

Medical Policy



Title: Artificial Intervertebral Disc: Cervical Spine

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| Related Policy: | ▪ <i>Artificial Intervertebral Disc: Lumbar Spine</i> |
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| Professional / Institutional |
| Original Effective Date: September 25, 2007 / October 23, 2008 |
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| Populations | Interventions | Comparators | Outcomes |
|--|--|---|--|
| Individuals: • With cervical radicular pain or myelopathy | Interventions of interest are: • Single-level cervical spine arthroplasty | Comparators of interest are: • Anterior cervical discectomy and fusion | Relevant outcomes include: • Symptoms • Morbid events • Functional outcomes • Quality of life • Treatment-related morbidity |
| Individuals: • With cervical radicular pain or myelopathy | Interventions of interest are: • Two-level cervical spine arthroplasty | Comparators of interest are: • Anterior cervical discectomy and fusion | Relevant outcomes include: • Symptoms • Morbid events • Functional outcomes |

| Populations | Interventions | Comparators | Outcomes |
|-------------|---------------|-------------|--|
| | | | <ul style="list-style-type: none"> • Quality of life • Treatment-related morbidity |

DESCRIPTION

Several prosthetic devices are currently available for cervical disc arthroplasty. Cervical disc arthroplasty is proposed as an alternative to anterior cervical discectomy and fusion for individuals with symptomatic cervical degenerative disc disease.

OBJECTIVE

The objective of this evidence review is to determine whether cervical disc arthroplasty improves the net health outcome compared with anterior cervical discectomy and fusion in individuals who have degenerative disc disease.

BACKGROUND

Cervical Degenerative Disc Disease

Cervical degenerative disc disease is a manifestation of spinal spondylosis that causes deterioration of the intervertebral discs of the cervical spine. Symptoms of cervical degenerative disc disease include arm pain, weakness, and paresthesias associated with cervical radiculopathy. Disc herniation, osteophytes, kyphosis, or instability that compress the spinal cord can result in myelopathy, which is manifested by subtle changes in gait or balance, and, in severe cases, leads to weakness in the arms or legs and numbness of the arms or hands. The prevalence of degenerative disc disease secondary to cervical spondylosis increases with age. An estimated 60% of individuals older than 40 years have radiographic evidence of cervical degenerative disc disease. By age 65 years, 95% of men and 70% of women have at least 1 degenerative change evident at the radiographic examination. It is estimated that approximately 5 million adults in the United States are disabled to an extent by spine-related disorders, although only a small fraction of those are clear candidates for spinal surgery.

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 patients. Anterior cervical discectomy and fusion involves an anterolateral surgical approach, decompression of the affected spinal level, discectomy, and placement of a PEEK (polyetheretherketone) or titanium interbody cage plus autograft or allograft bone in the prepared intervertebral space to stimulate healing and eventual fusion between the vertebral endplates. A metal anterior cervical plate is attached to the adjoining vertebral bodies to stabilize the fusion site, maintain neck lordosis, and reduce the need for prolonged postoperative brace application that is needed following anterior cervical discectomy and fusion without an anterior plate. Although there may be slight differences between autograft and allograft sources in the postoperative rate of union, clinical studies have

demonstrated similar rates of postoperative fusion (90% to 100%) and satisfactory outcomes using either bone source. Studies have suggested that altered adjacent-segment kinematics following fusion may lead to adjacent-level degenerative disc disease and the need for secondary surgery.

Cervical disc arthroplasty is proposed as an alternative to anterior cervical discectomy and fusion for patients with symptomatic cervical degenerative disc disease. 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.

REGULATORY STATUS

In 2007, the Prestige® ST Cervical Disc (Medtronic) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process as a class III device. The Prestige ST Cervical Disc is composed of stainless steel and is indicated in skeletally mature patients for reconstruction of the disc from C3 through C7 following single-level discectomy. The device is implanted using an open anterior approach. Intractable radiculopathy and/or myelopathy should be present, with at least 1 of the following items producing symptomatic nerve root and/or spinal cord compression as documented by patient history (eg, pain [neck and/or arm pain], functional deficit, and/or neurologic deficit) and radiographic studies (eg, magnetic resonance imaging, computed tomography, x-rays): herniated disc and/or osteophyte formation. The FDA required Medtronic (the Prestige disc manufacturer) to conduct a 7-year postapproval clinical study of the safety and function of the device and a 5 year enhanced surveillance study to more fully characterize adverse events in a broader patient population.

Another disc arthroplasty product, the ProDisc-C® (Synthes Spine), was approved by the FDA through the premarket approval process in 2007. As with the Prestige ST Cervical Disc, the FDA approval of ProDisc-C was made conditional on the 7 year follow-up of the 209 subjects included in the non-inferiority trial (discussed in the Rationale section), 7 year follow-up of 99 continued-access subjects, and a 5 year enhanced surveillance study to characterize more fully adverse events when the device is used under general conditions of use. The ProDisc-C Vivo is currently marketed by Centinal Spine.

More recently, continued FDA approval requires the completion of 2 postapproval studies. One study provides extended follow-up of the premarket pivotal cohort out to 7 years. The second study provides 10 year enhanced surveillance of adverse event data. Continued approval is contingent on the submission of annual reports, which include the number of devices sold, heterotopic ossification, device malfunction, device removal, other serious device-related complications, and analysis of all explanted discs.

Devices with FDA approval for use in the United States are described in Table 1. These devices are for 1 site or 2 contiguous sites, there are no devices approved for non-contiguous sites. FDA Product Code: MJO

