

## Medical Policy Manual

**Topic:** Artificial Intervertebral Disc

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**Section:** Surgery

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### IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

### DESCRIPTION

Artificial intervertebral discs, also known as intervertebral disc prostheses, are synthetic replacements for damaged intervertebral discs in the cervical or lumbar regions of the spine. These devices are being studied as a motion-preserving alternative to spinal fusion.

There are a number of artificial cervical and lumbar discs that are under investigation, some of which have received approval for marketing from the U.S. Food and Drug Administration (FDA):

Artificial Cervical Discs		
Device name	Manufacturer	FDA Approved?
Advent <sup>®</sup>	Orthofix <sup>®</sup>	No
BRYAN <sup>®</sup> disc	Medtronic	Yes – single level
Cadisc <sup>™</sup> -C	Rainier <sup>®</sup> Technology	No
Cervicore (metal on metal-cobalt-chromium-molybdenum)	Stryker	No IDE status revoked by FDA
Discover <sup>™</sup> (polyethylene on titanium alloy)	DePuy Synthes (formerly DePuy Spine, Inc.)	No IDE only

Artificial Cervical Discs		
Device name	Manufacturer	FDA Approved?
Freedom <sup>®</sup> Cervical Disc	AxioMed <sup>®</sup>	No
Kineflex <sup>®</sup> -C (cobalt-chromium-molybdenum)	SpinalMotion	No IDE only
M6 <sup>®</sup> -C	Spinal Kinetics <sup>™</sup>	No IDE only
Mobi-C <sup>®</sup>	LDR Spine USA	Yes 1- and 2-level
NeoDisc <sup>®</sup>	NuVasive <sup>®</sup>	No IDE only
PCM <sup>®</sup> (Porous Coated Motion ) Cervical Disc (polyethylene-on-metal)	Cervitech, now part of NuVasive <sup>®</sup>	Yes – single level
Prestige <sup>®</sup> Cervical Disc System (includes Prestige ST) (titanium-ceramic)	Medtronic	Yes – single level
Prestige <sup>®</sup> -LP Cervical Disc	Medtronic	Yes – single level
ProDisc <sup>®</sup> -C	DePuy Synthes	Yes – single level
SECURE <sup>®</sup> -C	Globus Medical	Yes – single level

Artificial Lumbar Discs		
Device name	Manufacturer	FDA Approved?
Activ-L <sup>™</sup>	Aesculap <sup>®</sup>	No
Cadisc <sup>™</sup> -L	Rainier <sup>®</sup> Technology	No
Charité <sup>®</sup>	<del>DePuy Spine, Inc.</del>	- Withdrawn from the market
FlexiCore <sup>®</sup>	Stryker	No
Freedom <sup>®</sup> Lumbar Disc (FLD)	AxioMed <sup>®</sup>	No
INMOTION <sup>®</sup> (formerly Charité <sup>®</sup> )	Depuy Spine <sup>™</sup>	Yes – single level. This device is a modification of the Charité design
M6 <sup>®</sup> -L	Spinal Kinetics <sup>™</sup>	No
Maverick <sup>®</sup>	Medtronic	No
ProDisc <sup>®</sup> -L	DePuy Synthes (formerly Synthes Spine)	Yes – single level
XL TDR <sup>®</sup>	NuVasive <sup>®</sup>	No

## MEDICAL POLICY CRITERIA

- I. Anterior total cervical disc replacement using an artificial intervertebral disc following complete decompression is considered **medically necessary** in skeletally mature patients with symptomatic cervical disc degeneration when *all* of the following criteria are met:
  - A. Disc replacement is limited to a single-level between C3 and C7
  - B. Diagnosis of cervical radiculopathy or myelopathy with radicular arm pain and

neurological deficit in a specific nerve root distribution or myelopathic level consistent with the neuroimaging and the operative cervical spinal level when *at least one* of the following criteria (1 or 2) are met:

1. There is clinical documentation that a minimum of 6 weeks of conservative nonoperative therapy failed to adequately treat the patient's symptoms, including *at least two* of the following therapies:
  - a. Use of narcotic or nonnarcotic analgesics, and/or nonsteroidal anti-inflammatory drugs (NSAIDs) if not contraindicated
  - b. Physical therapy
  - c. Alteration of activities, including but not limited to cessation of activities that exacerbate symptoms
2. Severe or rapidly progressive symptoms of nerve root or spinal cord compression requiring immediate surgical treatment (e.g., increasing numbness/tingling; increasing motor loss or  $\leq 3/5$  muscle strength)

