Simplify® Cervical Artificial Disc (Simplify Disc) Instructions for Use

Device Description

Simplify® Cervical Artificial Disc is a weight-bearing implant consisting of PEEK (polyetheretherketone) endplates and one semi-constrained, fully articulating, mobile zirconia toughened alumina (ZTA) ceramic core. Simplify® Cervical Artificial Disc is provided packaged and preassembled in one of twelve (12) configurations (Table A).

In addition to serrated surfaces, the inferior endplate has a midline fin and the superior endplate has two to three teeth to facilitate endplate fixation. Both endplates have concave articulating surfaces. The superior endplate's concave articulating surface features a retention ring which mates with the corresponding core retention feature.

The PEEK endplates are coated with a titanium plasma spray (TPS) coating on the bone contacting surfaces.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician who has appropriate training or experience.

IMPORTANT: Simplify® Cervical Artificial Disc is provided sterile. The instruments are provided non-sterile and must be sterilized using the validated instructions.

Table A: Simplify® Cervical Artificial Disc Sizes

Catalog #	Description
SM-4	Simplify® Cervical Artificial Disc Size SM, Height 4
SM-5	Simplify® Cervical Artificial Disc Size SM, Height 5
SM-6	Simplify® Cervical Artificial Disc Size SM, Height 6
MD-4	Simplify® Cervical Artificial Disc Size MD, Height 4
MD-5	Simplify® Cervical Artificial Disc Size MD, Height 5
MD-5L	Simplify® Cervical Artificial Disc Size MD, Height 5, 5° Lordosis
MD-6	Simplify® Cervical Artificial Disc Size MD, Height 6
MD-6L	Simplify® Cervical Artificial Disc Size MD, Height 6, 5° Lordosis
LG-5	Simplify® Cervical Artificial Disc Size LG, Height 5
LG-5L	Simplify® Cervical Artificial Disc Size LG, Height 5, 5° Lordosis
LG-6	Simplify® Cervical Artificial Disc Size LG, Height 6
LG-6L	Simplify® Cervical Artificial Disc Size LG, Height 6, 5° Lordosis

Table B: Simplify® Disc Instrument Set

Catalog #	Description
T-SM-4	Simplify® Trial, Size SM, Height 4
T-SM-5	Simplify® Trial, Size SM, Height 5
T-SM-6	Simplify® Trial, Size SM, Height 6
T-MD-4	Simplify® Trial, Size MD, Height 4
T-MD-5	Simplify® Trial, Size MD, Height 5
T-MD-6	Simplify® Trial, Size MD, Height 6
T-MD-5L	Simplify® Trial, Size MD, Height 5, 5° Lordosis
T-MD-6L	Simplify® Trial, Size MD, Height 6, 5° Lordosis
T-LG-5	Simplify® Trial, Size LG, Height 5
T-LG-6	Simplify® Trial, Size LG, Height 6
T-LG-5L	Simplify® Trial, Size LG, Height 5, 5° Lordosis
T-LG-6L	Simplify® Trial, Size LG, Height 6, 5° Lordosis
SC-SM-4	Simplify® Slot Cutter, Size SM, 4mm
SC-MD-4	Simplify® Slot Cutter, Size MD, 4mm
SC-SM-5/6	Simplify® Slot Cutter, Size SM, 5/6mm
SC-MD-5/6	Simplify® Slot Cutter, Size MD, 5/6mm
SC-LG-5/6	Simplify® Slot Cutter, Size LG, 5/6mm
I-SM	Simplify® Inserter, Size SM
I-MD	Simplify® Inserter, Size MD
I-LG	Simplify® Inserter, Size LG
SH	Simplify® Slide Hammer
TMP	Simplify® Tamp
AS	Simplify® Adjustable Stop
DG-SM	Simplify® Depth Gauge, Size SM
DG-MD	Simplify® Depth Gauge, Size MD
DG-LG	Simplify® Depth Gauge, Size LG
ID	Simplify® Intervertebral Distractor
CR-JL	Simplify® Jaws, Large
CR-JS	Simplify® Jaws, Small
CR-H	Simplify® Handle Core
CR-A	Simplify® Housing Assembly
CR-CG	Simplify® Core Gauge
OST	Simplify® Osteotome
TRAY	Simplify® Tray 3 Level

Simplify® Cervical Artificial Disc Instrument Set **(Table B)** is indicated to assist implantation of the Simplify® Cervical Artificial Disc.

Simplify® Cervical Artificial Disc, Instruments, and Surgical Technique are designed such that the device can be packaged, handled, and implanted as a single unit.

Indications

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

Contraindications

Simplify® Cervical Artificial Disc should not be implanted in patients with the following conditions:

- An active systemic infection or an infection at the operative site.
- Osteoporosis or osteopenia defined as DEXA bone mineral density T-score less than -1.5.
- Known allergy to the implant materials (PEEK, ceramic, titanium).
- Severe facet disease or facet degeneration.
- Bridging osteophytes.
- Marked cervical instability on neutral lateral or flexion/extension radiographs (e.g., radiographic signs of subluxation > 3.0mm or angulation of the disc space more than 11° greater than adjacent segments).
- Significant cervical anatomical deformity at the index levels or clinically compromised cervical vertebral bodies at the index levels due to current or past trauma (e.g., by radiographic appearance of fracture callus, malunion, or nonunion) or disease (e.g., ankylosing spondylitis, rheumatoid arthritis).

Warnings

- Simplify® Cervical Artificial Disc should only be used by surgeons who are experienced with anterior cervical spinal procedures and have undergone hands-on training in the use of this device. Only surgeons who are familiar with Simplify® Cervical Artificial Disc components, instruments, procedure, clinical applications, biomechanics, adverse events (AEs), and risks associated with Simplify® Cervical Artificial Disc should use this device. A lack of adequate experience and/or training may lead to a higher incidence of AEs, including neurological complications.
- Correct selection of the appropriate implant size and correct placement of Simplify® Cervical Artificial Disc are essential to ensure proper performance and functioning of the device. Information regarding implant size selection and correct implant placement is provided in the Simplify® Cervical Artificial Disc Surgical Technique Guide.
- Removal of the disc may be required during device re-positioning or for other surgical

considerations. This process could cause damage that is not visually apparent—if a disc is removed during the implantation procedure, a new device should be implanted in its place.

- Due to the proximity of vascular structures, neurological structures, and major organ systems to the implantation site, there are risks of serious or fatal hemorrhage and risks of neurological damage and/or injury to adjacent organs with the use of Simplify® Cervical Artificial Disc. Care must be taken to identify and protect these structures.
- There is a risk of heterotopic ossification associated with artificial cervical discs which could lead to reduced cervical motion or fusion at either the treated level(s) or adjacent levels.

Precautions

The safety and effectiveness of the Simplify® Cervical Artificial Disc has not been established in patients with the following conditions:

- Previous surgery at the level to be treated
- More than one neck surgery via anterior approach
- Axial neck pain as the solitary symptom
- History of an endocrine or metabolic disorder (e.g., Paget's disease) known to affect bone and mineral metabolism
- Current or extended use (>6 months) of any drug that may interfere with bony/soft tissue healing
- Insulin-dependent diabetes
- Renal Disease
- Auto-immune diseases

Preoperative:

- In order to minimize the risk of atraumatic periprosthetic vertebral fractures, surgeons must consider all co-morbidities, past and present medications, previous treatments, etc. Upon reviewing all relevant information, the surgeon must determine whether a bone density (DEXA) scan is prudent. If DEXA is performed, the patient should not receive the device if the DEXA bone mineral density T-score is <-1.5, as the patient may be osteoporotic or osteopenic.
- Patient selection is extremely important. In selecting patients for a total disc replacement, the following factors can be of extreme importance to the success of the procedure: the patient's occupation or activity level; a condition of senility, mental illness, alcoholism or drug abuse; certain degenerative diseases that may be so advanced at the time of implantation that the expected useful life of the device is substantially decreased, and medical conditions that may affect postoperative management, such as Alzheimer's disease and emphysema.
- The patient should be informed of the potential adverse effects (risks/complications) contained in this insert (see Safety Results / AEs).
- Information on the proper implant site preparation, implant size selection, and the use of surgical instrumentation for the Simplify® Cervical Artificial Disc is provided in the surgical technique guide and should be reviewed prior to surgery.
- Preoperative planning may be used to estimate the required implant size and to assure that the appropriate range of sizes is available for surgery. Correct selection of the appropriate implant sizes is extremely important to assure the placement and function of the disc. The procedure should not take place if the appropriate range of sizes are not available.

- The Simplify® Cervical Artificial Disc is intended to be used with the Simplify® Cervical Artificial Disc Instrument Set. The Simplify® Cervical Artificial Disc Instruments are reusable, supplied non-sterile and must be sterilized in accordance with the recommended cleaning and sterilization procedures prior to use.
- The Simplify® Cervical Artificial Disc is supplied sterile. It is not intended to be re-sterilized. Do not use if sterility is compromised.
- Examine all instruments prior to surgery for wear or damage. Instruments which have been used excessively may be more likely to break. Replace any worn or damaged instruments.

Intraoperative:

- Use aseptic technique when removing Simplify® Cervical Artificial Disc from the innermost packaging. Carefully inspect each device and its packaging for any signs of damage, including damage to the sterile barrier. Do not use the Simplify® Cervical Artificial Disc if the packaging is damaged or if the implant shows signs of damage.
- Ensure Simplify® Cervical Artificial Disc does not come into contact with hard objects that may damage the implant and render the implant functionally unreliable. Visual inspection of the prosthesis is recommended prior to implanting the device. If any part of the device appears damaged or not fully assembled, do not use.
- Take care not to over-distract the disc space.
- Excessive removal of endplate cortical bone may result in sub-optimal outcomes.
- Surgical implants must never be re-used or re-implanted. Even though the device appears undamaged, it may have small defects and internal stress patterns that may lead to early breakage.
- Simplify® Cervical Artificial Disc must not be used with instruments of spinal systems from other manufacturers.

Postoperative:

- Patients should be instructed in postoperative care procedures and should be advised of the importance of adhering to these procedures for successful treatment with the device. Heavy lifting (greater than 20lbs) should be avoided for 6 weeks, and impact sports should be avoided for 3 months.