Table 1. Cervical Disc Prostheses Approved for use in the United States

| Prosthesis | Manufacturer | Characteristics | FDA Approval | Year |
|------------------------------------|--|---|-----------------|-----------|
| Prestige ST | Medtronic | Stainless steel | P060018 | 2007 |
| ProDisc-C | Centinal Spine | 2 metal (cobalt-chromium alloy) endplates and a polyethylene insert | P070001 | 2007 |
| Bryan® Cervical Disc | Medtronic Sofamor Danek | 2 titanium-alloy shells encasing a polyurethane nucleus | P060023 | 2009 |
| PCM Cervical Disc® | NuVasive | PCM is a semi-constrained device consisting of 2 metal (cobalt-chromium alloy) endplates and a polyethylene insert | P100012 | 2012 |
| SECURE®-C | Globus Medical | Semi-constrained device with 2 metal (cobalt-chromium molybdenum alloy) endplates and a polyethylene insert | P100003 | 2012 |
| Mobi-C | Zimmer Biomet (previously LDR Spine) | Semi-constrained device with metal (cobalt-chromium alloy) endplates and a polyethylene insert; approved for both 1 and 2- levels | P110002/P110009 | 2013 |
| Prestige LP | Medtronic Sofamor Danek | Titanium-ceramic composite with a metal-on-metal bearing; approved for both 1- and 2-levels | P090029 | 2014/2016 |
| M6®-C | Orthofix (previously Spinal Kinetics) | Ultra-high molecular weight polyethylene weaved fiber creating a matrix (artificial annulus) within a sheath and titanium alloy endplates | P170036 | 2019 |
| Simplify® Cervical Artificial Disc | NuVasive (previously Simplify Medical) | PEEK endplates and a mobile ceramic core; MRI compatible | P200022/S003 | 2020/2021 |

FDA: U.S. Food and Drug Administration; MRI: magnetic resonance imaging; PCM: porous-coated motion; PEEK: polyetheretherketone.

POLICY

- A. Cervical disc arthroplasty may be considered **medically necessary** when **ALL** of the following criteria are met:
1. The device is approved by the U. S. Food and Drug Administration (FDA)
AND
 2. The individual is skeletally mature
AND
 3. The individual has intractable cervical radicular pain or myelopathy
 - a. which has failed at least 6 weeks of conservative nonoperative treatment, including an active pain management program or protocol, under the direction of a physician, with pharmacotherapy that addresses neuropathic pain and other pain sources AND physical therapy
OR
 - b. if the individual has severe or rapidly progressive symptoms of nerve root or spinal cord compression requiring hospitalization or immediate surgical treatment.**AND**
 4. Degeneration is documented by magnetic resonance imaging (MRI), computed tomography (CT), or myelography
AND
 5. Cervical degenerative disc disease is from C3 through C7
AND
 6. The individual is free from contraindication to cervical disc arthroplasty
- B. Simultaneous cervical disc arthroplasty at a second contiguous level may be considered **medically necessary** if the above criteria are met for each disc level, and the device is FDA-approved for 2 levels (e.g., Mobi-C®, Prestige LP™).
- C. Subsequent cervical disc arthroplasty at an adjacent level may be considered **medically necessary** when all of the following are met:
1. Criteria A 1 to A 6 above are met
AND
 2. The device is FDA-approved for 2 levels
AND
 3. The planned subsequent procedure is at a different cervical level than the initial cervical artificial disc replacement
AND
 4. Clinical documentation that the initial cervical disc arthroplasty is fully healed.

- D. Cervical disc arthroplasty is considered **experimental / investigational** for all other indications, including, but not limited to, the following:
1. Disc implantation at more than 2 levels
 2. Combined use of an artificial cervical disc and fusion
 3. Prior surgery at the treated level
 4. Previous fusion at another cervical level
 5. Translational instability
 6. Anatomical deformity (e.g., ankylosing spondylitis)
 7. Rheumatoid arthritis or other autoimmune disease
 8. Presence of facet arthritis
 9. Active infection
 10. Metabolic bone disease (e.g., osteoporosis, osteopenia, osteomalacia)
 11. Malignancy

POLICY GUIDELINES

- A. Experimental / Investigational uses for cervical disc arthroplasty are derived from pivotal trials' eligibility criteria. Notably, individuals with prior surgery at the treated level were generally excluded from pivotal trials of cervical disc prostheses approved for use in the United States.(Mummaneni et al, 2007; PMID 17355018)(Gornet et al, 2015; PMID 26230424)(Murrey et al, 2009; PMID 18774751)(Heller et al, 2009; PMID 19112337)(Hisey et al, 2015; PMID 25310394)(U.S. Food and Drug Administration (FDA), https://www.accessdata.fda.gov/cdrh_docs/pdf11/P110002b.pdf; Accessed February 27, 2024.)(Vaccaro et al, 2013; PMID 24335629)(U.S. Food and Drug Administration (FDA), https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100003b.pdf; Accessed February 26, 2024.)(Phillips et al, 2021; PMID 33096243)(U.S. Food and Drug Administration (FDA), <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P170036>, Accessed February 25, 2024)(U.S. Food and Drug Administration (FDA), https://www.accessdata.fda.gov/cdrh_docs/pdf20/P200022S003B.pdf, Accessed February 24, 2024.)(Coric et al, 2022; PMID 35364570)(U.S. Food and Drug Administration (FDA), <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P090029>; Accessed February 23, 2024.)(Davis et al, 2015; PMID 25380538)
- B. Uniquely, a pivotal trial with PCM (porous-coated motion) Cervical Disc® included approximately 12% of individuals with prior adjacent or non-adjacent single-level fusions.(Phillips et al, 2013; PMID 23591659)

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review was created with searches of the PubMed database. The most recent literature update was performed through February 27, 2024.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality

of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Clinical Context and Therapy Purpose

The purpose of artificial intervertebral disc arthroplasty of the cervical spine in individuals who have cervical radicular pain or myelopathy is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with symptomatic cervical degenerative disc disease.

Interventions

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

Comparators

Comparators of interest include anterior cervical discectomy and fusion. Cervical degenerative disc disease is initially treated conservatively using noninvasive measures (eg, rest, heat, ice, analgesics, anti-inflammatory agents, exercise). If symptoms do not improve or resolve within 6 weeks, or if symptoms progress, surgical intervention may be indicated. Candidates for surgical intervention have chronic pain or neurologic symptoms secondary to cervical degenerative disc disease and no contraindications for the procedure.

Outcomes

The general outcomes of interest are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity.

The Neck Disability Index is a validated multidimensional instrument that measures the effects of pain and disability on a patient's ability to manage everyday life.¹ It is a modification of the Oswestry Disability Index, based on responses to 10 questions that focus on neck pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping, and recreation. Response options to each question range from 1 to 5, with a lower numeric score representing a better pain and disability status for that variable. A total Neck Disability Index score is obtained by adding individual question scores and dividing by the maximum total of 50 if all questions are answered. Therefore, Neck Disability Index scores range from 0% to 100%, with a lower percentage indicating less pain and disability. Neurologic status is a composite measure of motor function, sensory function, and deep tendon reflexes. It is used to judge whether patients are within normative parameters for those categories based on physiologic measurement. The anterior functional spinal unit height is a radiographic measure of interdiscal space. Comparison of the immediate postoperative functional spinal unit height with the 6-week postoperative value shows whether the disc space has decreased, which indicates that graft or device subsidence has occurred. Other outcome measures may include the 36-Item Short-Form Health Survey Mental and Physical Component Summary scores, neck and arm pain status, patient satisfaction, patient global perceived effect, gait assessment, foraminal compression test, adjacent-level stability and measurements, return to work, and physician's perception.