C. Documented findings on MRI, CT, or other imaging are consistent with the patient's symptoms and demonstrate moderate to severe spinal stenosis, cord compression, or nerve root compression from *at least one* of the following at the operative level:

1. Herniated disc
2. Spondylosis, defined as the presence of osteophytes

D. The patient is an appropriate candidate for anterior cervical spinal surgery, including *absence of all* of the following contraindications:

1. Prior surgery at the operative level
2. Prior fusion at the same or any adjacent level or artificial disc placement at any cervical level
3. Radiographic confirmation of severe facet joint pathology of involved vertebral bodies
4. Concomitant conditions known to affect osteogenesis including any of the following:
  - a. Metabolic bone disease (e.g., gout, osteoporosis [T-score  $\leq -2.5$  by DXA], osteomalacia, Paget's disease)
  - b. Current or past history of primary or metastatic spinal malignancy
  - c. Conditions requiring daily high-dose oral steroids (e.g., rheumatoid arthritis)

II. Total cervical disc replacement that does not meet the medical necessity criteria in I.B-D above is considered **not medically necessary**.

III. Total disc replacement with artificial intervertebral discs is considered **investigational** for all

other indications, including but not limited to the following:

- A. Artificial intervertebral disc placement at more than one or more spinal levels
- B. Combination procedures with artificial disc(s) placement and fusion at an adjacent or distant spinal level (“hybrid” procedures)
- C. Spinal levels other than those between C3 and C7

## SCIENTIFIC EVIDENCE

### Background

Evaluating the safety and effectiveness of total disc replacement with artificial intervertebral discs (TDR) requires randomized comparisons with fusion, which is the current standard for surgical treatment of degenerative disc disease (DDD). In their 2008 guidance for studies for the total artificial disc, the U.S. Food and Drug Administration (FDA) recommended as the appropriate study design a multi-center, randomized, prospective, concurrently controlled clinical trial.<sup>[1]</sup> “Such a study design offers the benefits of prospectively acquired data. It also provides advantages over other types of study designs by offering greater control of all parameters and by addressing some of the biases introduced by the other study designs.”

- Randomization is necessary in evaluating any treatment in which improvements in pain and function are the most clinically relevant outcomes. Pain is a subjective outcome and can be influenced by nonspecific effects (e.g., placebo response, the natural history of the disease, and the severity of the condition). Random treatment assignment to either a control (standard of care) or treatment (procedure being studied) study group helps control for nonspecific effects. In addition, randomization promotes equal distribution of patient characteristics — clinical and demographic, known and unknown — across the study groups. Consequently, any difference in the outcome observed between the study groups may, with reasonable assuredness, be attributed to the treatment under investigation.
- Studies must include sufficient numbers of participants in order to eliminate the element of chance as an explanation of study outcomes, and to allow generalization of results.
- Postoperative follow-up of at least five years is recommended to assess the long-term effects of TDR on overall health outcomes.<sup>[2-7]</sup> Long-term data are required for the following reasons:
  - Patterns of degenerative changes following TDR or fusion take at least five years to become measurable; thus, the impact of motion preservation are unknown
  - The benefits of spinal surgery are known to deteriorate over time; therefore, it cannot be assumed that early benefits seen at one to two years following TDR will remain stable in the mid- and long-term.
  - Complications and adverse effects for spinal surgery tend to increase over time.

### Effectiveness

The extensive information in U.S. and international published literature for artificial intervertebral discs is encouraging and supports the need for further research.<sup>[2-5,8-14]</sup> Primary effectiveness outcomes include

symptom reduction and improved daily function. A secondary outcome of interest in most studies is the ability and time to return to work.

The advantage most often cited for TDR over fusion is the preservation of mobility at the operative level. The hypothesis is that this motion preservation may eliminate or slow the development of degenerative disc disease at adjacent vertebral levels compared with fusion. The available evidence reflects continued controversy on this hypothesis, and is insufficient to permit conclusions as to whether TDR affects the postsurgical development of clinically significant adjacent segment degenerative disc disease.