Potential Adverse Effects of Device on Health

Below is a list of the potential adverse effects (e.g., complications) identified from the Simplify® Cervical Artificial Disc clinical study results, approved device labeling for other cervical total disc replacement devices, and published scientific literature including: (1) those associated with any general surgical procedure; (2) those associated with anterior cervical spine surgery; and (3) those associated with a cervical artificial disc device, including the Simplify® Cervical Artificial Disc. In addition to the risks listed below, there is also the risk that surgery may not be effective in relieving symptoms or may cause worsening of symptoms. Additional surgery may be required to correct some of the adverse effects.

General Surgery Risks

General surgical risks are, but may not be limited to:

- Infection/abscess/cyst, localized or systemic
- Blood clots, including pulmonary emboli

- Medication and anesthesia reactions
- Phlebitis
- Pneumonia
- Atelectasis
- Soft tissue damage
- Septicemia
- Hemorrhage possibly requiring a blood transfusion, with possible transfusion reaction
- Myocardial infarction
- Paralysis
- Poor tissue healing
- Cerebrovascular accident (CVA)
- Death

Anterior Cervical Surgery Risks

Anterior cervical surgical risks are, but may not be limited to:

- Infection/abscess/cyst, localized or systemic
- Injury or damage to the trachea, esophagus, nerves or blood vessels
- Dysphagia
- Hoarseness
- Vocal cord paralysis
- Paresis
- Recurrent laryngeal nerve palsy
- Soft tissue damage
- Spinal cord damage
- Dural tear with cerebrospinal fluid leakage
- Arm weakness or numbness
- Bowel, bladder or sexual dysfunction
- Nerve root injury
- Airway obstruction
- Epidural hematoma or bleeding
- Epidural fibrosis
- Vertebral body fracture
- Dysesthesia or numbness
- Paresthesia
- Unresolved pain
- Surgical intervention at incorrect level
- Need for supplemental fixation
- Spinal instability
- Death

Cervical Artificial Disc Risks

Risks specific to cervical artificial discs, including the Simplify® Cervical Artificial Disc, are but may not be limited to:

- Infection/abscess/cyst, localized or systemic
- Allergic reaction to the implant materials

- Implant failure
- Device migration
- Device subsidence
- Device fatigue or fracture or breakage
- Device instability
- Separation of device components
- Placement difficulties, device malposition
- Improper device sizing
- Excessive device height loss
- Wear debris
- Disc space collapse
- Material degradation
- Excessive facet loading
- Kyphosis or hyper-extension
- Loss of flexibility
- Asymmetric range of motion
- Vertebral body fracture
- Spinal cord damage,
- Dural tear with cerebrospinal fluid leakage
- Soft tissue damage
- Epidural fibrosis
- Nerve injury, paralysis or weakness that is temporary or permanent
- Injury or damage to the trachea, esophagus, or blood vessels
- Epidural hematoma or bleeding
- Dysesthesia or numbness
- Paresthesia
- Failure to relieve symptoms including unresolved pain
- Additional surgery due to loss of fixation, infection or injury
- Spontaneous fusion due to heterotopic ossification, development of bridging bone or osteophytes
- Periarticular calcification and fusion
- Development of spinal conditions, including but not limited to spinal stenosis, spondylolisthesis, or retrolisthesis
- Removal, revision, reoperation or supplemental fixation of the disc
- Osteolysis, bone loss, or bone resorption
- Death

For the specific adverse events (AEs) that occurred in the Simplify® Cervical Artificial Disc, please refer to Section I.A.4 (one-level) and/or Section I.B.4 (two-level).

Simplify® Cervical Artificial Disc is nickel-free. Nickel is not intentionally added to the Simplify® Cervical Artificial Disc or its packaging, and sensitive analytical testing could not detect its presence. Therefore, Simplify® Cervical Artificial Disc does not contain nickel at a level that could result in an AE (allergic reaction or toxicity) and any potential release of nickel from the Simplify® Cervical Artificial Disc is very unlikely to present a risk to the patient.

NOTE: Additional surgery may be necessary to correct some of the adverse effects. During the procedure, if the Simplify® Cervical Artificial Disc cannot be visualized, a contrast media may be used.

Following completion of the procedure, patients should receive a postoperative treatment care protocol. Patients will be permitted to ambulate on the day of surgery, as tolerated, and, at the discretion of the surgeon, may wear a collar to support the neck (Philadelphia, Aspen, Miami J, 2 poster-orthosis, etc.) until the soft tissues of the neck have healed.

I. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant conducted two clinical studies to establish a reasonable assurance of safety and effectiveness of replacement of the degenerated native disc with the Simplify® Cervical Artificial Disc in skeletally mature patients for reconstruction of the disc at one or two contiguous levels from C3-C7 following discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and manifested by at least one of the following conditions confirmed by radiographic imaging (e.g., X-rays, computed tomography (CT), magnetic resonance imaging (MRI)): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels. A summary of the clinical studies is presented below.

A. One-Level IDE Study (G140154)

1. Study Design

Subjects in the Simplify® Cervical Artificial Disc pivotal study ("Simplify® Cervical Artificial Disc IDE study") were treated between February 2016 and February 2018. The database for this PMA reflects data collected through March 2020 and included 150 Simplify® Cervical Artificial Disc subjects (166 including training subjects) at 16 sites and 133 ACDF subjects treated at 21 sites. Control subjects were treated between July 2005 and August 2007.

The prospective, non-randomized, historically controlled, multi-center study was performed in the United States under IDE #G140154. The ACDF data was from a previous multi-center, prospective, randomized concurrently-controlled cervical disc IDE study performed in the United States. This previous study incorporated a similar study design, indications for use, study entry

criteria, study endpoints, and data collected. The two studies were not identical, and differences were identified in some categories and are discussed below.

A statistical plan utilizing propensity score (PS) modeling was developed to incorporate the historical control and to match the baseline covariates to the Simplify® Cervical Artificial Disc group. The resultant PS Selected study cohort used for the primary analysis population thus included all investigational Simplify® Cervical Artificial Disc subjects (excluding training subjects) and historical control subjects (excluding trimmed subjects) and is termed the "Primary Analysis Set."

Clinical Inclusion and Exclusion Criteria

To be eligible for the Simplify® Cervical Artificial Disc IDE study, subjects had to be eligible for a fusion procedure and meet all of the inclusion criteria and none of the exclusion criteria:

Table 1: Study Inclusion/Exclusion Criteria

Study Inclusion Criteria	Study Exclusion Criteria

• Be between 18 and 60 years of age;
• Have symptoms of cervical degenerative disc disease (DDD) at ***one cervical level*** from C3 to C7 defined as intractable radiculopathy (arm pain and /or a neurological deficit) with or without neck pain or myelopathy due to a single-level abnormality localized to the level of the disc space and radiographic evidence of at least one of the following;
  • Spondylosis (defined by the presence of osteophytes or dark disc) on CT or MRI or;
  • Disc height decreased by ≥ 1 mm when compared to adjacent levels on radiographic film, CT, or MRI or
  • Disc herniation on CT or MRI;
• Have at least one of the following radiculopathy or myelopathy symptoms in neck and/or arm;
  • Pain or paresthesias in a specific nerve root distribution from C3 to C7,
  • Decreased muscle strength of at least one level on the 0-5 scale, or
  • Abnormal sensation, including hyperesthesia or hypoesthesia.
• Have at least one of the following:
  • At least six weeks of prior conservative treatment (e.g., physical therapy and/or use of anti-inflammatory medications and muscle relaxants at the manufacturer's recommended therapeutic dose);
  • The presence of progressive symptoms (e.g., increasing numbness or tingling) or
  • Signs of nerve root compression.
• Have a Neck Disability Index (NDI) greater than or equal to 40 on a scale of 100 (moderate disability);
	• Marked cervical instability on resting lateral or flexion/ extension X-ray (translation > 3 mm or > 11 degrees rotation to that of either adjacent non-treatment level);
	• Non-discogenic neck pain or non-discogenic source of symptoms (e.g., tumor, rotator cuff injury, etc.);
	• Radiographic confirmation of severe facet disease or facet degeneration;
	• Bridging osteophytes;
	• Less than 2 degrees of motion at index level;
	• Prior surgery at the level to be treated, except laminotomy without accompanying facetectomy;
	• Prior fusion or artificial disc replacement at any cervical level;
	• More than one neck surgery via anterior approach;
	• Previous trauma to the C3-C7 levels resulting in compression or bursting;
	• Documented presence of a free nuclear fragment at cervical levels other than the study level;
	• Axial neck pain only (no radicular or myelopathy symptoms);
	• Symptomatic DDD at more than one cervical level;
	• Severe myelopathy (less than 3/5 muscle strength);
	• Any paralysis;
	• Recent history (within previous six months) of chemical or alcohol dependence;
	• Active systemic infection;
	• Infection at the site of surgery;
	• Prior disc space infection or osteomyelitis in the cervical spine;
	• Any terminal, systemic or autoimmune disease;

Study Inclusion Criteria	Study Exclusion Criteria

• Be appropriate for treatment using an anterior surgical approach;
• Be likely to return for all follow-up visits[1] and
• Be willing and able to provide Informed Consent for study participation.
 	
Muscle strength will be graded for the deltoid (C5), biceps (C6), and triceps (C7) according to a 6-point scale where 0 = no movement, 1 = trace of muscle contraction; 2 = active movement without gravity; 3 = active movement against gravity; 4 = active movement against gravity/resistance; and 5 = normal response. [2]
 	
For the purpose of this study, conservative therapy may include, but is not limited to, injections of steroids, physical therapy, bracing, traction, acupuncture, yoga, life style changes, neck support or massage chairs, exercise, ice, heat, massage, water therapy, chiropractic, and medications prescribed for pain, muscle tightness, muscle cramping or inflammation of muscles or nerves or other symptoms typically involved with chronic neck conditions such as DDD.
	• Metabolic bone disease (e.g., osteoporosis/osteopenia [3], gout, osteomalacia, Paget's disease);
	• Any disease, condition or surgery which might impair healing, such as;
	  • Diabetes mellitus requiring daily insulin management,
	  • Active malignancy,
	  • History of metastatic malignancy.
	• Current or extended use (> 6 months) of any drug known to interfere with bone or soft tissue healing;
	• Known PEEK, ceramic, titanium allergy;
	• Arachnoiditis;
	• Significant cervical anatomical deformity at the index level or clinically compromised cervical vertebral bodies at the index level due to current or past trauma (e.g., by radiographic appearance of fracture callus, malunion, or nonunion) or disease (e.g., ankylosing spondylitis, rheumatoid arthritis);
	• Currently experiencing an episode of major mental illness (psychosis, major affective disorder, or schizophrenia), or manifesting physical symptoms without a diagnosable medical condition to account for the symptoms, which may indicate symptoms of psychological rather than physical origin;
	• Pregnancy at time of enrollment, or planning to become pregnant, since this would contraindicate surgery [4];
	• Use of spinal stimulator at any cervical level prior to surgery;
	• Currently a prisoner;
	• Currently involved in spinal litigation which may influence the subjects reporting of symptoms **or**
	• Participation in any other investigational drug, biologic or medical device study within the last 30 days prior to study surgery.