REVIEW OF EVIDENCE

Systematic Reviews

Hu et al (2016) published a systematic review and meta-analysis of 8 RCTs (N=2368) reporting mid-term outcomes (at least 48 months) comparing artificial intervertebral disc arthroplasty with anterior cervical discectomy and fusion.² This meta-analysis had the highest AMSTAR rating out of 14 meta-analyses published between 2011 and 2017.³ 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,^{4,5} and 3 reported on Neck Disability Index success.^{4,5,6} 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=.01). Pooled data also showed a significant benefit of cervical disc arthroplasty for secondary procedures at the index level (6 studies)^{4,5,7,8,9,10}; (RR, 0.40; 95% CI, 0.28 to 0.58; p<.001) and at the adjacent level (5 studies)^{4,7,9,10,11}; (RR, 0.42; 95% CI, 0.26 to 0.70; p<.002). These trials and outcome measures are detailed below.

Latka et al (2019) conducted a meta-analysis of RCTs on cervical disc arthroplasty to evaluate safety and long-term efficacy for reducing adjacent segment degeneration.¹² The authors 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=.002) along with the frequency of dysphagia/dysphonia (odds ratio [OR], 0.69; 95% CI, 0.49 to 0.98; p=.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=.0001). Another meta-analysis by Toci et al (2022) that included 19 RCTs

(N=4655) likewise found a lower risk of adjacent segment degeneration with cervical disc arthroplasty compared to anterior cervical discectomy with fusion (14.4% vs. 19.7%; $p<.001$), as well as adjacent segment disease (3.8% vs. 6.1%; $p<.001$) and reoperation rates (3.1% vs. 6.1%; $p<.001$).¹³

Similar findings were reported by Deng et al (2020) in a meta-analysis of 9 studies with 48 to 120 months of follow-up.¹⁴ Symptomatic adjacent-level disease requiring surgery was significantly lower following cervical disc arthroplasty compared to anterior cervical discectomy and fusion. Likewise, a meta-analysis by Peng et al that included 30 RCTs (N range, 79 to 545) and compared cervical disc arthroplasty to anterior cervical discectomy with fusion in patients with cervical degenerative disc disease with either radiculopathy or myelopathy found improved overall success, neurological success, and Neck Disability Index success with cervical disc arthroplasty.¹⁵ Follow-up ranged from 1 to 10 years and most studies included single-level cervical disc arthroplasty.

Single-Level Cervical Disc Arthroplasty

The pivotal trials of 9 artificial cervical discs are described in Table 2 (Kineflex is no longer marketed). 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 ($p=.005$) 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; $p=.01$), 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 ($p=.146$).

Table 2. Summary of Pivotal Study Characteristics of Cervical Artificial Intervertebral Discs

| Study | Device | Design | Primary Outcome Measure | Participants | Interventions | |
|--|-------------|---------------------------------|---|---|----------------------|-------|
| | | | | | CDA | ACDF |
| Mummaneni et al (2007) ¹⁶ , | Prestige ST | Multicenter non-inferiority RCT | 3 primary outcome variables were used in the Prestige pivotal trial: a 15-point | Patients with nonaxial pain and other symptoms secondary to | Prestige ST (n=276) | n=265 |

| Study | Device | Design | Primary Outcome Measure | Participants | Interventions | |
|---|----------------------------|---------------------------------|---|--|---------------------|--|
| | | | improvement in NDI score, neurologic status, and functional spinal unit height. | radiculopathy or myelopathy | | |
| Gornet et al (2015) ^{17,} | Prestige LP | Multicenter non-inferiority RCT | Primary outcomes were neurologic success, individual success, and overall success. | Patients with nonaxial pain and other symptoms secondary to radiculopathy or myelopathy | Prestige LP (n=280) | n=265 historical controls from the Prestige ST trial |
| Murray et al (2009) ^{18,} | ProDisc-C | Multicenter non-inferiority RCT | Improvement in VAS pain and intensity (neck and arm), VAS satisfaction, NDI score, neurological exam, device success, adverse event occurrence, and SF-36 questionnaire | Patients with nonaxial pain and other symptoms secondary to radiculopathy or myelopathy unresponsive to nonoperative treatment for at least 6 weeks | ProDisc-C (n=103) | n=106 |
| Heller et al (2009) ^{19,} | Bryan Cervical Disc | Multicenter non-inferiority RCT | Success on all of the following: ≥ 15 -point improvement in NDI score, neurologic improvement, no serious adverse events related to the implant or subsequent surgical procedure, and no subsequent surgery or intervention. | Patients with radiculopathy or myelopathy from single-level cervical disc disease secondary to disc herniation that had not responded to at least 6 weeks of nonoperative management | Bryan disc (n=242) | n=223 |
| Hisey et al (2014) ^{20,} FDA SSED ^{21,} | Mobi-C Single level | Multicenter non-inferiority RCT | Composite overall success score (not defined by authors) | Patients with discogenic neck and/or arm pain with degeneration of the disc with radiculopathy or myeloradiculopathy from C3 to C7 at 1 level without prior cervical fusion | Mobi-C (n=169) | n=87 |
| Phillips et al (2013) ^{22,} | Porous Coated Motion (PCM) | Multicenter non-inferiority RCT | Composite measure of overall success measured at 24-weeks post-operatively, defined as at least 20% improvement in NDI; | Patients with single-level symptomatic cervical spondylosis with radiculopathy | PCM (n=224) | n=192 |