- There is controversy in the published literature as to whether fusion of a spinal segment leads to early degeneration in adjacent segments.<sup>[15-23]</sup>
- It is unknown whether TDR results in a reduction in adjacent segment degeneration (ASD) compared with fusion.<sup>[24,25]</sup>
- It is unknown to what degree any degenerative changes to adjacent segments following spinal surgery may be clinically relevant or impact clinical outcomes.<sup>[5,6,26-28]</sup>
- The pivotal trials used in the FDA approval process reported that motion at the *operative* level did not correlate with clinical success.<sup>[29-33]</sup>
- These FDA trials also demonstrated that the motion at the *adjacent* levels, as measured by dynamic radiographs, was not significantly different for the TDR groups compared with the fusion control groups.
- As part of FDA approval for marketing of these devices, sponsors are prohibited from making any claims or suggestions relating preservation of motion with clinical success.
- FDA also prohibited any mention by TDR sponsors of prevention of adjacent level disease.

### Safety

Investigation is ongoing regarding the long-term safety, complications, and reoperation rates for TDR compared with other therapies. Specific concerns include the following:

- The rate of failure of the TDR device itself is unknown compared with other therapies, including the durability and replacement rates.<sup>[26-28,34,35]</sup>
- It is unknown if subsequent surgical options are limited if revision is needed due to complications or device failure.<sup>[34-38][39]</sup>
- It is unknown how TDR impacts the rate of degenerative disc disease in adjacent discs compared to other therapies.<sup>[24,40-44]</sup>
- It is unknown whether TDR increases the rate of degeneration in the facet joints at the level of the implant compared to other therapies.

Specific complications reported in the literature to date include the following:<sup>[34-38,45-64]</sup>

- Allergic reaction to implant materials
- Vertebral body and pedicle fractures
- Lymphocytic<sup>[65]</sup> or granulomatous<sup>[66]</sup> reaction to metal-on-metal artificial disc requiring revision (pseudotumor formation)
- Excessive wear, bending or breakage of any component of the artificial disc device
- Loosening, migration, or dislodging of the artificial disc device
- Collapse of the artificial disc device into the bone (subsidence), migration, or extrusion

- Fusion, heterotopic ossification, and osteophyte formation at the index or adjacent levels can cause loss of motion and nerve root compression
- Errors in positioning, angle, or prosthesis size (e.g., under sizing)
- Wear debris from the polyethylene and metallic components of the prostheses with associated inflammation have been found in surrounding tissue<sup>[67]</sup>
- Spinal cord compression with possible spinal cord injury requiring implant removal and fusion.
- Chronic inflammatory reaction and osteolysis has been found in periprosthetic tissue.
- Concerns have been published related to the release of metallic ions into the body due to friction on the metallic components of the prosthesis during movement. The long-term effect of these ions in the body is unknown
- Acquired spondylolysis
- Dysphagia<sup>[68]</sup>
- Retrograde ejaculation has been reported following lumbar TDR in some men
- Hypopharyngeal injury leading to dyspnea and subcutaneous emphysema
- Documented complications during removal of failed lumbar discs included accidental lesions to major blood vessels, small bowel, and ureter, and profound bleeding from bone
- Incomplete paraplegia following artificial cervical disc dislocation<sup>[69]</sup>

## Literature Appraisal: Single-level Cervical Discs

### Technology Assessments

Two recent technology assessments reported the following results:

- The BlueCross BlueShield Association Technology Evaluation Center (TEC) conducted a technology assessment of mid-term (4-5 year) outcomes in 2011<sup>[70]</sup> which updated prior assessments in 2007<sup>[2]</sup> and 2009<sup>[3]</sup>. The TEC assessment concluded that although results beyond two years follow-up are consistent with continued noninferiority of artificial discs and lower cumulative reoperation rates, uncertainty remains due to the low follow-up rates<sup>[71,72]</sup>.
- In 2010 the American Academy of Orthopaedic Surgeons (AAOS) published a technology overview comparing outcomes of cervical TDR with anterior cervical fusion.<sup>[73]</sup> This is the most current version of the AAOS technology overview which included 7 studies and reported the following comparisons between TDR and cervical discectomy and fusion:
  - Most studies considering patient characteristics that predict successful outcomes for cervical TDR compared with fusion “did not report or conduct the appropriate statistical analyses.”
  - The majority of scores for pain and functional levels were found to be inconclusive or have no statistically significant difference between TDR and fusion. Several studies reported better outcomes in Neck Disability Index measures for TDR up to 3 months postoperatively; however, these differences were not present or were inconclusive at longer follow-up.
  - The revision rates for TDR and fusion could not be compared because the studies did not report secondary surgical procedures similarly.
  - The rate of adverse events in the included studies was inconclusive.
  - Economic analyses found no statistically significant differences in hospital length of stay for these two procedures. Patients who received TDR returned to work in significantly fewer days (range 14-16 days) than patients who underwent fusion. However, no

statistically significant difference was found in the number of patients who returned to work, including heavy work, at 24 months.