[1] Please note that patients who live significant distances away from a treatment center are statistically likely to be present for treatment, but are not likely to return for all follow-up visits. For this reason, patients who live over **150** miles from a treatment center were not eligible for treatment in this clinical study without **prior approval** from the study Sponsor.

[2] *See* Hacker *et al.*, *supra* note 7, at 2648; Aids to the Investigation of Peripheral Nerve Injuries (UK Medical Research Council, War Memorandum No. 7 (2d ed. Rev. 1943).

[3] Patients at risk for osteoporosis/osteopenia must be screened using a dual X-ray absorptiometry scan (DXA). Patients meeting the WHO definition for osteoporosis/osteopenia for risk of fracture, i.e., have a bone mineral content greater than 1.5 standard deviations below the mean for young, healthy adults (DXA score), were ineligible for study participation.

[4] Pregnancy during participation in this study was also discouraged, since pregnancy may prohibit exposure to X-rays during necessary follow-up timeframes.

Control
Control subjects received ACDF. The historical control was collected from the control arm of a previously completed multi-center, prospective, randomized non-inferiority clinical trial. Comparison of the data collected from the Simplify® Cervical Artificial Disc Pivotal IDE study and historical ACDF control demonstrated that the cohorts were comparable, though not identical.

- A detailed comparison of the indications and inclusion/exclusion criteria of the historical ACDF cohort and the Simplify® Cervical Artificial Disc IDE study protocol was conducted to determine if the historical data were adequate to serve as comparator and support a PMA application. The sponsor reviewed the protocol and case report forms as submitted to the FDA. Based on this review and discussion with FDA, it was determined that the historical study was similar to the IDE study in its Indications for Use and Inclusion/Exclusion criteria.
- The historical study collected the parameters used to calculate overall success, success of the individual components of the composite primary endpoint, secondary endpoints, and safety assessments per the defined assessments in the Simplify® Cervical Artificial Disc IDE study protocol.

A PS method was used to address selection bias in the observational study design when pooling data from the historical control and actively enrolled Simplify® Cervical Artificial Disc group. The objective of the observational design was to select from the candidate pool of historical controls those subjects whose baseline covariate distribution was approximately the same as Simplify® Cervical Artificial Disc subjects within PS subclasses. The final Primary Analysis set included all 150 Simplify® Cervical Artificial Disc subjects (166 including training subjects) and 117 of 133 historical control subjects. Rigorous statistical criteria and graphical analyses demonstrated that within PS subclasses, Simplify® Cervical Artificial Disc subjects and PS-selected historical controls had approximately the same multivariate baseline covariate distribution.

Postoperative Care
Following completion of the procedure, recommended postoperative care regimen was implemented.

Subjects were encouraged to return to normal activity with the following guidelines:

- Use of a soft collar (at the discretion of the surgeon)
- Ambulation on day of surgery progressing to aerobic walking over the course of 6 weeks
- Gradually increase cervical range of motion
- No heavy lifting (greater than 20 lbs) for 6 weeks and then progress to more resistive exercise
- No impact sports for 3 months

Follow-up Schedule

All subjects were evaluated preoperatively, postoperatively (up to 2-weeks post-treatment) and postoperatively at 6 weeks (±2 weeks), 3 months (±2 weeks), 6 months (±1 month), 1 year (±2 months), 2 years (±2 months), and annually thereafter (±2 months). The following parameters (**Table 2**) were measured throughout the study:

Table 2: Simplify® Cervical Artificial Disc IDE Study Assessment Schedule

Evaluation	Preop	Treatment	Postop	6 Weeks	3 Months	6 Months	12 Months	24 Months
Informed Consent	X							
Medical History & Physical Examination	X							
DXA ***(as described in protocol)***	X							
AP & Lateral X-rays	X		X	X	X	X	X	X
Flexion & Extension X-rays	X				X	X	X	X
Lateral bending X-rays	X					X	X	X
MRI ***(Simplify® Cervical Artificial Disc Subjects only)***	X							X
Radiographic Core Lab Assessments	X		X	X	X	X	X	X
Dysphagia Handicap Index ***(Simplify® Cervical Artificial Disc Subjects only)***	X			X	X	X	X	X
Neck Disability Index (NDI)	X			X	X	X	X	X
SF-12v2 Health Survey ***(Simplify® Cervical Artificial Disc Subjects only)***	X					X	X	X
Visual Analog Scale (VAS)	X		X	X	X	X	X	X
Odom's Criteria			X	X	X	X	X	X
Neurologic Exam	X		X	X	X	X	X	X
Medications Taken	X		X	X	X	X	X	X
Work Status	X				X	X	X	X
Treatment Assessments		X						
Treatment Satisfaction Assessment							X	X
AE Assessment	N/A	*As Needed*						

Clinical Endpoints

The effectiveness of the Simplify® Cervical Artificial Disc was assessed using a composite endpoint, as described below. Effectiveness was further evaluated by assessing improvement in the Neck Disability Index (NDI), neck and arm pain based on a Visual Analog Scale (VAS), and health-related quality of life using the short-form questionnaire (SF-12v2), work status, as well as patient satisfaction of the Simplify® Cervical Artificial Disc group compared to the historical ACDF control group. Similar criteria were used to measure success in both groups.

The safety of the Simplify® Cervical Artificial Disc was assessed by comparison to the historical ACDF control group with respect to the nature and frequency of AEs (overall and in terms of seriousness and relationship to the implant), subsequent index level surgical procedures and maintenance or improvement in neurological status.

<u>Primary Endpoints</u>

The study hypothesis for the Simplify® Cervical Artificial Disc IDE study was that the Month 24 (i.e., 24 months postoperatively) composite clinical success (CCS) rate of the Simplify® Cervical Artificial Disc would be no worse than conventional ACDF when success of ACDF is evaluated at Month 24 in patients with intractable radiculopathy (arm pain and/or a neurological deficit) with

or without neck pain or myelopathy due to a single-level abnormality localized to the level of the disc space at one level from C3 to C7 that are unresponsive to conservative management or have presence of progressive symptoms.

- Individual success for the investigational Simplify® Cervical Artificial Disc is defined as at least a 15 point (out of 100) improvement in NDI percentage at Month 24 compared with baseline; maintenance or improvement in neurologic status at Month 24 compared with baseline; no device failures or revision, reoperation, removal and/or supplemental fixation within 24 months of index procedure; and the absence of major AEs within 24 months as defined below.
- Individual success for the historical control ACDF device is defined as at least a 15 point (out of 100) improvement in NDI percentage at Month 24 compared with baseline; maintenance or improvement in neurologic status at Month 24 compared with baseline; no device failures or revision, reoperation, removal and/or supplemental fixation within 24 months; and the absence of major AEs within 24 months as defined below.

Device failure is defined as breakage, migration, or mechanical failure of the components. For purpose of determining individual patient success, a major AE is defined as any of the following which are definitely related to the device system or to a device component as determined by the Clinical Events Committee (CEC):

- Permanent neurologic damage or permanent nerve root injury related to a level at or below the level treated;
- Implant or component breakage or migration that does not require revision, reoperation or removal, but causes persistent or moderate to severe dysphagia and/or
- Patient death.

Per the FDA Guidance for the Preparation of IDEs for Spinal Systems, the following definitions apply:

- Reoperation – Any surgical procedure at the index level that does not involve modification, addition or removal of any components of the device in the postoperative or follow-up period.
- Revision – Any procedure in the postoperative or follow-up period that adjusts, modifies, or removes part of the original implant configuration with or without replacement of a component – may include adjusting the position of the original configuration in the postoperative or follow-up period.
- Removal – A procedure where the entire device is removed with or without replacement of the device in the postoperative or follow-up period.
- Supplemental fixation – A procedure in which additional instrumentation not under study is implanted (e.g., supplemental placement of a rod/ screw system).

<u>Secondary Endpoints</u>

Secondary objectives, measured in both groups (except as noted), included:

- Clinically significant improvement in one or more radicular symptoms or myelopathy at Month 24 compared to baseline for the investigational Simplify® Cervical Artificial Disc and the historical control ACDF subjects. The data collected reflect the number of subjects who improved (numbers are stratified to reflect clinical improvement), who remain unchanged, and who deteriorated at each study timepoint. These endpoints are graded and defined as follows:
    - VAS for the following pain locations:
        - Neck and arm pain (to allow comparison to historical ACDF control);
        - Neck, Arm (Right/Left) pain (Simplify® Cervical Artificial Disc group only);

      Changes of at least 20 mm on a 100 mm scale is regarded as clinically significant.
    - Motor status - A change of one or more grade levels in muscle strength is regarded as clinically significant.
    - Sensory status - Sensation is graded as normal or abnormal (diminished or absent). Any changes from abnormal to normal or absent to diminished is regarded as clinically significant improvement.
- Time to recovery (earliest time at which a minimum 15-point (out of 100) NDI improvement is reached).
- Disc height at Month 24 compared to baseline.
- Adjacent level deterioration at Month 24 compared to baseline.
- Displacement or migration of the device defined as a change of 3mm or greater compared to the position at implantation.
- Treatment satisfaction at Month 24.
- Health-related Quality of Life Survey (SF-12v2) at Month 24 compared to baseline (Simplify® Cervical Artificial Disc group only).
- Dysphagia Handicap Index (DHI scale) at Month 24 compared to baseline (Simplify® Cervical Artificial Disc group only).
- Facet deterioration at Month 24 compared to baseline (Simplify® Cervical Artificial Disc group only).
- Results at Month 24 as categorized by the physician according to Odom's Criteria.