| Study | Device | Design | Primary Outcome Measure | Participants | Interventions | |
|---|------------------------|--|---|---|------------------|---|
| | | | absence of reoperation, revision, or removal; maintenance or improvement in neurological status; and absence of major complications during follow-up period | and/or myelopathy unresponsive to nonoperative treatment | | |
| Vacarro et al (2013) ²³ , FDA SSED ²⁴ , | Secure C | Multicenter non-inferiority RCT | Composite measure of overall success measured at 24 months post-operatively, defined as improvement of at least 25% in NDI; no device failure requiring revision, removal or reoperation; and absence of major complications. | Patients with intractable degenerative cervical radiculopathy (arm pain and/or a neurological deficit) at 1 level from C3 to C7 | Secure C (n=151) | n=140 |
| Phillips et al (2021); FDA SSED: M6-C ^{25,26} , | M6-C | Multicenter non-randomized pragmatic trial | Improvement of NDI >15 pts, maintenance or improvement in neurologic function, and no serious adverse events or supplemental surgical procedures. | Patients with intractable degenerative cervical radiculopathy (arm pain and/or a neurological deficit) at 1 level from C3 to C7 | M6-C (n=160) | 189 propensity-matched controls selected from concurrent ACDF patients and a previous IDE study |
| FDA SSED: Simplify Cervical Disk ²⁷ , | Simplify Cervical Disc | Multicenter non-inferiority RCT | Improvement of NDI >15 pts, maintenance or improvement in neurologic function, and no serious adverse events or supplemental surgical procedures. | Patients with intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain or myelopathy at 1 level from C3 to C7 | Simplify (n=150) | n=133 historical controls from a previous IDE study from 2005-2007 |

ACDF: anterior cervical discectomy and fusion; CDA: cervical disc arthroplasty; FDA : U.S. Food and Drug Administration ; IDE: investigational device exemption; NDI: Neck Disability Index; RCT: randomized controlled trial; SF-36: short form-36; VAS: visual analog scale; SSED: summary of safety and effectiveness.

Table 3. Summary of Pivotal Randomized Controlled Trial Results

| Outcomes | 24 Months | | | 36 to 48 Months | | | 60 Months | | | 84 Months | | | 120 Months | | |
|---------------------|---|-------------------------------|----------------------|-----------------|------|---|-----------|------|---|------------------------------------|-------|------|------------|-------|---|
| | CDA | ACDF | p | CDA | ACDF | p | CDA | ACDF | p | CD A | AC DF | p | CD A | AC DF | p |
| Prestige ST | Mummaneni et al (2007) ^{16,} | | | | | | | | | Burkus et al (2014) ^{28,} | | | | | |
| n | 223 | 198 | | | | | | | | 21 | 18 | | | | |
| Overall Success | 79.3% | 67.8% | .004 for superiority | | | | | | | 72.6% | 60.0% | .008 | | | |
| NDI | mean improvement, 36 points | mean improvement, 33.6 points | Met non-Inferiority | | | | | | | -37.5 | -31.9 | | | | |
| Neurologic Success | 92.8% | 84.3% | .005 | | | | | | | 88.2% | 79.7% | .011 | | | |
| Secondary Surgeries | 1.1% | 3.4% | .0492 | | | | | | | 4.8% | 13.7% | | | | |
| Prestige LP | Gornet et al (2015) ^{17,} | | | | | | | | | | | | | | |
| n | 272 | 223 | | | | | | | | | | | | | |
| Overall Success | mean difference, -0.111 (95% CrI, -0.196 to -0.026) | | Superiority | | | | | | | | | | | | |
| NDI | | | | | | | | | | | | | | | |
| Neurologic Success | 93.5% | 83.5% | Superiority | | | | | | | | | | | | |
| Secondary Surgeries | 28.6% | 34% | | | | | | | | | | | | | |

| Outcomes | 24 Months | | | 36 to 48 Months | | | 60 Months | | | 84 Months | | | 120 Months | | |
|----------------------------|-------------------------------------|------------------|----------------------|---|-----------|-------|---|-------|-------|--------------------------------------|-----|------|--------------------------------------|-------|------|
| ProDisc C | Murray et al (2009) ¹⁸ , | | | Delamarter et al (2010) ²⁹ , | | | Zigler et al (2013) Delamarter et al (2013) ^{30,31} , | | | Janssen et al (2015) ¹⁰ , | | | | | |
| n | 101 | 101 | | 75 | 67 | | 72 | 61 | | 152/209 (72.7%) | | | | | |
| Overall Success | 72.3% | 68.3% | Met non-inferiority | | | | | | | | | | | | |
| NDI | 21.4±20.2 points | 20.5±18.4 points | 1.0 | 20.3±18.6 | 21.2±14.9 | | 50% to 60% | | NS | | | | | | |
| Neurologic Success | 90.9% | 88% | .638 | 88.9% | 74.4% | .0665 | 90.3% | 91.7% | NS | 88% | 89% | NS | | | |
| Secondary Surgeries | 1.8% | 8.5% | .003 | 2.9% | 11.3% | .0292 | 2.9% | 14.5% | .0079 | 7% | 18% | .009 | | | |
| Bryan Cervical Disc | Heller et al (2009) ¹⁹ , | | | Sasso et al (2011) ⁵ , | | | | | | | | | Lavelle et al (2018) ³² , | | |
| n | 230 (95%) | 194 (87%) | | 181 (75%) | 138 (62%) | | | | | | | | 128 | 104 | |
| Overall Success | 82.6% | 72.7% | .010 for superiority | 85.1% | 72.5% | .004 | | | | | | | 81.3% | 66.3% | .005 |
| NDI Success | 86% | 78.9% | .035 for superiority | | | | | | | | | | -38.3 | -31.1 | .01 |
| Arm Pain Score | 19.1 | 21.5 | .194 | 16.6 | 22.4 | .028 | | | | | | | -58.9 | -51.6 | .60 |
| Neurologic Success | 93.9% | 90.2% | Met noninferiority | | | NS | | | | | | | 92.1% | 95.1% | .82 |

