due to disc herniation and/or osteophyte formation and confirmed by radiographic imaging (computed tomography, magnetic resonance imaging, x-ray). The device is implanted via an anterior approach. Patients should have failed at least six weeks of conservative treatment or exhibit progressive neurological symptoms, which could lead to permanent impairment. (P170036)
Mobi-C® (2013)	Single level or two contiguous levels C3-C7	The device is placed between two adjacent neck bones (cervical vertebrae) to replace a diseased cervical disc that is causing arm pain and/or weakness or numbness. The device is intended for skeletally mature patients to replace a cervical disc in the neck (from C3-C7) following removal of the disc for conditions that result from a diseased or bulging disc at one or wo adjacent spinal levels. (P110002 or P110009)
PCM Cervical Disc	Single level C3-C7	The device is placed between two adjacent neck bones (vertebrae) to replace a diseased cervical disc causing arm pain and/or weakness or

(2012)		numbness. The device is intended to be used in skeletally mature patients to replace a cervical disc from C3-C7 following removal of the disc for conditions that result from a diseased or bulging disc (intractable radiculopathy or myelopathy) at only one level. (P100012).
Prestige® Cervical Disc System (2007)	Single level C3-C7	The device is indicated in skeletally mature patients for reconstruction of the disc from C3-C7 following single-level discectomy for intractable radiculopathy and/or myelopathy. The device is implanted via an open anterior approach. Intractable radiculopathy and/or myelopathy should present with at least one of the following items producing symptomatic nerve root and/or spinal cord compression which is documented by patient history (e.g., pain [neck and/or arm pain], functional deficit, and/or neurological deficit), and radiographic studies (e.g., CT, MRI, x-rays, etc.): 1) herniated disc, and/or 2) osteophyte formation. The safety and effectiveness of the device has not been established in patients who have not undergone at least six weeks of conservative treatment or had signs of progression or spinal cord/nerve root compression with continued non-operative care. (P060018)
Prestige LP® Cervical Disc (2014; 2016 received approval for implantation at two levels)	Single level or two contiguous levels C3-C7	It is indicated in skeletally mature patients for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and at least one of the following conditions confirmed by imaging (CT, MRI, x-ray): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels.
Prestige® ST Cervical Disc System (2007)	Single level C3-C7	Received FDA premarket application (PMA) approval as a class III device in 2007.
ProDisc-C® Total Disc Replacement (2007)	Single level C3-C7	The device is indicated for skeletally mature patients for reconstruction of the disc from C3-C7 following single-level discectomy for intractable symptomatic cervical disc disease (SCDD). Symptomatic cervical disc disease is defined as neck or arm (radicular) pain and/or a functional/neurological deficit with at least one of the following conditions confirmed by imaging (CT, MRI, or x-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes) and/or loss of disc height. The device is implanted via an open anterior approach. Patients should have failed

		at least six weeks of non-operative treatment prior to implantation. (P070001).
Simplify® Cervical Artificial Disc (2020)	Single level or two contiguous levels C3-C7	The device has PEEK endplates and a mobile ceramic core and is MRI compatible. (P200022)
SECURE®-C Cervical Disc (2012)	Single level C3-C7	The device is intended to be used in skeletally mature patients to replace a cervical disc in the neck (from C3-C7) following removal of the disc for conditions that result from a diseased or bulging disc (intractable radiculopathy or myelopathy) at only one level. (P100003)

Cervical Disc Prostheses Device(s) Under Investigation in the U.S.

- Freedom® AxioMed FDA IDE trial
- Kineflex C Spinal Motion FDA IDE clinical trial complete

IDE: investigational device exemption

FDA Approved Lumbar Artificial Discs

Implant & Approval Year	Approved Vertebral Level(s)	Description
ActivL® Artificial Disc (2018)	Single level L4-S1	The device is intended for disc reconstruction between the fourth and fifth lumbar or fifth lumbar and first sacral vertebrae to treat symptomatic degenerative disc disease (DDD). The weight-bearing total disc replacement (TDR) is intended to match the rotational motion of the lumbar disc in response to physiologic motion. (P120024)
Charite Artificial Disc (2004)	Single level from L4-S1	The device is approved for indications for the which define DDD as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. According to the FDA-approved labeling, these DDD patients should have no more than 3 mm of spondylolisthesis at the involved level. Patients receiving the device should have failed at least six months of conservative treatment prior to implantation. (P040006)

ProDisc®-L (2017)	Single level from L3-S1	The device is indicated for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one level from L3-S 1. 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 should have failed at least six months of conservative treatment prior to implantation. (P050010)

Devices without current approval in the United States

Device	Description
FlexiCore® Artificial Disc (Stryker Spine)	The metal-on-metal device for the lumbar spine has completed the investigational device exemption trial as part of the FDA approval process and is currently being used under continued access.
INMOTION® lumbar artificial disc (DePuy Spine)	The is a modification of the Charité® device with a change in name under the same premarket approval. The INMOTION® is not currently marketed in the United States.
Kineflex-L™ (Spinal Motion)	The device is a 3-piece, modular, metal-on-metal implant. An FDA advisory committee meeting on the Kineflex-L, scheduled in 2013, but was canceled without explanation.
Maverick™ artificial disc (Medtronic)	The device not marketed in the United States due to patent infringement litigation.