2. <u>Accountability of PMA Cohort</u>

One-hundred sixty-six (166) subjects were enrolled in the Simplify® Cervical Artificial Disc population. Of these, 16 Simplify® Cervical Artificial Disc subjects were training subjects. The historical ACDF control population included 133 subjects.

The 283 available subjects (150 Simplify® Cervical Artificial Disc (excluding training subjects) and 133 historical ACDF control) were assessed via the PS subclassification sequential model-building process. After applying an established heuristic for 3 iterations, a total of 150 Simplify® Cervical Artificial Disc and 117 historical ACDF control subjects were retained in the final PS designed sample. Inclusion into a PS subclass is the observational study analogue to randomized treatment allocation. When accounting for the PS design, there was excellent balance across all considered baseline covariates. For subjects at Month 24, the visit compliance rates were 97% for Simplify® Cervical Artificial Disc subjects and 86% for the PS Selected ACDF subjects.

The subject accountability for Month 12 and Month 24 clinical evaluations is presented in **Table 3** and **Figure 1**.

Table 3: Subject Accounting Summary (Primary Analysis Population)

	Month 12		Month 24	
	I	C	I	C
Accounting				
(1) Theoretical follow-up	150	117	150	117
(2) Cumulative Death	0	0	0	0
(3a) Intra-Op Deviations	2	0	2	0
(3b) Cumulative SSI Failures	1	2	4	5
(4) Not Yet Overdue	0	0	0	0
(5) Deaths+SSI failures+Intra-Op Deviations among theoretically due	3	2	6	5
(6) Expected Due [(6)=(1)-(4)-(5)]	147	115	144	112
(7) SSI failures+Intra-Op Deviations among theoretically due	3	2	6	5
(8) Expected due+SSI failures+Intra-Op Deviations among theoretically Due [(8)=(6)+(7)]	150	117	150	117
All Evaluated Accounting (Actual^{B}) Among Expected Due Procedures				
(9) Procedures with any clinical data in interval†	144	101	139	96
(10) Visit Compliance (%)	98%	88%	97%	86%
(11) Change in NDI	143	100	138	96
(12) Change in VAS	142	100	139	95
(13) Neuro evaluations	143	100	139	95
(14) Composite Clinical Success (CCS)			136	91
(15) Actual^{B} % Follow-up for CCS			94%	81%
Within Window Accounting (Actual^{A}) Among Expected Due Procedures				
(16) Procedures with any clinical data in interval†	141	89	128	79
(17) Visit Compliance (%)	96%	77%	89%	71%
(18) Change in NDI	140	88	127	79
(19) Change in VAS	139	88	128	79
(20) Neuro evaluations	140	88	128	78
(21) Composite Clinical Success (CCS)			125	74
(22) Actual^{A} % Follow-up for CCS			87%	66%

† Change in NDI, change in VAS, or Neuro overall status;
Source: Table Follow-up Compliance.sas; Analyzed: 27AUG2020

Actual^{A}: Patients with complete data for each endpoint, within window.
Actual^{B}: Patients with any follow-up data reviewed or evaluated by investigator ("all evaluated" accounting).

(1) Theoretical follow-up: The theoretical follow-up is the number of devices at one level that would have been examined if all subjects returned on the exact anniversary of their respective initial surgery dates. The date of database closure for these analyses was March 27th, 2020. All subjects were theoretically due for Month 12 and Month 24 follow-up at the date of database closure.

(2) Cumulative deaths: Cumulative deaths up to the date of the exact anniversary defining the current interval. Deaths occurring after the exact anniversary are recorded in the next interval.

(3a) Intraop Deviations: Subjects who were to be treated with Simplify® Cervical Artificial Disc but converted to alternate treatment intraoperatively. Intraoperative deviation subjects are considered a treatment failure in the CCS primary endpoint calculation and censored at day 0 for secondary surgical intervention (SSI) and device survivorship. At the time of surgery, due to anatomical challenges the surgeons could not implant the total disc replacement (TDR) for 2 subjects enrolled to be treated with Simplify® Cervical Artificial Disc and performed an ACDF surgery. Since these 2 subjects do not meet the definition of an SSI, they are accounted for

separately. They were considered a treatment failure in the CCS primary endpoint calculation and censored at day 0 for SSIs and device survivorship.

(3b) Cumulative SSI Failures: Failures are defined as any result that removes the subject from further evaluation of effectiveness, that is, these Failures are "***terminal failures***". As per FDA Guidance (2004), failure includes subsequent SSIs categorized as reoperations, revisions, removals, reoperations or supplemental fixation. It also includes other severe AEs or other parameters that would define the device as ineffective or unsafe from that point on. Failures are counted up to the date of the exact anniversary defining the current interval. Terminal failures occurring after the exact anniversary are recorded in the next interval. Terminal failures on this row do not include radiographic failure since radiographic failure does not remove a subject from the study. It also does not include clinical failures determined on the basis of clinical scores such NDI, VAS, or deteriorating neurological status because these types of failure do not remove the subject from further follow-up. Although the cumulative number of failures is recorded on this row, only failures among devices that are theoretically due for that interval are subtracted from theoretically due to determine the number expected due for clinical indices.

(4) Not Yet Overdue: Includes subjects whose surgical anniversary has occurred; however, clinical data has not yet been collected (i.e., NDI or VAS/NRS is currently unavailable) but the subject is still in the protocol specified follow-up window. Such subjects may yet be observed and so follow-up compliance estimates account for this by removing such subjects from the denominator as well as from the numerator when determining compliance ratios.

(5) Deaths+SSI Failures+Intraop Deviations among theoretically due: This row records the sum of deaths, SSI Failures, and Intraop Deviations among those theoretically due for follow-up according to the exact anniversary of the scheduled follow-up visit. Only deaths, SSI Failures, and Intraop Deviations among procedures that are theoretically due for that interval are subtracted from theoretically due to determine the number expected due for clinical index evaluation.

(6) Expected due for clinic visit: This row is the number of subjects expected for a given time interval. These include the theoretical number of subjects who were due to be evaluated, less the number of subjects who died or who were considered failures by that time interval and less the subjects in the "Not yet overdue" category. **Expected = Theoretical - [Deaths + Failures + Not yet overdue]** where the counts of the numbers of Deaths, Failures, and Not yet overdue are determined from among the theoretically due subjects. This row serves as denominator for evaluation % follow-up for clinical indices (e.g., NDI, VAS/NRS). The Expected row includes subjects lost to follow-up, and major protocol violations are included in the expected group for all timepoints.

(7) SSI Failures + Intraop Deviations among theoretical due: SSI failures and intraop deviations among theoretically due is the count of theoretically due Failures that need to be "added back" to the number of expected due to serve as the correct denominator for CCS counts when determining CCS follow-up compliance.

(8) Expected due + SSI Failures + Intraop Deviations among theoretical due: Expected due plus theoretical due Failures is computed by adding expected due in row (6) to the number of cumulative Failures among theoretically due devices in row (7). This row serves as the denominator for composite clinical success (CCS) outcomes since CCS status is known for subjects with a Failure as defined in row (3).

(9) and (16) Procedures with any clinical data in interval: These rows indicate the number of subjects with any clinical data that report a change in NDI, VAS, or neurological status for all evaluated subjects among expected due subjects **(9)** and for all subjects that are within window among expected due subjects **(16)**.

(10) and (17) Visit Compliance (%): These rows indicate the percentage of subjects compliant with the specified visit scheduled for all evaluated subjects among expected due subjects **(10)** and for all subjects that are within window among expected due subjects **(17)**.

(11) and (18) Change in NDI: These rows indicate the number of subjects reporting a change in NDI for all evaluated subjects among expected due procedures **(11)** and for all subjects that are within window among expected due procedures **(18)**.

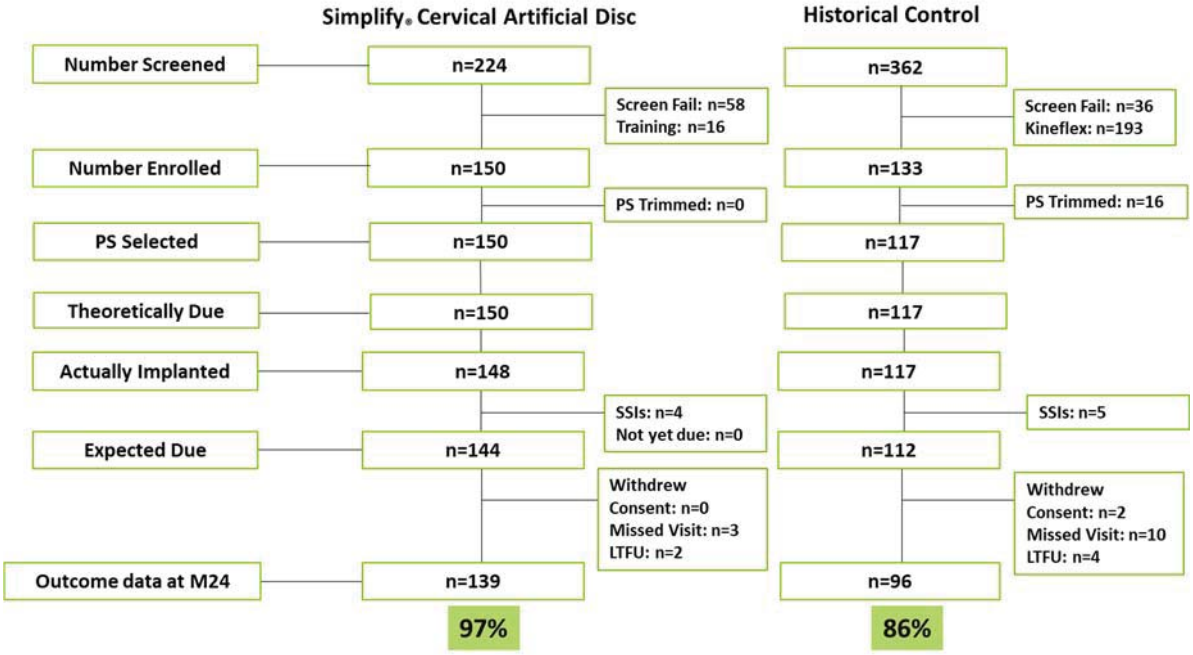
(12) and (19) Change in VAS: These rows indicate the number of subjects reporting a change in VAS for all evaluated subjects among expected due procedures **(12)** and for all subjects that are within window among expected due procedures **(19)**.