| Outcomes | 24 Months | | | 36 to 48 Months | | | 60 Months | | | 84 Months | | | 120 Months | | |
|-------------------------|---|-------|---------------------|-----------------------------------|-------|---------------------|--------------------------------------|-------------|---------------------|---------------------------------------|-------|---------------------|------------|------|-------|
| | Secondary Surgeries | | | | 7.8% | 8.6% | NS | | | | | | | 9.7% | 15.8% |
| Mobi-C (1 level) | Hisey et al (2014) ²⁰ , FDA SSED ²¹ , | | | Hisey et al (2015) ⁹ , | | | Hisey et al (2016) ³³ , | | | Radcliff et al (2017) ³⁴ , | | | | | |
| n | 164 | 81 | | | | | 85.5% | 78.9% | | | | | | | |
| Overall Success | 73.7% | 65.3% | Met non-inferiority | 69.5% | 58.7% | Met non-inferiority | 61.9% | 52.2% | Met non-inferiority | 55.2% | 50.0% | Met non-inferiority | | | |
| NDI | | | Met non-inferiority | | | | | | | | | Met non-inferiority | | | |
| Secondary Surgeries | 1.2% | 6.2% | | 3% | 9.9% | <.05 | 4.9% | 17.3% | <.01 | 3% | 12.3% | <.05 | | | |
| PCM | Phillips et al (2013) ²² , | | | | | | Phillips et al (2015) ⁶ , | | | | | | | | |
| n | 189 | 151 | Per protocol | | | | 163 (74.8%) | 130 (70.3%) | | | | | | | |
| Overall Success | 75.1% | 64.9% | Superiority | | | | | | | | | | | | |
| NDI success | 83.4% | 81.5% | .667 | | | | 85% | 74.2% | .026 | | | | | | |
| Neurologic Success | 94.7% | 89.5% | .100 | | | | 92.4% | 87.5% | .229 | | | | | | |
| Secondary Surgeries | 5.2% | 5.4% | | | | | 8.1% | 12.0% | NS | | | | | | |

| Outcomes | 24 Months | | | 36 to 48 Months | | | 60 Months | | | 84 Months | | | 120 Months | | |
|---------------------|--|-------|---------------------|------------------------|--|--|------------------|--|--|------------------|--|--|-------------------|--|--|
| Secur C | Vacarro et al (2013) ²³ , FDA SSED ²⁴ , | | | | | | | | | | | | | | |
| n | 87% | | | | | | | | | | | | | | |
| Overall Success | 83.8% | 73.2% | Met non-inferiority | | | | | | | | | | | | |
| NDI Success | 89.2% | 84.5% | Met non-inferiority | | | | | | | | | | | | |
| Neurologic Success | 96.0% | 94.9% | Met non-inferiority | | | | | | | | | | | | |
| Secondary Surgeries | 2.5% | 9.7% | | | | | | | | | | | | | |
| M6-C | Phillips et al (2021) ²⁶ , FDA SSED: M6-C ²⁵ , | | | | | | | | | | | | | | |
| n | 160 | 189 | | | | | | | | | | | | | |
| Overall Success | 86.8% | 79.3% | Met non-inferiority | | | | | | | | | | | | |
| NDI Success | 90.5% | 85.1% | | | | | | | | | | | | | |
| Neurologic Success | 93.3% | 87.2% | | | | | | | | | | | | | |
| Secondary Surgeries | 1.9% | 4.8% | | | | | | | | | | | | | |
| Pain Medication | 14% | 38.2% | <.001 | | | | | | | | | | | | |

| Outcomes | 24 Months | | | 36 to 48 Months | | | 60 Months | | | 84 Months | | | 120 Months | | |
|-------------------------------|--|-------|-------|-----------------|--|--|-----------|--|--|-----------|--|--|------------|--|--|
| | | | | | | | | | | | | | | | |
| Simplify Cervical Disc | FDA SSED: Simplify Cervical Disk ²⁷ | | | | | | | | | | | | | | |
| n | 150 | 133 | | | | | | | | | | | | | |
| Overall Success | 93% | 73.6% | <.001 | | | | | | | | | | | | |
| NDI Success | 97.9% | 88% | .009 | | | | | | | | | | | | |
| Neurologic Success | 99.3% | 94.7% | | | | | | | | | | | | | |
| Secondary Surgeries | 2.9% | 2.9% | .979 | | | | | | | | | | | | |
| Pain Medication | 10.8% | 36.8% | | | | | | | | | | | | | |

ACDF: anterior cervical discectomy and fusion; CDA: cervical disc arthroplasty; CrI: credible interval; FDA SSED: U.S. Food and Drug Administration Summary of Safety and Effectiveness; NDI: Neck Disability Index; NS: not significant; PCM: porous coated motion.

Most available products have efficacy and safety results published up to 10 years post-operative. The group originally studying the Bryan Cervical Disc recently published 20-year follow-up data.^{35,36} Forty-seven patients with single-level cervical radiculopathy were randomized to either Bryan cervical disc or anterior cervical discectomy and fusion for an FDA Investigational Device Exemption trial. At 20-years follow-up, both groups showed significantly better Neck Disability Index scores and Visual Analog Scale arm and neck pain scores compared to preoperative scores. There was no significant difference between cervical disc arthroplasty and discectomy and fusion groups in Neck Disability Index scores or Visual Analog Scale pain scores. Reoperations since the first procedure were reported in 41.7% of patients who initially underwent discectomy and fusion and 10% of cervical disc arthroplasty patients (p=.039). These data continue to demonstrate the long-term benefits with cervical disc arthroplasty.

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. Twenty-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 postapproval 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.

Two-Level Cervical Disc Arthroplasty

Table 4 summarizes key characteristics of RCTs that evaluated cervical disc arthroplasty at 2 continuous levels.

In 2021, the Simplify Cervical Disc received FDA approval for implantation at 2 levels (previously approved for implantation at only 1 level). Overall success was achieved in 86.7% of Simplify Cervical Disc patients and 77.1% of anterior cervical discectomy and fusion controls at 24 months follow-up (Table 5).³⁷

In 2016, the Prestige LP received FDA approval for implantation at 2 levels.³⁸ 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%, respectively (Table 5). Table 5 provides data on patients who reached follow-ups at intervals up to 120 months. 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.

Two and 4-year results from the 2-level Mobi-C investigational device exemption trial were reported by Davis et al (2013, 2015) with 5- and 7-year results published by Radcliff et al (2016, 2017).^{8,39,40,34} Clinically relevant heterotopic ossification (grade III or IV) was observed in 29.7% of the Mobi-C patients at 5 years, but the Mobi-C patients had significantly less adjacent-segment degeneration (50.7%) than anterior cervical discectomy and fusion patients (90.5%; p<.001).