## Systematic Reviews and Meta-analyses

### *Effectiveness*

A number of systematic reviews and meta-analyses of studies comparing the outcomes of cervical TDR with those of fusion also noted that the majority of randomized trials were limited to 2 year follow-up data.<sup>[74-81]</sup> While all reported promising outcomes 2 years postoperatively, long-term data from well-designed randomized controlled trials (RCTs) was lacking. Authors continue to recommend ongoing RCTs to determine longer-term outcomes. The most comprehensive review was a 2013 Cochrane systematic review with a meta-analysis of 9 studies (2,400 patients) with 1 to 2 years of follow-up.<sup>[82]</sup> As in other reviews, the evidence quality of the 9 included RCTs<sup>[61,83-90]</sup> was graded as very low to moderate due in part to the non-blinded outcome measures. Results of the TDR group were statistically better than the anterior cervical discectomy and fusion (ACDF) group for many of the primary comparisons, but differences were small (<10% of the scale) and not considered to be clinically relevant. No significant difference between AIDA and fusion was found for adjacent level surgery.

### *Safety and Reoperation Rates*

Anderson and Hashimoto conducted a 2012 systematic review of studies comparing the long-term safety of TDR and fusion.<sup>[91]</sup> The primary safety issues were long-term complication rates, rates and causes of repeat surgery, and how these rates change over time. Both comparative and non-comparative studies with at least 48 months followup were included in the review. Two RCTs compared cervical TDR with fusion at 4-5 years follow-up. The rate of repeat surgeries was similar. One small subset of an RCT reported lower rates of adjacent disc heterotopic ossification in TDR patients. The rates of other adverse events were similar between the TDR and fusion groups. The authors rated the current level of evidence on TDR safety outcomes as low and called for additional comparative studies with follow-up of at least 4 years.

Investigators in the FDA IDE trials for the Prestige, ProDisc-C, Bryan, Kineflex-C, and Mobi-C artificial cervical discs have reported lower reoperation rates following single-level TDR (mean 4.3%) compared with single-level fusion (mean 9%) at 2-years follow-up. Singh et al. considered this reoperation rate within 2 years after fusion to be unusually high.<sup>[92]</sup> Thus, the authors conducted a retrospective review of 176 fusion patients in their clinical practice and compared their reoperation rates with those of the IDE trials. All patients had at least 2 years follow-up and met the inclusion criteria in the IDE trials. Final outcomes were available on 159 patients; the rate of reoperation within 2 years was 2.1% for single-level fusion. Even with longer follow-up (mean 3.5 years) including multilevel cases, their reoperation rate was only 7.6%. While this retrospective study design is considered unreliable, the outcomes suggest possible threshold differences for reoperation in the fusion arm of the IDE trials compared with the threshold in a clinical setting. The question also arises as to whether the reoperation threshold differed between the TDR and the fusion arms within each of the IDE trials

### *Segmental Motion and Adjacent Level Degeneration*

In a 2012 meta-analysis on range of motion (ROM), Chen et al. reviewed studies in which pre- and postoperative ROM measurements of both the index and adjacent levels were reported.<sup>[93]</sup> Ten studies were included with a total of 974 patients. The authors found no significant changes in ROM at the

index level following TDR. However, there was an increase in ROM at the adjacent levels that was similar to the changes seen following fusion. It is this compensatory increased ROM at adjacent segments that has been behind the hypothesis that fusion may increase adjacent level degeneration. The authors concluded that the results of this meta-analysis suggested that the protective effect against adjacent segment degeneration might not be as good as has been believed, and long-term evidence is still needed.

In 2012 two systematic reviews and one meta-analysis compared adjacent segment disease after at least two years following TDR or fusion.<sup>[42-44]</sup> All three reports concluded that, to date, there is no evidence that TDR decreases adjacent segment disease compared with fusion.