(13) and (20) Neuro evaluations: These rows indicate the number of subjects reporting a change in neurological status for all evaluated subjects among expected due procedures **(13)** and for all subjects that are within window among expected due procedures **(20)**.

(14) and (21) Composite Clinical Success: These rows indicate the number of subjects with enough data available for evaluation of clinical composite success for all evaluated subjects among expected due procedures **(14)** and for all subjects that are within window among expected due procedures **(21)**.

(15) and (22) Actual Follow-up for CCS: These rows indicate the percentage of subjects with follow-up data available used to evaluate CCS for all evaluated subjects among expected due procedures **(15)** and for all subjects that are within window among expected due procedures **(22)**.

Figure 1. Subject Accountability Tree



3. Study Population Demographics and Baseline Parameters

After adjusting for PS subclass, the demographic data appear to demonstrate that the treatment groups were well-balanced and no statistically significant differences were noted in the demographic characteristics and categorical values (**Table 4** and **Table 5**). The mean baseline preoperative assessments for NDI, VAS Neck and Arm, and baseline radiographic parameters were also similar between treatment groups. Baseline VAS Neck and Arm were significantly

higher in the Simplify® Cervical Artificial Disc group; however, when adjusting for PS subclass, there was no significant difference between groups, indicating similar neck pain and function.

Table 4: Summary of Demographic and Baseline Continuous Variables (Clinical) (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
All																
Age (years)	150	43.0	8.9	43.2	18.1	60.9	117	44.1	7.0	43.9	23.6	59.3	0.765	-0.3	-2.5	1.8
BMI (kg/m^2)	150	27.5	5.2	26.6	18.2	40.3	117	28.7	5.6	27.3	19.5	48.4	0.914	0.1	-1.3	1.5
Height (inches)	150	67.7	4.0	67.0	59.0	76.0	117	67.3	4.1	67.0	57.0	79.0	0.927	-0.1	-1.1	1.0
Weight (pounds)	150	180.3	42.9	178.5	103.0	308.0	117	185.3	41.4	180.0	103.0	298.0	0.855	1.1	-10.4	12.5
Female																
Age (years)	91	43.0	8.7	43.1	18.1	60.4	68	44.7	6.8	45.6	30.5	58.8	0.678	-0.6	-3.3	2.1
BMI (kg/m^2)	91	26.7	5.5	25.5	18.2	40.3	68	28.9	6.5	27.1	19.5	48.4	0.404	-0.8	-2.8	1.1
Height (inches)	91	65.3	2.5	65.0	59.0	72.0	68	65.0	3.0	66.0	57.0	72.0	0.416	-0.4	-1.3	0.5
Weight (pounds)	91	162.2	36.2	160.0	103.0	265.0	68	173.7	40.9	167.0	103.0	292.0	0.343	-6.3	-19.4	6.8
Male																
Age (years)	59	42.8	9.2	43.9	22.1	60.9	49	43.2	7.2	43.7	23.6	59.3	0.797	-0.5	-4.1	3.2
BMI (kg/m^2)	59	28.7	4.5	27.4	21.5	39.5	49	28.4	4.0	27.5	20.5	38.3	0.177	1.3	-0.6	3.2
Height (inches)	59	71.4	2.9	72.0	64.0	76.0	49	70.4	3.1	70.0	66.0	79.0	0.440	0.5	-0.8	1.9
Weight (pounds)	59	208.2	37.4	195.0	150.0	308.0	49	201.4	36.7	200.0	127.0	298.0	0.171	11.7	-5.1	28.4
Clinical Scores																
Neck Disability Index	150	63.3	12.5	61.0	40.0	94.0	117	62.4	12.6	64.0	40.0	90.0	0.950	0.1	-3.3	3.5
VAS Neck and Arm	150	81.6	12.4	84.0	41.0	100.0	117	77.6	13.5	79.0	42.0	100.0	0.717	0.6	-2.7	4.0
VAS Neck	150	77.1	18.2	81.0	0.0	100.0										
VAS Left Arm	150	54.3	36.3	67.5	0.0	100.0										
VAS Right Arm	150	48.8	39.4	60.0	0.0	100.0										
DHI Score	150	6.2	8.8	3.0	0.0	50.0										
SF12 PCS	150	31.1	7.4	30.3	11.2	56.1										
SF12 MCS	150	42.4	12.2	42.3	15.6	67.5										
Radiography																
Disc Angle	148	2.1	4.5	2.4	-8.2	14.0	116	2.6	4.4	2.4	-8.4	14.0	0.249	-0.7	-1.9	0.5
Average Disc Height	148	3.3	0.7	3.3	1.1	5.7	115	3.3	0.8	3.2	1.4	5.2	0.813	0.0	-0.2	0.2
Anterior Disc Height	148	3.6	1.0	3.5	1.6	6.5	115	3.6	1.1	3.5	1.4	6.9	0.419	-0.1	-0.4	0.2
Posterior Disc Height	148	3.0	0.9	3.1	0.6	5.4	115	2.9	0.9	2.8	0.9	5.2	0.537	0.1	-0.2	0.3
Rotation	143	7.3	4.2	6.4	0.0	21.4	110	7.3	4.4	6.8	-0.8	19.0	0.588	-0.3	-1.5	0.9
Translation (mm)	143	0.7	0.5	0.6	0.0	2.4	109	0.8	0.6	0.7	-0.1	2.7	0.061	-0.1	-0.3	0.0
Translation (%)	143	4.6	3.1	3.9	0.0	13.9	110	5.2	3.9	4.6	-0.7	16.0	0.090	-0.8	-1.8	0.1
AP Rotation	144	6.1	2.8	5.6	0.3	15.4	106	5.2	3.1	4.7	0.0	12.9	0.211	0.5	-0.3	1.4
Spondylolisthesis (mm)	148	0.9	1.0	0.9	-1.8	3.9	115	1.2	0.9	1.0	-0.5	3.8	0.078	-0.2	-0.5	0.0
Spondylolisthesis (%)	148	6.0	6.1	5.7	-10.5	24.9	116	7.4	5.8	6.1	-4.1	25.7	0.091	-1.4	-3.1	0.2

*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Baseline Demo.sas; Analyzed: 14MAY2020

Table 5: Summary of Baseline Categorical Variables – (Primary Analysis Population)

	Simplify® Cervical Artificial Disc			ACDF			Group Difference*			
	N	n	%**	N	n	%**	p	Δ	LB	UB
Conservative Therapy with Injection	150	70	46.7%	117	52	44.4%	0.953	0.4%	-12.6%	13.4%
Conservative Therapy with Narcotics	150	66	44.0%	117	67	57.3%	0.994	0.1%	-13.5%	13.6%
Neurological Motor Deficit	150	53	35.3%	117	62	53.0%	0.772	0.2%	-15.7%	11.5%
Neurological Sensory Deficit	150	66	44.0%	117	66	49.6%	0.855	-0.1%	-14.2%	11.7%
Work Status = Employed	150	120	80.0%	117	82	70.1%	0.617	2.9%	-8.1%	13.9%

*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model. **Unadjusted proportions calculated as x/n.
Source: Table Clinical Follow-up.sas; Analyzed: 19JUN2020

Table 6 summarizes the available race and ethnicity data. Please note, complete race and ethnicity data were not collected.

Table 6: Summary of Demographic and Baseline Variables – Race and Ethnicity (Primary Analysis Population)

	Simplify Disc			ACDF			
	N	n	%	N	n	%	p*
Race and Ethnicity							0.822
Caucasian		131	87.3%		103	88.0%	
Black	150	10	6.7%	117	7	6.0%	
Hispanic		4	2.7%		6	5.1%	
Other		5	3.3%		1	0.9%	

*p-value adjusted for PS subclass using two-way analysis of variance with race dichotomized as Caucasian vs. Non-Caucasian.
Source: Tables Baseline Demo.sas; Analyzed: 27FEB2020

The radiographic findings used to qualify a subject for enrollment are provided with post-hoc nominal measures of significance are presented in **Table 7**.

Table 7: Summary of Baseline Variables – Radiographic Data (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p**	Δ	LB	UB
Spondylosis (defined by the presence of osteophytes or dark disc on CT/MRI†	150	72	48.0%	117	66	56.4%	0.490	-5.7%	-18.6%	7.2%
Decrease disc height ≥1mm compared to adjacent levels on x-rays, CT, or MRI	150	59	39.3%	117	53	45.3%	0.490	-4.7%	-17.4%	8.0%
Disc herniation on CT or MRI	150	139	92.7%	117	98	83.8%	0.117	8.0%	-0.6%	16.6%

*Post-hoc nominal Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model. **PS adjusted Hochberg p-values corrected for multiplicity (3 tests). †Historical control criterion wording reads 'degenerated / dark disc on MRI'.
Source: IR3 - Question 7c.sas; Analyzed: 10JUN2020

Table 8: Summary of Operative Continuous Variables (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Operative Time (minutes)	150	73.6	21.8	70.0	32.0	170.0	117	74.0	27.1	69.0	29.0	157.0	0.987	-0.05	-6.66	6.55
Blood Loss (cc)	150	31.2	38.6	20.0	0.0	250.0	117	42.4	33.9	30.0	0.0	200.0	0.013	-12.62	-22.55	-2.69
Length of Stay (days)	150	0.6	1.9	0.0	0.0	23.0	117	1.1	0.5	1.0	0.0	3.0	0.134	-0.31	-0.71	0.09

*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.

Source: Tables Intra-op.sas; Analyzed: 09JAN2020

As evidenced by Table 8, a statistically significant difference was observed in blood loss, favoring the Simplify® Cervical Artificial Disc subjects. The mean blood loss for the Simplify® Cervical Artificial Disc subjects was 31.22cc while the mean blood loss for the historical ACDF control subjects was 42.4cc. The operative time and length of stay were not significantly different.