A number of other devices are under study in FDA Investigational Device Exemption (IDE) trials in the United States.

PRIOR APPROVAL

Not applicable.

POLICY

Cervical Artificial Disc: Initial
The use of an artificial intervertebral cervical disc prosthesis may be considered **medically necessary** when the individual has met **all of the following criteria:**

- Is skeletally mature with documented closure of growth plates; **and**
- Has **one of the following**:

- intractable cervical radicular pain with motor or sensory deficits; **or**
- myelopathy as evidenced by **one of the following**;
  - Bilateral upper or lower extremity weakness, numbness, or pain; **or**
  - Gastrointestinal dysfunction and other etiologies excluded (e.g., bowel or bladder); **or**
  - A physical exam positive for spasticity and other etiologies excluded; **or**
  - Bilateral loss of dexterity; **or**
  - Gait disturbances and other etiologies excluded; **and**

- Has failed at least six weeks of consistent conservative treatment, corresponding with the current pain episode, within the last year, to include **all of the following**:
  - Pharmacotherapy (i.e., prescription-strength analgesics, steroids, and/or NSAIDs); **and**
  - Provider directed physical therapy (PT) program; **and**
  - Activity modification; **and**

  Note: The following circumstances would be considered an exception to completing the above conservative therapy requirements;
  - *if the patient has severe or rapidly progressive symptoms of nerve root or spinal cord compression requiring hospitalization or immediate surgical treatment; or*
  - *Documentation of physical therapy which is contraindicated as explained by the physical therapist's or physician's clinical.*
- Anatomic derangement is documented by magnetic resonance imaging (MRI), computed tomography (CT), or myelography noting **one of the following**:
  - Herniated nucleus pulposus; **or**
  - Spondylosis (degenerative disc disease and osteoarthritis); **or**
- The planned implant is approved by the U.S. Food and Drug Administration (FDA); **and**
- Will be utilized at the number of levels based on the FDA approval for that device; **and**
  - *Note:*
    - *One level to include but not limited to: Bryan cervical disc, M6-C cervical disc, MOBI-C cervical disc, PCM cervical disc, Prestige cervical disc system, Prestige LP cervical disc system, ProDisc-C total disc replacement, SECURE-C artificial cervical disc, Simplify cervical artificial disc*
    - *Two contiguous levels to include but not limited to: MOBI-C cervical disc, Prestige-LP Cervical Disc, Simplify cervical artificial disc*
- Will be utilized within cervical disc(s) C3 through C7; **and**
- The individual is free from contraindications for an artificial intervertebral cervical disc prothesis as identified on the device FDA label. (*Each device may*

have its own contraindications. See the Cervical Artificial Disc: Investigational, list below for some identified contraindications)

Cervical Artificial Disc: Subsequent
The use of a subsequent artificial intervertebral cervical disc prosthesis at an adjacent level may be considered **medically necessary** when all of the following are met:

- Initial criteria above are met; **and**
- The device is FDA-approved for two levels; **and**
- The planned subsequent procedure is at a different cervical level than the initial cervical artificial disc replacement; **and**
- Clinical documentation confirms the initial artificial intervertebral cervical disc prothesis implantation is fully healed.

Cervical Artificial Disc: Revision
Revision of an artificial intervertebral cervical disc prosthesis may be considered **medically necessary** when imaging confirms failure of the implanted device (e.g., loosening, dislodgement, fracture, discitis infection) and the individual meets the criteria for a one- or two-level implant as noted above.

Cervical Artificial Disc: Investigational
An artificial intervertebral cervical disc prosthesis is considered **investigational** when the criteria above has not been met and for all other indications, including but not limited to the following due to a lack of evidence demonstrating an impact on improved net health outcomes:

- Active systemic infection or infection localized to the site of implantation
- Allergy or sensitivity to implant materials (e.g., cobalt, chromium, titanium, polyethylene)
- Anatomic deformity (e.g., ankylosing spondylitis)
- Chronic non-specific neck or arm pain of an unknown etiology
- Combined use of an artificial cervical disc and fusion (hybrid construct)
- Malignancy
- Metabolic bone disease (e.g., osteoporosis, osteopenia, osteomalacia)
- Non-FDA–approved cervical disc prosthesis
- Ossification of the posterior longitudinal ligament
- Planned procedure will lead to disc implantation at more than two levels
- Presence of severe facet arthritis at the surgical level
- Previous fusion at another cervical level (hybrid construct)
- Prior surgery at the proposed treated level
- Rheumatoid arthritis or other autoimmune disease
- Translational instability (Clinically significant cervical instability on resting or lateral flexion/extension plain X-rays defined as kyphotic deformity/significant reversal or lordosis or spondylolisthesis)

Lumbar Artificial Disc: Initial

The use of an artificial intervertebral lumbar disc prosthesis may be considered **medically necessary** when the individual has met **all of the following criteria:**