### Randomized Controlled Trials

A number of published randomized trials have reported outcomes less than 5 years following fusion or TDR.<sup>[6,72,83-86,94-103]</sup> Data from randomized, controlled trials of sufficient duration to begin to measure long-term health outcomes ( $\geq 5$  years) are now becoming available.<sup>[71,72,104-107]</sup>

All of these studies had significant design and analysis limitations that hinder interpretation of the data including the following examples:

- Small study populations limit the ability to rule out the role of chance as an explanation of study findings.<sup>[5,86,94,95,97,108]</sup>
- The report on the 2-year outcomes of the FDA trial for the PRESTIGE cervical disc was an interim analysis that included only 80% of the TDR group and 75% of the fusion control group.<sup>[85]</sup> The Burkus et al article reporting 5-year outcomes of this trial was again an interim report that included only 50% of the 533 participants from the 2-year study who agreed to participate in the extended study.<sup>[71]</sup> This subset analysis included only the first 271 participants (50%) to reach the 5-year postoperative milestone.
- Well-executed randomization is particularly important in studies which include subjective outcomes such as pain, patient satisfaction, and quality of life. This was not achieved in the FDA trial for the Bryan cervical disc.<sup>[84,109]</sup> Of the 582 patients initially randomized, 117 (37 from the TDR group and 80 from the fusion group) declined surgery. This 20% loss of patients following randomization undermines the randomization, potentially confounding the treatment effect observed. This flaw is compounded in this study by the treatment crossover of 13 patients following randomization, 12 from the TDR group to the fusion group and one from the fusion group to the TDR group. Since patients were not blinded to their treatment assignment, this crossover after randomization likely reflects patient bias toward which treatment they felt would be most beneficial.
- The study endpoints were unclear, inconsistent or incomplete. For example, in the study on which FDA approval for the PRESTIGE device was based, the primary endpoint was the patient's "overall success" which was calculated using: Neck Disability Index (NDI) scores; ill-defined neurological status scores; and the absence of implant or related surgical adverse events or "second surgery classified as a failure". Other components of pain and function (i.e., SF-36 scores, neck and arm pain scale scores) were evaluated separately but were not included in determining overall success. In addition, the criteria by which a second surgery is classified as a success or failure were not defined.
- The population studied may not be reflective of typical surgical candidates for DDD. Although the inclusion criteria for the FDA trials only required six weeks of medical management, the AAOS guidance for the design of clinical trial of artificial intervertebral discs recommends six months of conservative therapy before the patient is considered a surgical candidate.<sup>[110]</sup>

## Conclusions

Despite the numerous methodologic limitations of the available studies, including limited long-term data, the use of single-level artificial cervical discs has gained increasing acceptance in the U.S. This is due, in part, to the desire for cervical motion preservation in the fairly young candidates for cervical TDR. In addition, the short- to mid-term outcomes of RCTs have consistently reported primary outcomes following single-level cervical TDR to be at least equivalent to those following cervical fusion. In addition, TDR patients required shorter postoperative hospitalization and returned to work more quickly than fusion patients, though the rate of patients able to return to work was equivalent at 6 months follow-up.<sup>[80]</sup>

## **Literature Appraisal: Single-level Lumbar Discs**

### Technology Assessment

- An updated TEC Assessment in February 2007 reviewed the evidence on artificial lumbar disc replacement devices.<sup>[4]</sup> No additional RCTs had been published since the FDA approval of the ProDisc-L in 2006. The Assessment found that both the Charité and ProDisc-L trials had been evaluated with one randomized clinical trial, designed as a noninferiority trial, with the comparator being fusion. The lower-than-expected success rates of fusion in the Charité and ProDisc-L trials raised questions regarding the validity of a noninferiority trial and the noninferiority margin selected. The Charité trial showed little evidence of superiority, and the ProDisc-L analysis was problematic because of missing values and uncertain outcomes for all patients. Given the invasiveness of the procedure, there were no obvious short-term advantages. In terms of the long-term goal of reducing stress on adjacent levels, the duration of follow-up was insufficient for evaluation.