Table 4. Summary of Pivotal Randomized Controlled Trial Characteristics of Cervical Disc Arthroplasty at 2 Continuous Levels

| Study | Device | Design | Blinding | Primary Outcome Measure | Participants | Interventions | |
|----------------------------------|------------------------|----------------------------|----------|---|--|--------------------------------|--|
| | | | | | | CDA | ACDF |
| Coric et al (2022) ³⁷ | Simplify Cervical Disc | Multicenter non-randomized | None | Improvement of NDI >15 pts, maintenance or improvement in neurologic function, and no serious adverse events or | Patients with 2-level, symptomatic cervical disc disease with medically refractory radiculopathy and/or myelopathy | Simplify Cervical Disc (n=182) | n=170 historical controls from a previous IDE study from the mid-2000s |

| Study | Device | Design | Blinding | Primary Outcome Measure | Participants | Interventions |
|-----------------------------------|-------------|-----------------------------------|---|----------------------------------|--|--|
| | | | | supplemental surgical procedures | | |
| FFDA SSED (2016) ^{41,} | Prestige LP | Multicenter non-inferiority trial | Unknown | Overall success ^a | Patients with 2-level, symptomatic cervical disc disease with medically refractory radiculopathy and/or myelopathy | Prestige LP at 2 contiguous levels (n=209) n=188 |
| Davis et al (2013) ^{39,} | Mobi-C | Multicenter RCT | Patient and independent review blinding; radiologist not able to be blinded | Overall Success ^a | Patients with 2-level, symptomatic cervical disc disease with medically refractory radiculopathy and/or myelopathy | Mobi-C at 2 contiguous levels (n=225) n=105 |

ACDF: anterior cervical discectomy and fusion; CDA: cervical disc arthroplasty; FDA SSED: U.S. Food and Drug Administration Summary of Safety and Effectiveness; IDE: investigational device exemption; NDI: neck disability index; RCT: randomized controlled trial.

^aOverall success was achieved if the postoperative score improvement in the NDI was ≥15 points, neurological status did not worsen, and no serious implant/surgical procedure–associated adverse event, or second surgery, which was deemed “failure”, occurred.

Table 5. Follow-Up and Success Rates for 2-Level Cervical Discs Compared With 2-Level Anterior Cervical Discectomy and Fusion

| Outcomes | 24 Months | | | 48 Months | | | 60 Months | | | 84 Months | | | 120 Months | | |
|-------------------------------|-----------------------------------|------------|---|-----------|-------|---|-----------|-------|---|-----------|-------|---|------------|------|---|
| | CDA | ACD F | p | CDA | ACD F | p | CDA | ACD F | p | CDA | ACD F | p | CDA | ACDF | p |
| Simplify Cervical Disc | Coric et al (2022) ^{37,} | | | | | | | | | | | | | | |
| n (%) | 182 (100%) | 170 (100%) | | | | | | | | | | | | | |

| Outcomes | 24 Months | | | 48 Months | | | 60 Months | | | 84 Months | | | 120 Months | | |
|-------------------------------------|--------------------------|-----------------|-------------|-----------------|-----------------|-------------|-----------------|----------------|-------------|----------------|---------------|-------------|--------------------------------------|-----------|-------------|
| | Overall success % | 86.7 % | 77.1 % | <.05 | | | | | | | | | | | |
| NDI Success n/N (%) | 156/168 (92.3%) | 106/127 (85.5%) | <.10 | | | | | | | | | | | | |
| Neurologic Success | 168/168 (100%) | 125/128 (97.7%) | NA | | | | | | | | | | | | |
| No additional surgery | 177/181 (97.8%) | 152/166 (91.6%) | <.10 | | | | | | | | | | | | |
| No SAEs due to implant or procedure | 176/182 (96.3%) | 158/170 (94.7%) | >.50 | | | | | | | | | | | | |
| Prestige LP | FDA SSED ⁴¹ , | | | | | | | | | | | | Gornet et al (2019) ^{a42} , | | |
| n (%) | 199 (95) | 160 (86) | | 185 (89) | 149 (80) | | 166 (80) | 138 (74) | | 126 (67) | 99 (58) | | 148 (86%a) | 118 (85%) | |
| Overall success n/N (%) | 162/199 (81.4%) | 111/160 (69.4%) | Superiority | 151/185 (81.6%) | 105/149 (70.5%) | | 132/166 (79.6%) | 91/138 (65.5%) | | 99/126 (78.6%) | 62/99 (62.6%) | | 80.4 % | 62.2 % | Superiority |
| NDI Success | 87.9 % | 79.2 % | Superiority | 89.7 % | 82.3 % | Superiority | 89.2 % | 77.8 % | Superiority | 87.0 % | 75.6 % | Superiority | 88.4 % | 76.5 % | Superiority |
| Neurologic Success | 91.5 % | 86.2 % | NS | 90.3 % | 83.8 % | Superiority | 90.4 % | 87.5 % | NS | 91.6 % | 82.1 % | Superiority | 92.6 % | 86.1 % | Superiority |
| Secondary | 2.4 % | 3.2 % | | | | | | | | | | | 13.7 % | 35.5 % | Significant |

| Outcomes | 24 Months | | | 48 Months | | | 60 Months | | | 84 Months | | | 120 Months | | |
|---------------------|------------------------------------|-------|--------|-----------------------------------|-------|-------|---------------------------------------|-------|-------------|---------------------------------------|-------|-------------|------------|--|--|
| | | | | | | | | | | | | | | | |
| Surgeries | | | | | | | | | | | | | | | |
| Mobi-C | Davis et al (2013) ³⁹ , | | | Davis et al (2015) ⁸ , | | | Radcliff et al (2016) ⁴⁰ , | | | Radcliff et al (2017) ³⁴ , | | | | | |
| n | 225 | 105 | | 89.0% | 81.2% | | 90.7% | 86.7% | | 84.4% | 75% | | | | |
| Overall success | 69.7% | 37.4% | <.0001 | 66.0% | 36.0% | | 61% | 31% | <.001 | 60.8% | 34.6% | Superiority | | | |
| NDI Success | 78.2% | 61.8% | <.05 | 79.3% | 53.4% | <.001 | | | Significant | 79.0% | 58.9% | <.05 | | | |
| Secondary Surgeries | 3.1% | 11.4% | | 4.0% | 15.2% | | 7.1% | 21.0% | <.001 | 4.4% | 16.2% | <.05 | | | |

ACDF: anterior cervical discectomy and fusion; CDA: cervical disc arthroplasty; FDA: SSED: US Food and Drug Administration Summary of Safety and Effectiveness; NA: not applicable; NS: not significantly different; SAE: serious adverse event.