Table 9: Summary of Operative Categorical Variables (Primary Analysis Population)

	Simplify Disc (N= 150)		ACDF (N= 117)	
	n	%	n	%
C3/C4	3	2%	3	3%
C4/C5	7	5%	6	5%
C5/C6	80	53%	71	61%
C6/C7	60	40%	37	32%
Posterior Ligament Cut				
No	6	4%	17	15%
Yes	144	96%	91	78%
Not available	0	0%	9	8%
Device Size				
Height 4	**58**	**39%**		
SM-4	22	15%		
MD-4	36	24%		
Height 5	**78**	**53%**		
SM-5	9	6%		
SM-5S	18	12%		
MD-5	20	14%		
MD-5L	12	8%		
LG-5	10	7%		
LG-5L	9	6%		
Height 6	**12**	**8%**		
SM-6	1	1%		
MD-6	1	1%		
MD-6L	0	0%		
LG-6	8	5%		
LG-6L	2	1%		

Source: Tables Intra-op.sas; Analyzed: 09JAN2020

As evidenced by **Table 9**, the majority of procedures occurred in C5/C6 and C6/C7 for both the Simplify® Cervical Artificial Disc subjects and historical ACDF control subjects.

4. Safety and Effectiveness Results

Please note: The counts and percentages provided for the Simplify® Cervical Artificial Disc and ACDF control groups correspond to the values unadjusted for PS subclass. The device group difference and 95% confidence interval lower bound (LB) and upper bound (UB) are calculated controlling for PS subclass, accounting for why the reported difference does not match the difference between the presented unadjusted percentages.

Safety Results

Similar rates of any AE and any serious adverse event (SAE) occurred in the Simplify® Cervical Artificial Disc cohort and the historical ACDF control cohort through Month 24 (safety results shown through postoperative day 790, the end of the Month 24 visit window). Over the same timecourse, a similar rate of device- and procedure-related AEs occurred in both groups. While

not significantly different, the Simplify® Cervical Artificial Disc subjects experienced a numerically greater number of AEs (245 events in 98 subjects) than the historical ACDF control subjects (192 events in 69 subjects) (**Table 10**).

Table 10: Comparisons of Summary AE Rates between Simplify® Cervical Artificial Disc and ACDF Groups (Primary Analysis Population through Day 790)

	Simplify Disc (N= 150)			ACDF (N= 117)			Group Difference*			
	Events	Subjs	%‖	Events	Subjs	%‖	p	Δ	LB	UB
Adverse Events										
All	245	98	65.3%	192	69	59.0%	0.234	8.0%	-4.5%	20.5%
Device Related†	77	54	36.0%	86	46	39.3%	0.364	-6.1%	-18.6%	6.4%
Device Related - Definitely	2	1	0.7%	1	1	0.9%	0.663	-0.5%	-2.7%	1.7%
Procedure Related†	108	64	42.7%	93	49	41.9%	0.823	-1.5%	-14.2%	11.2%
Procedure Related - Definitely	24	16	10.7%	7	6	5.1%	0.298	3.4%	-3.1%	9.9%
Serious Adverse Events										
All	26	16	10.7%	24	16	13.7%	0.686	1.5%	-6.5%	9.5%
Device Related†	5	5	3.3%	9	5	4.3%	0.825	0.5%	-4.0%	5.0%
Major	0	0	0.0%	0	0	0.0%				
Device Related - Definitely	1	1	0.7%	0	0	0.0%				
Procedure Related†	11	5	3.3%	9	5	4.3%	0.825	0.5%	-4.0%	5.0%
Procedure Related - Definitely	6	1	0.7%	0	0	0.0%				
AE by Severity										
Mild	112	58	38.7%	68	43	36.8%	0.912	0.7%	-11.7%	13.2%
Moderate	103	59	39.3%	99	40	34.2%	0.307	6.8%	-5.5%	19.1%
Severe	30	21	14.0%	22	15	12.8%	0.241	4.9%	-3.3%	13.2%
Life Threatening	0	0	0.0%	3	2	1.7%				
SAE by Severity										
Mild	1	1	0.7%	0	0	0.0%				
Moderate	2	2	1.3%	7	7	6.0%	0.155	-3.4%	-8.3%	1.5%
Severe	23	15	10.0%	14	10	8.5%	0.230	4.0%	-3.0%	10.9%
Life Threatening	0	0	0.0%	3	2	1.7%				
Death										
All	0	0	0.0%	0	0	0.0%				

*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model;
Comparisons with less than 6 subjects in each group includes PS as a continuous variable (df=1) for model stability;
‖Percentage of subjects experiencing specific event; † Definite, probable, possibly, and unknown;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - AE Summary - Primary.sas; Analyzed: 28APR2020

Counts and percentages of subjects with specific AEs are presented in **Table 11** and counts of AEs by timecourse are presented in **Table 12**. The most commonly occurring events reported to have occurred in the Simplify® Cervical Artificial Disc cohort include radiculopathy (n=35), spasm (n=24), and inflammation conditions, such as discitis, joint and other types of inflammation (n=17). In the historical ACDF control cohort, the most commonly reported AEs include radiculopathy (n=29), pain with narcotic given (n=29), and pain with no narcotic given (n=18). Through Month 24, the nature and incidence of specific AEs were comparable in the two study groups.

Table 11. Counts and Percentages of Subjects with Specific AEs – (Primary Analysis Population through Day 790)

	Simplify Disc (N= 150)			ACDF (N= 117)			Group Difference*			
	Events	Subjs	%‖	Events	Subjs	%‖	p	Δ	LB	UB
All Events	245	98	65.3%	192	69	59.0%	0.234	8.0%	-4.5%	20.5%
Spasm	24	23	15.3%	6	5	4.3%	0.012	10.8%	3.6%	18.1%
Trauma	11	11	7.3%	8	7	6.0%	0.271	3.2%	-2.6%	9.0%
Other	15	13	8.7%	8	6	5.1%	0.381	3.0%	-3.3%	9.2%
Infection (All Other Infections - NOT at cervical surgical site)	13	9	6.0%	7	5	4.3%	0.377	2.6%	-2.8%	8.0%
Dysphagia	9	8	5.3%	3	3	2.6%	0.342	2.6%	-2.3%	7.4%
Injury To Muscles Or Organs	4	4	2.7%	1	1	0.9%	0.164	2.3%	-0.7%	5.4%
Psychological Illness	5	5	3.3%	2	2	1.7%	0.432	1.7%	-2.2%	5.6%
Allergic Reaction	6	5	3.3%	1	1	0.9%	0.400	1.6%	-1.8%	5.0%
Soft Tissue Damage	3	3	2.0%	1	1	0.9%	0.161	1.4%	-1.1%	4.0%
Pneumonia	2	2	1.3%	1	1	0.9%	0.258	0.7%	-1.2%	2.6%
Surgical Wound Dehiscence	2	2	1.3%	1	1	0.9%	0.979	0.0%	-2.5%	2.6%
Tingling - increased from pre-op or prior visit	1	1	0.7%	2	2	1.7%	0.935	-0.1%	-2.0%	1.9%
Implant/Joint Noise	1	1	0.7%	1	1	0.9%	0.848	-0.2%	-2.5%	2.0%
Cardiac Event	1	1	0.7%	1	1	0.9%	0.848	-0.2%	-2.5%	2.0%
Spinal Stenosis	1	1	0.7%	1	1	0.9%	0.663	-0.5%	-2.7%	1.7%
Facet Joint Deterioration	1	1	0.7%	2	2	1.7%	0.635	-0.6%	-3.4%	2.1%
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	17	15	10.0%	14	12	10.3%	0.856	-0.7%	-8.4%	6.9%
Numbness - increased from pre-op or prior visit	8	7	4.7%	8	5	4.3%	0.748	-0.9%	-6.2%	4.4%
Adjacent Segment Degeneration	11	10	6.7%	8	8	6.8%	0.791	-0.9%	-7.4%	5.5%
Weakness - increased from pre-op or prior visit	2	2	1.3%	2	2	1.7%	0.429	-1.1%	-4.2%	1.9%
Radiculopathy	35	29	19.3%	29	21	17.9%	0.753	-1.7%	-11.8%	8.4%
Pseudoarthrosis	1	1	0.7%	4	4	3.4%	0.161	-2.8%	-6.7%	1.1%
Pain (No Narcotic Given)	15	14	9.3%	18	15	12.8%	0.305	-4.4%	-12.5%	3.8%
Compressive Neuropathy	4	4	2.7%	10	9	7.7%	0.035	-6.4%	-12.4%	-0.4%
Headache	8	6	4.0%	14	12	10.3%	0.008	-9.1%	-16.1%	-2.1%
Pain (Narcotic Given)	11	11	7.3%	29	21	17.9%	0.011	-11.6%	-20.4%	-2.8%
Gastrointestinal Complications Including Ileus, Nausea and Vomiting	8	7	4.7%	0	0	0.0%				
Infection Localized To Cervical Surgical Site	5	5	3.3%	0	0	0.0%				
Surgery At A Location Other than the Spine	8	4	2.7%	0	0	0.0%				
Hematoma or Seroma	2	2	1.3%	0	0	0.0%				
Tremors	2	2	1.3%	0	0	0.0%				
Difficulty With Urination	2	2	1.3%	0	0	0.0%				
Otitis Media	1	1	0.7%	0	0	0.0%				
Stroke	1	1	0.7%	0	0	0.0%				
Esophageal Perforation	1	1	0.7%	0	0	0.0%				
Hypertension	1	1	0.7%	0	0	0.0%				
Ischemia	1	1	0.7%	0	0	0.0%				
Deep w ound infection localized to cervical surgical site	1	1	0.7%	0	0	0.0%				
Skin disorders	1	1	0.7%	0	0	0.0%				
Airw ay Obstruction	0	0	0.0%	1	1	0.9%				
Dural Injury	0	0	0.0%	1	1	0.9%				
Dysphonia	0	0	0.0%	1	1	0.9%				
Implant Collapse Or Subsidence	0	0	0.0%	1	1	0.9%				
Pulmonary Embolism	0	0	0.0%	1	1	0.9%				
Thrombosis	0	0	0.0%	1	1	0.9%				
Sw elling (Edema)	0	0	0.0%	1	1	0.9%				
Hypotension	0	0	0.0%	1	1	0.9%				
Cancer	0	0	0.0%	2	2	1.7%				