The assessment made the following conclusions:

- Given what is known about fusion as a comparator treatment, neither of the noninferiority trials provided convincing evidence of efficacy
  - The evidence supporting the effectiveness of the ProDisc -L and Charité artificial disc was limited
  - There was no immediately discernible advantage to use of the artificial disc.
- A 2013 update of this TEC assessment evaluated the 5-year follow-up from the pivotal trial of the ProDisc-L.<sup>[111]</sup> The Assessment made the following conclusions:
    - Additional study of the ProDisc-L in an appropriately powered clinical trial with minimum 5-year follow-up is needed to confirm the results of the investigational device exemption (IDE) trial in patients with single-level chronic symptomatic DDD 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 disk—that it maintains range of motion and thereby reduces the risk of adjacent-level segment degeneration better than fusion—remains subject to debate.

### Systematic Reviews

In 2010, two systematic reviews concluded that high-quality RCTs with a relevant control group and long-term follow-up are needed to evaluate the effectiveness and safety of artificial lumbar disc replacement.<sup>[22,112]</sup>

A 2012 systematic review by Wang et al<sup>[113]</sup> reported on a pooled analysis of two randomized controlled trials<sup>[114,115]</sup> that compared the risk of adjacent segment pathology (ASP) following lumbar artificial disc replacement with those following lumbar fusion. The overall strength of the evidence was graded as “moderate”, defined as moderate confidence that the evidence reflects the true effect, and further research may change the confidence in the estimate of effect and may change the estimate. The consensus statement was that this evidence demonstrated the risk of ASP requiring surgery is likely greater after fusion, but the risk is still quite rare. The strength of the statement was graded as weak due to the study limitations which included the lack of evaluation by an independent observer in both studies, and a high loss to follow-up in the Guyer et al study, increasing the risk of bias. Also, the confidence interval was relatively wide, which was attributed to the rarity of lumbar ASP and the limited number of ASP events. In addition, it is unclear whether different lumbar artificial discs can be generalized as essentially equal. The authors concluded that more studies are needed on this topic.

### Randomized Controlled Trials

The following studies were not included in the systematic reviews summarized above:

- The five-year results of the extension of the initial 2-year pivotal study for the ProDisc®-L were summarized in 2012 by two investigators from one site of this multicenter study.<sup>[116]</sup> The 5-year results have not been published as a full-length article by the research group. Out of an original 236 patients randomized, 193 (81.8%) were included in the 5-year follow-up (137 ProDisc-L and 56 controls). Results showed non-inferiority, but not superiority of artificial disc replacement, with 53.7% of ProDisc-L patients and 50.0% of fusion patients achieving overall success at 5 years compared with 63.5% and 45.1% at 2 years for the ProDisc-L and fusion groups, respectively. This change in overall success in ProDisc-L patients between 2 and 5 years indicates a possible decrement in response over time with the artificial disc. This decrement in response rate was not observed in the standard fusion group and resulted in convergence of the primary outcome measures between groups over time.

Several of the individual components of the primary outcome measure were also statistically better in the ProDisc-L group at 2 years, but were no longer significantly different at 5 years. For example, at 5 years ODI scores improved by 15% or more in 78.6% of ProDisc-L patients compared to 76.5% of controls. A similar percentage of patients maintained or improved SF-36 physical component scores compared with baseline (81.3% ProDisc-L and 74.0% fusion), and overall neurologic success was obtained in 88.8% of ProDisc-L patients and 89.6% of fusion patients. Secondary surgeries at the index level occurred in 8% of ProDisc-L patients and 12% of fusion patients (p value not reported). Device success, defined as the absence of any reoperation required to modify or remove implants and no need for supplemental fixation, was achieved in 93.3% of ProDisc-L patients and 93.2% of fusion patients. Analysis of visual analog scores (VAS) for pain excluded patients who had secondary surgical interventions (11 ProDisc®-L and 5 fusion). For the ProDisc-L group, VAS improved from a mean of 75.9 at baseline to 37.1 at 5 years. Mean VAS for the fusion group improved from 74.9 at baseline to 40.0 at 5 years. There was no significant difference in VAS between the groups. Narcotic use decreased from a baseline of 84% to 44.6% of ProDisc-L patients and from 76% to 42.5% of fusion patients.