^a Not all sites were involved in the 10 yr follow-up. Patients who died (n=5) or had withdrawn from the study (n=25) were also excluded from the analysis.

Post hoc analysis of data from the pivotal 1- and 2-level Mobi-C trials was reported by Bae et al (2015).⁴³ The comparison showed no significant differences between 1- and 2-level cervical disc arthroplasty on clinical outcomes (Neck Disability Index, Visual Analog Scale and 12-Item Short-Form Health Survey scores), major complication rates (4.3% for 1-level cervical disc arthroplasty vs. 4.0% for 2-level cervical disc arthroplasty), or subsequent surgery rates (3.0% of 1-level vs. 4.0% of 2-level). Clinically relevant heterotopic ossification was observed in 23.8% of 1-level patients and 25.7% of 2-level patients. Huppert et al (2011) compared outcomes between single-level (n=175) and multilevel (2 to 4 levels, n=56) cervical disc arthroplasty with the Mobi-C device in a prospective multicenter study from Europe.⁴⁴ 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.

Section Summary: Two-Level Cervical Disc Arthroplasty

The FDA approval of Simplify Cervical Disc for implantation at 2 levels (previously approved for implantation at only 1 level) was based on superiority to 2-level anterior cervical discectomy and fusion in overall success at 2-year follow-up.

The FDA approval for the Prestige LP disc at 2 levels was based on superiority to 2-level anterior cervical discectomy and fusion 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 the 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.

Registry Data

Staub et al (2016) evaluated the clinical effectiveness of cervical disc arthroplasty for 987 patients in the Spine Tango registry.⁴⁵ The primary outcome measures were 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 ($p=.04$) and 0.7 points in arm pain ($p=.02$); the mean Core Outcome Measures Index score difference was 0.8 points ($p=.01$). 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% ; $p=.02$) and Core Outcome Measures Index score (81.6% vs. 67.9% ; $p<.01$) 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 to 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% ; $p=.05$), 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.

MacDowall et al compared 5-year outcomes of cervical disc arthroplasty and anterior cervical discectomy and fusion from the Swedish Spine Registry.⁴⁶ 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 ; $p=.28$) between the groups. There were also no differences between the groups in EuroQol-5 Dimensions or in pain scores for the neck and arm.

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

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 to 4) after cervical disc arthroplasty included 8 studies (N=617 patients).⁴⁷ 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.

Nunley et al (2018) evaluated the effect of heterotopic ossification on clinical outcomes.⁴⁸ 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 ($p=.04$), 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.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2015 Input

In response to requests, input was received from 3 physician specialty societies and 2 academic medical centers while this policy was under review in 2015. There was agreement that cervical disc replacement may be medically necessary under specified conditions. Likewise, there was agreement that combined use of an artificial disc and fusion over 2 levels was investigational. Input was mixed on the medical necessity of 2-level artificial intervertebral disc arthroplasty.

2009 Input

In response to requests, input was received from 2 physician specialty societies and 2 academic medical centers while this policy was under review in 2009. Input did not support the conclusion that artificial intervertebral disc arthroplasty is investigational.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

International Society for the Advancement of Spine Surgery

In 2021, the International Society for the Advancement of Spine Surgery issued a position statement on cervical and lumbar disc replacement.⁴⁹ Based on a review of the available evidence-based scientific literature, the Society "strongly supports both cervical and lumbar total disc replacements, including multi-level use as approved by the FDA [Food and Drug Administration], as safe and effective treatment alternatives to fusion in appropriately selected patients. FDA study guidelines and labelling regarding inclusion and exclusion criteria should be followed for use."

National Institute for Health and Care Excellence

In 2010, NICE issued guidance on the artificial cervical disc, concluding that:⁵⁰

"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 the preservation of mobility, occurrence of adjacent segment disease, and avoidance of revision surgery."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 6.

Table 6. Summary of Key Trials

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---------------------------|--|---------------------------|------------------------|
| <i>Ongoing</i> | | | |
| NCT05691231 ^a | Long-Term Assessment of the Safety and Performance of the NuVasive Simplify Disc at Two Levels | 158 | May 2029 |
| NCT05740176 ^a | A Multi-Center, Prospective, Historically Controlled Pivotal Trial Comparing the Safety and Effectiveness of the Synergy Disc to Anterior Cervical Discectomy and Fusion in Patients With Two-Level Symptomatic Cervical Degenerative Disc Disease (DDD) | 200 | Dec 2025 |
| NCT05489822 ^a | Sponsor-initiated, Prospective, Single-center, Non-interventional Clinical Observational Study to Evaluate the VERTICALE® Cervical System in Spine Surgery According to Its Intended Use. | 20 | Apr 2026 |
| NCT04520776 ^a | A Multicenter, Prospective, Randomized, Clinical Trial Comparing the Safety and Effectiveness of the BAGUERA®C Cervical Disc Prosthesis to the Mobi-C® Cervical Disc for the Treatment of Patients With Symptomatic Cervical Disc Disease at a Single Level | 284 | Feb 2026 |
| NCT04564885 ^a | A Multicenter, Prospective, Randomized, Clinical Trial Comparing the Safety and Effectiveness of the BAGUERA®C Cervical Disc Prosthesis to the Mobi-C® Cervical Disc for the Treatment of Patients With Symptomatic Cervical Disc Disease at Two Contiguous Levels | 300 | Oct 2025 |
| NCT03367052 | Clinical and Radiological Outcomes of a 7-year Follow-up, Multi-center, Prospective, Randomized, Controlled Trial: Two-level Cervical ProDisc-C Vivo Versus Hybrid Construct. | 542 | Dec 2025 |
| NCT04469231 ^a | A Multi-Center, Prospective, Historically Controlled Pivotal Trial Comparing The Safety And Effectiveness Of The Synergy Disc To Anterior Cervical Discectomy And Fusion In Patients With One-Level Symptomatic Cervical Degenerative Disc Disease (DDD) | 175 | Jan 2026 |
| <i>Unpublished</i> | | | |
| NCT03123549 ^a | Clinical Study Protocol for the Investigation Of The Two Level Simplify® Cervical Artificial Disc | 182 | Mar 2022 |
| NCT02667067 ^a | Clinical Study Protocol for the Investigation Of The Simplify® Cervical Artificial Disc | 150 | Jul 2021 |