*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model;
Comparisons with less than 6 subjects in each group includes PS as a continuous variable (df=1) for model stability;
‖Percentage of subjects experiencing specific event; † Definite, probable, possibly, and unknown;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - All AEs - Primary.sas; Analyzed: 11JUN2020

Table 12: Counts of Specific AEs by Time of Occurrence – (Primary Analysis Population through Day 790) (I = Simplify® Cervical Artificial Disc, C = ACDF)

	Days Post-Op																	
	Missing		0-2		2-30		30-90		90-180		180-365		365-730		730-790		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
All Events	0	0	8	8	35	16	50	30	51	43	51	41	48	44	2	10	245	192
Radiculopathy	0	0	0	2	5	1	6	6	6	8	9	3	9	6	0	3	35	29
Spasm	0	0	0	0	2	0	3	2	9	3	6	1	4	0	0	0	24	6
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	0	0	0	0	2	0	4	1	3	1	1	5	7	7	0	0	17	14
Pain (No Narcotic Given)	0	0	0	0	2	3	3	2	7	5	1	3	2	5	0	0	15	18
Other	0	0	0	1	1	0	4	1	1	1	6	4	2	0	1	1	15	8
Infection (All Other Infections - NOT at cervical surgical site)	0	0	0	0	2	3	3	1	2	1	2	2	4	0	0	0	13	7
Pain (Narcotic Given)	0	0	0	0	1	1	3	4	3	9	1	7	3	5	0	3	11	29
Trauma	0	0	0	0	0	1	3	1	1	0	3	4	4	2	0	0	11	8
Adjacent Segment Degeneration	0	0	0	0	0	0	1	2	2	0	3	0	4	4	1	2	11	8
Dysphagia	0	0	0	0	3	0	3	1	2	2	1	0	0	0	0	0	9	3
Numbness - increased from pre-op or prior visit	0	0	1	0	2	0	3	3	1	2	1	2	0	1	0	0	8	8
Surgery At A Location Other than the Spine	0	0	1	0	1	0	3	0	0	0	2	0	1	0	0	0	8	0
Gastrointestinal Complications Including Ileus, Nausea and Vomiting	0	0	0	0	1	0	2	0	0	0	3	0	2	0	0	0	8	0
Headache	0	0	0	0	1	0	1	1	4	6	2	2	0	4	0	1	8	14
Allergic Reaction	0	0	4	1	1	0	0	0	0	0	1	0	0	0	0	0	6	1
Infection Localized To Cervical Surgical Site	0	0	0	0	4	0	1	0	0	0	0	0	0	0	0	0	5	0
Psychological Illness	0	0	0	0	1	1	0	0	2	0	1	1	1	0	0	0	5	2
Compressive Neuropathy	0	0	0	2	0	2	0	0	1	1	2	3	1	2	0	0	4	10
Injury To Muscles Or Organs	0	0	0	0	0	0	1	0	2	0	1	1	0	0	0	0	4	1
Soft Tissue Damage	0	0	0	1	0	0	1	0	0	0	1	0	1	0	0	0	3	1
Hematoma or Seroma	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	2	0
Pneumonia	0	0	0	0	0	0	2	1	0	0	0	0	0	0	0	0	2	1
Tremors	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	2	0
Weakness - increased from pre-op or prior visit	0	0	0	0	0	0	1	1	1	0	0	0	0	1	0	0	2	2
Difficulty With Urination	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	2	0
Surgical Wound Dehiscence	0	0	0	0	2	1	0	0	0	0	0	0	0	0	0	0	2	1
Facet Joint Deterioration	0	0	0	0	0	1	0	0	1	1	0	0	0	0	0	0	1	2
Otitis Media	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Pseudoarthrosis	0	0	0	0	0	0	0	0	0	1	0	2	1	1	0	0	1	4
Spinal Stenosis	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	1
Tingling - increased from pre-op or prior visit	0	0	0	0	0	0	0	0	1	0	0	0	0	2	0	0	1	2
Cardiac Event	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Implant/Joint Noise	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	1
Stroke	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Esophageal Perforation	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Hypertension	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Ischemia	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Deep wound infection localized to cervical surgical site	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Skin disorders	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Airway Obstruction	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Dural Injury	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Dysphonia	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Implant Collapse Or Subsidence	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Pulmonary Embolism	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
Thrombosis	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
Swelling (Edema)	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Hypotension	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Cancer	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	2

‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - All AEs - Primary.sas; Analyzed: 11JUN2020

Definitely Device-Related AEs

There were two events in one subject in the Simplify® Cervical Artificial Disc group and one event in the historical ACDF control group that were determined to be definitely device-related by the

CEC. In the Simplify® Cervical Artificial Disc group, the definitely device-related AE rate was 0.7% (2/150), with the two events related to implant/joint noise and inflammation. In the historical ACDF control group, the definitely device-related AE rate was 0.9% (1/117), with the event being related to pseudarthrosis. Additional details regarding the device-related AEs are presented in **Table 13** below.

Table 13: Counts and Percentages of Subjects with Specific Definitely Device Related AE– (Primary Analysis Population through Day 790)

	Simplify Disc (N= 150)			ACDF (N= 117)			Group Difference*			
	Events	Subjs	%‖	Events	Subjs	%‖	p	Δ	LB	UB
All Events	2	1	0.7%	1	1	0.9%	0.663	-0.5%	-2.7%	1.7%
Implant/Joint Noise	1	1	0.7%	0	0	0.0%				
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	1	1	0.7%	0	0	0.0%				
Pseudoarthrosis	0	0	0.0%	1	1	0.9%				

*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model;
Comparisons with less than 6 subjects in each group includes PS as a continuous variable (df=1) for model stability;
‖Percentage of subjects experiencing specific event; † Definite, probable, possibly, and unknown;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Definitely Device Related - Primary.sas; Analyzed: 11JUN2020

Table 14 includes a timecourse of definitely device-related AEs for all subjects in the study through postoperative day 790 by day of occurrence. As shown below, the definitely device-related events occurred 365-730 days postoperatively.

Table 14: Definitely Device-Related AEs (Timecourse) by Code (Primary Analysis Population through Day 790)

	Days Post-Op																	
	Missing		0-2		2-30		30-90		90-180		180-365		365-730		730-790		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
All Events	0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	2	1
Implant/Joint Noise	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Pseudoarthrosis	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1

‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Definitely Device Related - Primary.sas; Analyzed: 11JUN2020

Table 15 includes definitely device-related AEs by severity for subjects in the Simplify® Cervical Artificial Disc group through postoperative day 790. As shown below, one event was categorized as mild in severity and the other was categorized as severe.

Table 15: Definitely Device-Related AEs (Severity) by Code (Simplify® Cervical Artificial Disc Group, N=150)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	1	50.0%	0	0.0%	1	50.0%	0	0.0%	2
Implant/Joint Noise	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1

*Percentage of total events;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Definitely Device Related - Primary.sas; Analyzed: 11JUN2020

Table 16 includes definitely device-related AEs by severity for subjects in the historical ACDF control group through postoperative day 790. As shown below, the one event designated as definitely device-related was categorized as moderate in severity.

Table 16: Definitely Device-Related AEs (Severity) by Code (Historical ACDF Control Group, N=117)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Pseudoarthrosis	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1

*Percentage of total events;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Definitely Device Related - Primary.sas; Analyzed: 11JUN2020

Definitely Device- or Procedure- Related AEs

Table 17 through **Table 20** present AEs that were determined by the CEC to be 'definitely' related to the device or procedure.

Table 17 includes definitely device- or procedure-related AEs by code for all subjects in the study through postoperative day 790. As shown below, sixteen (16) subjects in the Simplify® Cervical Artificial Disc group and six (6) subjects in the historical ACDF control group had 'definitely' device- or procedure-related events. The most commonly occurring AEs categorized as definitely device- or procedure-related in the Simplify® Cervical Artificial Disc cohort were allergic reaction (2.7% - 4/150), infection localized to cervical surgical site (2.7% - 4/150), and dysphagia (2.0% - 3/150). In the historical ACDF control cohort, the most commonly occurring AEs categorized as definitely device- or procedure-related were dysphagia (0.9% - 1/117), cardiac event (0.9% - 1/117), and surgical wound dehiscence (0.9% - 1/117).

Table 17: Definitely Device- or Procedure-Related AEs by Code (Primary Analysis Population through Day 790)

	Simplify Disc (N= 150)			ACDF (N= 117)			Group Difference*			
	Events	Subjs	%	Events	Subjs	%	p	Δ	LB	UB
All Events	26	16	10.7%	7	6	5.1%	0.298	3.4%	-3.1%	9.9%
Dysphagia	3	3	2.0%	1	1	0.9%	0.261	1.6%	-1.1%	4.3%
Cardiac Event	1	1	0.7%	1	1	0.9%	0.848	-0.2%	-2.5%	2.0%
Surgical Wound Dehiscence	1	1	0.7%	1	1	0.9%	0.663	-0.5%	-2.7%	1.7%
Infection Localized To Cervical Surgical Site	4	4	2.7%	0	0	0.0%				
Allergic Reaction	5	4	2.7%	0	0	0.0%				
Hematoma or Seroma	2	2	1.3%	0	0	0.0%				
Surgery At A Location Other than the Spine	5	1	0.7%	0	0	0.0%				
Implant/Joint Noise	1	1	0.7%	0	0	0.0%				
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	1	1	0.7%	0	0	0.0%				
Spasm	1	1	0.7%	0	0	0.0%				
Esophageal Perforation	1	1	0.7%	0	0	0.0%				
Deep wound infection localized to cervical surgical site	1	1	0.7%	0	0	0.0%				
Pseudoarthrosis	0	0	0.0%	1	1	0.9%				
Infection (All Other Infections - NOT at cervical surgical site)	0	0	0.0%	1	1	0.9%				
Radiculopathy	0	0	0.0%	2	1	0.9%				

*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model;
Comparisons with less than 6 subjects in each group includes PS as a continuous variable (df=1) for model stability;
|Percentage of subjects experiencing specific event; † Definite, probable, possibly, and unknown;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Definitely Device or Procedure Related - Primary.sas; Analyzed: 11JUN2020

Table 18 includes a timecourse of definitely device- or procedure-related AEs for all subjects in the study through postoperative day 790 by day of occurrence. As shown below, majority of procedure-related events occurred within the first 3 months (0-90 days postop) of treatment.