- In 2009, Berg et al. published 2-year follow-up of an RCT of 1- and 2- level total disc replacement.<sup>[114]</sup> Five-year follow-up of patients in this study was reported in 2013.<sup>[117]</sup> Patients with symptomatic degenerative disc disease in 1 or 2 motion segments between L3 and S1 were randomly assigned to 1 of 3 total disc replacement devices (Charité, ProDisc, or Maverick, n=80) or to instrumented fusion (n=72). The randomization was stratified for number of levels, with 56% of total disc replacement patients having 1-level surgery compared to 46% of fusion patients. Only patients who did not have a preference to the type of treatment were enrolled in the trial, and they were informed of the result of randomization upon arrival at the hospital for surgery. No patient left the study when informed of the randomization. There was 100% follow-up at the 1- and 2-year assessments, and 99.3% follow-up at the 5-year assessment.

The primary outcome, which does not appear to be a validated measure, was a global assessment of back pain consisting of “total relief”, “much better”, “better”, “unchanged”, or “worse”. The percentage of patients in the disc replacement group who reported being pain-free was 30% at the 1- and 2-year follow-up, and 38% at 5-year follow-up. In the fusion group, 10% reported being pain-free at 1 year and 15% reported being pain-free at 2 and 5 years. At 5 years, a similar percentage of patients reported being either totally pain free or much better (72.5% for disc replacement and 66.7% for fusion). The total disc replacement group showed lower mean VAS for pain at 1 and 2 years (25.4 vs. 29.2, respectively) and had better outcome scores on a quality-of-life scale (EQ-5D) and the ODI at 1 year (19.5 vs. 24.9, respectively) but not the 2-year follow-up (20.0 vs. 23.0, respectively). At 5-years, the disc replacement group had modestly improved outcome scores for both VAS back pain (23 vs. 31) and ODI (17 vs. 23).

The most common cause of reoperation in the disc replacement group was to fuse the index level that was believed to cause persistent or recurrent pain (5%). The most common cause of reoperation in the fusion group was operation at an adjacent level (7%). Twenty-two disc replacement patients underwent postoperative facet block due to remaining pain. Twenty fusion patients had their instrumentation removed due to persistent or recurrent pain. The investigators found no association between achievement of surgical goals (absence of mobility with fusion and maintenance of mobility with disc replacement) and clinical outcomes at 2 years.

The remaining published randomized trials of TDR in the lumbar spine do not permit conclusions regarding long-term health outcomes.<sup>[114,118-123]</sup> Data from these studies are unreliable due to the following methodologic limitations which undermine the validity of the results:

- All of the authors of articles related to the FDA trials for the CHARITE and ProDisc-L discs specifically noted that two years follow-up does not allow conclusions about the impact of TDR on adjacent-level DDD compared with fusion.
- In the pivotal trial for the ProDisc-L, conclusions are not possible due to missing data. Eleven percent of fusion patients and 7.5% of ProDisc-L patients were excluded from the results. No intent-to-treat analysis was provided.

### Conclusion

Current evidence is insufficient to permit conclusions about the long-term benefits and safety of total disc replacement in the lumbar spine.

### **Literature Appraisal: Multilevel and Combination TDR/fusion**

In August, 2013 the Mobi-C received PMA approval from the FDA for implantation following discectomy at two contiguous cervical spinal levels between C3 and C7.<sup>[124]</sup> This approval was based on an industry-sponsored multicenter non-inferiority IDE study of artificial cervical disc placements (n=225 randomized, 9 training) compared with fusion (n=105) at 1- and 2-levels. At 24-months follow-up, complete data was available for 195 (92.4%) Mobi-C patients and 81 (91%) fusion patients. On average, all patients showed significant improvement on pain measurements, with the TDR patients having significantly greater improvement compared with the fusion group. Adjacent-level degeneration was observed in the superior segment in 13.1% of TDR patients and 33.3% of fusion patients. Adjacent-level degeneration was observed in the inferior segment in 2.9% of TDR patients and 18.1% of fusion patients. However, while the stated aim of the study was for safety and effectiveness of the Mobi-C disc at 2 contiguous levels, it also stated that the study included both 1- and 2-level treatment arms. Thus, it appears that the reported outcomes did not include a direct comparison of outcomes for 2-level TDR with 2-level fusion. Further randomized comparisons are needed that compare multi-level TDR with fusion at the same levels.