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

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

| REVISIONS | |
|------------------|--|
| 09-23-2008 | In Description section: |
| | <ul style="list-style-type: none"> ▪ Updated wording |
| | In Policy section: |
| | <ul style="list-style-type: none"> ▪ Removed "Removal or revision of artificial disc(s) is a non-covered service." |
| 05-18-2010 | In Coding section: |
| | <ul style="list-style-type: none"> ▪ Removed CPT codes 0096T, 0098T |
| | Added Rationale section |
| | Updated Description Section |
| 03-08-2013 | Updated Coding Section: |
| | <ul style="list-style-type: none"> ▪ Updated wording for the following CPT codes: 0092T, 0095T (effective 01-01-09) ▪ Added CPT codes: 22856, 22861, 22864, 0098T (effective 01-01-09) ▪ Deleted CPT codes: 0090T, 0093T (effective 01-01-09) |
| | Updated Rationale and References Sections |
| 03-08-2013 | Description section updated |

| REVISIONS | |
|------------------|--|
| | Rational section updated |
| | In Coding section: <ul style="list-style-type: none"> ▪ Coding notations added. |
| | References updated |
| 01-01-2015 | In Coding section: <ul style="list-style-type: none"> ▪ Added CPT Codes: 22858, 0375T (Effective January 1, 2015) ▪ Deleted CPT Code: 0092T (Effective January 1, 2015) |
| 08-05-2015 | Description section updated |
| | In Policy section: <ul style="list-style-type: none"> ▪ Revised policy from: "Artificial intervertebral discs are considered experimental / investigational for treatment of disorders of the cervical spine, including degenerative disc disease." to: "A. Cervical artificial intervertebral disc implantation may be considered medically necessary when ALL of the following criteria are met: 1. The device is approved by FDA AND 2. The patient is skeletally mature AND 3. The patient has intractable cervical radicular pain or myelopathy a. which has failed at least 6 weeks of conservative nonoperative treatment, including active pain management program or protocol, under the direction of a physician, with pharmacotherapy that addresses neuropathic pain and other pain sources AND physical therapy; OR b. if the patient has severe or rapidly progressive symptoms of nerve root or spinal cord compression requiring hospitalization or immediate surgical treatment. AND 4. Degeneration is documented by magnetic resonance imaging (MRI), computed tomography (CT), or myelography AND 5. Cervical degenerative disc disease is limited to a single level from C3-C7 AND 6. The patient is free from contraindication to cervical artificial intervertebral disc implantation B. Cervical artificial intervertebral disc implantation is considered experimental / investigational for all other indications, including, but not limited to, the following: 1. Disc implantation at more than 1 level 2. Combined use of an artificial cervical disc and fusion 3. Prior surgery at the treated level 4. Previous fusion at another cervical level 5. Multilevel disc disease 6. Translational instability 7. Anatomical deformity (e.g., ankylosing spondylitis) 8. Rheumatoid arthritis or other autoimmune disease 9. Presence of facet arthritis 10. Active infection 11. Metabolic bone disease (e.g., osteoporosis, osteopenia, osteomalacia) 12. Malignancy" |
| | Rationale section updated |
| | In Coding section: <ul style="list-style-type: none"> ▪ ICD-9 and ICD-10 Codes added. |
| | References updated |
| 10-12-2016 | Description section updated |
| | In Policy section: |

| REVISIONS | |
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| | <ul style="list-style-type: none"> ▪ In Item A 5 removed "limited to a single level" to read "Cervical degenerative disc disease is from C3-C7" ▪ Added medically necessary indications of: "B. Simultaneous cervical artificial intervertebral disc implantation at a second contiguous level may be considered medically necessary if the above criteria are met for each disc level, and the device is FDA-approved for 2 levels (i.e., Mobi-C, Prestige LP)." and "C. Subsequent cervical artificial intervertebral disc implantation at an adjacent level may be considered medically necessary when all of the following are met: 1. Criteria 1 to 6 above are met; AND 2. The device is FDA-approved for 2 levels; AND 3. The planned subsequent procedure is at a different cervical level than the initial cervical artificial disc replacement; AND 4. Clinical documentation that the initial cervical artificial intervertebral disc implantation is fully healed." |
| | Rationale section updated |
| | In Coding section: <ul style="list-style-type: none"> ▪ ICD-10 Codes Effective 10-01-2016: M50.021, M50.022, M50.023, M50.11, M50.121, M50.122, M50.123, M50.221, M50.222, M50.223, M50.321, M50.322, M50.323, M54.12 ▪ ICD-10 Codes Termed 09-30-2016: M50.02, M50.22, M50.32 |
| | References updated |
| 05-23-2018 | Description section updated |
| | Rationale section updated |
| | References updated |
| 07-17-2019 | Description section updated |
| | Rationale section updated |
| | References updated |
| 01-01-2020 | In Coding section: <ul style="list-style-type: none"> ▪ Deleted CPT Code: 0375T |
| 08-21-2020 | Description section updated |
| | In Policy section: <ul style="list-style-type: none"> ▪ In Items A, A 6, B, C, C 4, and D revised "cervical artificial intervertebral disc implantation" to read "cervical disc arthroplasty". This is no change to the intent of the policy. ▪ In Item C 1 added "A" to read "Criteria A 1 to A 6 above". This added location clarification and is no change to the intent of the policy. |
| | Rationale section updated |
| | In Coding section: <ul style="list-style-type: none"> ▪ Removed coding notations (no coding changes) |
| | References updated |
| 06-03-2021 | Description section updated |
| | Rationale section updated |
| | References updated |
| 07-01-2022 | Updated Description Section |
| | Updated Rationale Section |
| | Updated Coding Section <ul style="list-style-type: none"> ▪ Converted ICD-10 codes to ranges |
| | Updated References Section |
| 05-23-2023 | Updated Description Section |
| | Updated Policy Guideline Section <ul style="list-style-type: none"> ▪ Added Policy Guidelines |

| REVISIONS | |
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| | Updated Rationale Section |
| | Updated Coding Section <ul style="list-style-type: none"> ▪ Removed ICD-10 codes |
| | Updated References Section |
| 05-28-2024 | Updated Description Section |
| | Updated Rationale Section |
| | Updated Coding Section <ul style="list-style-type: none"> ▪ Removed 22899 |
| | Updated References Section |

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