- Is skeletally mature with documented closure of growth plates; **and**
- Has chronic, unremitting, discogenic low back pain
- Single level, degenerative disc disease (DDD) is confirmed by a complex imaging study (e.g., Computed Tomography (CT), Magnetic Resonance Imaging (MRI)); **and**
- Has failed at least six weeks of consistent conservative treatment corresponding with the current pain episode, within the last year, to include **all of the following**:
    - Pharmacotherapy (i.e., prescription-strength analgesics, steroids, and/or NSAIDs); **and**
    - Provider directed physical therapy (PT) program; **and**
    - Activity modification; **and**

  Note: The following circumstances would be considered an exception to completing the above conservative therapy requirements;
    - *if the patient has severe or rapidly progressive symptoms of nerve root or spinal cord compression requiring hospitalization or immediate surgical treatment; or*
    - *Documentation of physical therapy which is contraindicated as explained by the physical therapist's or physician's clinical.*
- The device is approved by the U.S. Food and Drug Administration (FDA); **and**
- The specified implant will be inserted at the FDA approved spinal level specific to the implant to be used; **and**
- The individual is free from contraindications for an artificial intervertebral lumbar disc prothesis as identified on the device FDA label. *(Each device may have its own contraindications. See the Lumbar Artificial Disc: Investigational, list below for some identified contraindications)*

Lumbar Artificial Disc: Revision

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

Lumbar Artificial Disc: Investigational

A lumbar disc arthroplasty prosthesis is considered **investigational** when the criteria above has not been met and for all other indications, including but not limited to the following due to a lack of evidence demonstrating an impact on improved net health outcomes:

- Active systemic infection or infection localized to the site of implantation,
- Allergy or sensitivity to implant materials (e.g., cobalt, chromium, titanium, polyethylene)

- Chronic non-specific lumbar pain of an unknown etiology
- Combined use of a prosthesis and spinal fusion (hybrid construct)
- Lumbosacral spinal fracture
- Malignancy
- Metabolic bone disease (e.g., osteoporosis, osteopenia, osteomalacia)
- Moderate or severe facet arthropathy or pars defect at the operative level on a preoperative magnetic resonance imaging (MRI) scan, computed tomography (CT) scan or plain film
- Non-FDA–approved lumbar disc prosthesis
- Off-label use
    - This includes but is not limited to the implanted lumbar level or number of treatment levels approved by the FDA.
- Previous fusion at another lumbar level (hybrid construct)
- Previous lumbar spine surgery where the previous surgery destabilized the spine or where the spine at the level of the previous surgery is an alternate source of pain
- Presence of severe facet arthritis at the surgical level
- Rheumatoid arthritis or other autoimmune disease
- Scoliosis of the lumbosacral spine
- Vascular, urological, or other peritoneal or retroperitoneal pathology that may preclude safe and adequate spine exposure as required for the surgery

Policy Guidelines

Required Documentation

- Clinical notes that document the requesting surgeon personally evaluated the individual before submitting a request for surgery (except in cases of malignancy, trauma, infection, or rapidly progressive neurologic symptoms)
- Detailed documentation of extent and response to non-operative conservative therapy, if applicable, including outcomes of any procedural interventions, medications used and physical therapy/physiatrist notes
- Copy of radiologist's report(s) for diagnostic imaging (MRIs, CTs, etc.) completed within the past 12 months. Imaging must be performed and read by an independent radiologist.

Tobacco Use

- Evidence shows that tobacco use is considered a risk factor for poor healing. Tobacco use (e.g., cigarettes, cigars, pipes, vaping, or smokeless tobacco in the form of chew or snuff) within the previous four weeks is a contraindication for the procedure. If the patient utilizes tobacco, tobacco cessation should be encouraged.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 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)
- 0164T Removal of total disc arthroplasty, anterior approach, lumbar, each additional interspace
- 0165T Revision of total disc arthroplasty, anterior approach, lumbar, each additional interspace
- 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
- 22857 Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression); single interspace, lumbar
- 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)
- 22860 Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression); second interspace, lumbar (List separately in addition to code for primary procedure)
- 22861 Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, single interspace; cervical
- 22862 Revision including replacement of total disc arthroplasty (artificial disc) anterior approach, single interspace; lumbar
- 22864 Removal of total disc arthroplasty (artificial disc), anterior approach, single interspace; cervical
- 22865 Removal of total disc arthroplasty (artificial disc), anterior approach, single interspace; lumbar
- 22899 Unlisted procedure, spine

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POLICY HISTORY		
Date	**Reason**	**Action**
March 2022	Annual Review	Policy Revised
March 2021	Annual Review	Policy Revised
March 2020	Annual Review	Policy Revised
March 2019	Annual Review	Policy Revised
March 2018	Annual Review	Policy Revised
March 2017	Annual Review	Policy Revised
April 2016	Annual Review	Policy Revised

August 2015	Interim Review	Policy Revised
May 2015	Annual Review	Policy Revised
February 2015	Annual Review	Policy Revised
February 2014	Annual Review	Policy Renewed
March 2013	Annual Review	Policy Renewed
March 2012	Annual Review	Policy Renewed
April 2011	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
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