There are currently no lumbar artificial intervertebral discs with FDA approval for use at more than one spinal level. Studies on multilevel TDR and on combined TDR and fusion, also referred to as a hybrid procedure, are limited to small feasibility studies or have been included as a subset of RCTs with single-level TDR.<sup>[125-127]</sup> This preliminary evidence does not permit conclusions about the long-term benefits and safety of these uses of artificial intervertebral discs.

## **Clinical Practice Guidelines**

### Cervical Discs

There is currently only one evidence-based clinical practice guideline from U.S. neurosurgery or orthopedic professional associations that addresses cervical TDR.

#### *North American Spine Society (NASS)*

The 2011 NASS guidelines for cervical radiculopathy suggested TDR and fusion as comparable in short-term outcomes for single level degenerative cervical radiculopathy.<sup>[128]</sup> This was a grade B recommendation based on fair evidence defined as Level II or III studies with consistent findings. Additional recommendations focused on future research and included the need to validate purported advantages of TDR with long-term follow-up for clinical outcomes, revision surgery, and adjacent segment disease. Subgroup analysis of soft versus hard disc, and foraminal versus paracentral pathology were also recommended.

### Lumbar Discs

There is currently only one evidence-based clinical practice guideline from U.S. neurosurgery or orthopedic professional associations that addresses lumbar TDR. Guidelines from the American Pain Society (APS) rated the current evidence as “insufficient to adequately evaluate long-term benefits and harms of vertebral disc replacement” for the following reasons:<sup>[129]</sup>

- The trial results were only applicable to a narrowly defined subset of patients
- Interpretation the trial for the Charité disc was difficult because the fusion technique used in the trial is no longer widely used
- All trials had been industry-funded

- Data on long-term (beyond 2 years) benefits and harms following TDR are limited

## Summary

Current evidence consists mainly of studies with short- to mid-term outcomes. Long-term data is beginning to become available, but methodological limitations of the studies, such as large loss to follow-up, make interpretation of outcomes difficult. Despite the lack of long-term data, the use of single-level artificial cervical discs is becoming more widespread in the U.S. Given the increasing acceptance of these devices, single-level placement of an artificial intervertebral disc in a cervical spinal level between C3 and C7 may be considered medically necessary for carefully selected patients.

Current evidence is insufficient to determine whether the use of artificial intervertebral discs other than for single-level placement in the certain segments of the cervical spine improves outcomes in the short or long term compared with spinal fusion, the current standard of care for multilevel disc disease. In addition, there are no clinical practice guidelines from U.S. professional societies that recommend the use of these devices in the non-cervical spine. Therefore, all other uses of artificial intervertebral discs are considered investigational, including but are not limited to placement in more than one spinal level, placement at spinal levels other than cervical segments between C3 and C7, and techniques that combine artificial disc placement with spinal fusion at an adjacent or distant level.

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## CROSS REFERENCES

[Percutaneous Intradiscal Electrothermal Annuloplasty \(IDET\) and Percutaneous Intradiscal Radiofrequency Thermocoagulation](#), Surgery, Policy No. 118

[Total Facet Arthroplasty](#), Surgery, Policy No. 171

[Image-Guided Minimally Invasive Spinal Decompression \(IG-MSD\) for Spinal Stenosis](#), Surgery, Policy No. 176

[Lumbar Spinal Fusion](#), Surgery, Policy No. 187

CODES	NUMBER	DESCRIPTION
CPT	22856	Total disc arthroplasty (artificial disc), anterior approach, including discectomy with end plate preparation (includes osteophylectomy 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
	22861	Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, single interspace; cervical
	22862	lumbar
	22864	Removal of total disc arthroplasty (artificial disc), anterior approach, single interspace; cervical
	22865	Removal of total disc arthroplasty (artificial disc), anterior approach, lumbar, single interspace
	0092T	Total disc arthroplasty (artificial disc), anterior approach, including discectomy with end plate preparation (includes osteophylectomy for nerve root or spinal cord decompression and microdissection), each additional interspace, cervical (List separately in addition to code for primary procedure)
	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)
	0163T	Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression), each additional interspace, lumbar (List separately in addition to code for primary procedure)
	0164T	Removal of total disc arthroplasty (artificial disc), anterior approach, each additional interspace, lumbar (List separately in addition to code for primary procedure)
	0165T	Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, each additional interspace, lumbar (List separately in addition to code for primary procedure)

CODES	NUMBER	DESCRIPTION
HCPCS	None	