Table 18: Definitely Device- or Procedure-Related AEs (Timecourse) by Code (Primary Analysis Population through Day 790)

	Days Post-Op																	
	Missing		0-2		2-30		30-90		90-180		180-365		365-730		730-790		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
All Events	0	0	7	3	12	2	5	1	0	0	0	0	2	1	0	0	26	7
Surgery At A Location Other than the Spine	0	0	1	0	1	0	3	0	0	0	0	0	0	0	0	0	5	0
Allergic Reaction	0	0	4	0	1	0	0	0	0	0	0	0	0	0	0	0	5	0
Infection Localized To Cervical Surgical Site	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	4	0
Dysphagia	0	0	0	0	1	0	2	1	0	0	0	0	0	0	0	0	3	1
Hematoma or Seroma	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	2	0
Cardiac Event	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Implant/Joint Noise	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Spasm	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Esophageal Perforation	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Surgical Wound Dehiscence	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1
Deep wound infection localized to cervical surgical site	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Pseudoarthrosis	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
Infection (All Other Infections - NOT at cervical surgical site)	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Radiculopathy	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2

‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Definitely Device or Procedure Related - Primary.sas; Analyzed: 11JUN2020

Table 19 includes definitely device- or procedure-related AEs by severity for subjects in the Simplify® Cervical Artificial Disc group through postoperative day 790. As shown below, there were no life-threatening definitely procedure-related events in the Simplify® Cervical Artificial Disc group. The most commonly occurring AEs categorized as definitely device- or procedure-related in the Simplify® Cervical Artificial Disc cohort include surgery at a location other than the spine (n=5 *(one subject experienced a complication during the TDR procedure (esophageal perforation) resulting in five (5) subsequent procedures to repair the perforation)*), allergic reaction (n=5), and infection localized to cervical surgical site (n=4).

Table 19: Definitely Device- or Procedure-Related AEs (Severity) by Code (Simplify® Cervical Artificial Disc Group, N=150)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	9	34.6%	9	34.6%	8	30.8%	0	0.0%	26
Surgery At A Location Other than the Spine	0	0.0%	0	0.0%	5	100.0%	0	0.0%	5
Allergic Reaction	2	40.0%	3	60.0%	0	0.0%	0	0.0%	5
Infection Localized To Cervical Surgical Site	2	50.0%	2	50.0%	0	0.0%	0	0.0%	4
Dysphagia	2	66.7%	1	33.3%	0	0.0%	0	0.0%	3
Hematoma or Seroma	2	100.0%	0	0.0%	0	0.0%	0	0.0%	2
Cardiac Event	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Implant/Joint Noise	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1
Spasm	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Esophageal Perforation	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1
Surgical Wound Dehiscence	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Deep w ound infection localized to cervical surgical site	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1

*Percentage of total events;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Definitely Device or Procedure Related - Primary.sas; Analyzed: 11JUN2020

Table 20 includes all definitely device- or procedure-related AEs by severity for subjects in the historical ACDF control group through postoperative day 790. As shown below, there were no severe or life-threatening definitely device- or procedure-related events in the historical ACDF control group. The most commonly occurring AEs categorized as definitely device- or procedure-related in the historical ACDF control cohort include radiculopathy (n=2) and dysphagia (n=2).

Table 20: Definitely Device- or Procedure-Related AEs (Severity) by Code (Historical ACDF Control Group, N=117)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	3	42.9%	4	57.1%	0	0.0%	0	0.0%	7
Radiculopathy	0	0.0%	2	100.0%	0	0.0%	0	0.0%	2
Dysphagia	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Pseudoarthrosis	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Cardiac Event	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Infection (All Other Infections - NOT at cervical surgical site)	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Surgical Wound Dehiscence	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1

*Percentage of total events;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Definitely Device or Procedure Related - Primary.sas; Analyzed: 11JUN2020

Serious Adverse Events

There were a total of 26 SAEs in the Simplify® Cervical Artificial Disc group in 16 subjects and 24 SAEs in 16 subjects in the historical ACDF control group (**Table 21**). There were no significant differences in SAE rates between groups. The most commonly occurring events categorized as SAEs in the Simplify® Cervical Artificial Disc cohort were infection at a location other than the

cervical surgical site (1.3% - 2/150), pain with narcotic given (1.3% - 2/150), adjacent segment degeneration (1.3% - 2/150), and surgery at a location other than the spine (1.3% - 2/150). In the historical ACDF control cohort, the most commonly occurring events categorized as SAEs were pain with narcotic given (2.6% - 3/117) and adjacent segment degeneration (2.6% - 3/117).

Table 21: Counts and Percentages of Subjects with Specific SAE– (Primary Analysis Population through Day 790)

	Simplify Disc (N= 150)			ACDF (N= 117)			Group Difference*			
	Events	Subjs	%‖	Events	Subjs	%‖	p	Δ	LB	UB
All Events	26	16	10.7%	24	16	13.7%	0.686	1.5%	-6.5%	9.5%
Infection (All Other Infections - NOT at cervical surgical site)	2	2	1.3%	2	1	0.9%	0.826	0.3%	-2.3%	2.9%
Pseudoarthrosis	1	1	0.7%	1	1	0.9%	0.772	0.2%	-1.5%	2.0%
Trauma	1	1	0.7%	1	1	0.9%	0.594	0.2%	-1.1%	1.5%
Headache	1	1	0.7%	1	1	0.9%	0.848	-0.2%	-2.5%	2.0%
Radiculopathy	1	1	0.7%	4	2	1.7%	0.779	-0.3%	-2.7%	2.1%
Psychological Illness	1	1	0.7%	1	1	0.9%	0.365	-0.4%	-2.1%	1.3%
Pain (Narcotic Given)	2	2	1.3%	3	3	2.6%	0.518	-1.2%	-4.9%	2.4%
Adjacent Segment Degeneration	3	2	1.3%	3	3	2.6%	0.341	-1.8%	-5.4%	1.9%
Surgery At A Location Other than the Spine	5	2	1.3%	0	0	0.0%				
Gastrointestinal Complications Including Ileus, Nausea and Vomiting	2	2	1.3%	0	0	0.0%				
Pneumonia	1	1	0.7%	0	0	0.0%				
Spinal Stenosis	1	1	0.7%	0	0	0.0%				
Inflammation Conditions, Such As Discitis, Joint And Other Types Of Inflammation	1	1	0.7%	0	0	0.0%				
Esophageal Perforation	1	1	0.7%	0	0	0.0%				
Infection Localized To Cervical Surgical Site	1	1	0.7%	0	0	0.0%				
Ischemia	1	1	0.7%	0	0	0.0%				
Deep w ound infection localized to cervical surgical site	1	1	0.7%	0	0	0.0%				
Implant Collapse Or Subsidence	0	0	0.0%	1	1	0.9%				
Pain (No Narcotic Given)	0	0	0.0%	2	2	1.7%				
Pulmonary Embolism	0	0	0.0%	1	1	0.9%				
Thrombosis	0	0	0.0%	1	1	0.9%				
Other	0	0	0.0%	1	1	0.9%				
Cancer	0	0	0.0%	2	2	1.7%				

*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model;
Comparisons with less than 6 subjects in each group includes PS as a continuous variable (df=1) for model stability;
‖Percentage of subjects experiencing specific event; † Definite, probable, possibly, and unknown;
‡ Subjects censored at Index level secondary surgical interventions.
Source: Tables Safety - Serious AEs - Primary.sas; Analyzed: 11JUN2020

No subjects in the historical ACDF control group had definitely device-related SAEs. One (1) subject in the Simplify® Cervical Artificial Disc group had a SAE that was determined by the CEC to be 'definitely' device-related. The AE was categorized as 'inflammation conditions, such as discitis, joint and other types of inflammation' and occurred 365-730 days postoperatively. The event was categorized as severe.

Secondary Surgical Intervention

Some AEs resulted in SSIs that were prospectively classified as revisions, removals, reoperations or supplemental fixations, qualified as study failures in accordance with FDA's Guidance Document, Clinical Data Presentations for Orthopedic Device Applications (2004) and were reviewed and adjudicated by the CEC.

There were 4 SSIs in the Simplify® Cervical Artificial Disc group and 6 SSIs in the historical ACDF control group through Month 24 (postoperative day 790).

Based on the results presented in **Table 22**, a total of four (4) SSIs occurred in the Simplify® Cervical Artificial Disc group and six (6) SSIs occurred in the ACDF group. Of the ACDF SSIs, one (1) occurred on postoperative day 746 (post 2-year anniversary but prior to close of Month 24 window) and is therefore not included in the subject accounting table and overall success table.

The timecourse of these events (Table 21) demonstrates that the majority of SSIs occurred between 12 and 24 months in both groups; however, meaningful conclusions cannot be made with respect to timing due to the low number of SSI events in both groups.

Table 22: Surgical Intervention Timecourse by Treatment Type – (Primary Analysis Population through Day 790)

Treatment Group	SSI Type	Event Timecourse (months)					Total (events)
		<1.5	1.5-3	3-6	6-12	12-24	
Simplify® Cervical Artificial Disc (N=150)	Removal	-	1	-	-	1	2
	Revision	-	-	-	-	-	0
	Reoperation	-	-	-	-	1	1
	Supplemental Fixation	-	-	-	-	1	1
ACDF (N=117)	Removal	-	-	2	-	3*	5
	Revision	-	-	-	-	1	1
	Reoperation	-	-	-	-	-	0
	Supplemental Fixation	-	-	-	-	-	0

**One SSI occurred on day 746 (post 2-year anniversary but prior to close of Month 24 window) and is therefore not included in the survival analysis, subject accounting table, and overall success table.*

The procedure and reason for SSI are detailed below in **Table 23**. Of the four (4) SSIs observed in the Simplify® Cervical Artificial Disc cohort, two (2) resulted in device removal. Of the six (6) SSIs reported in the historical ACDF control cohort, five (5) resulted in device removal.

Table 23: Surgical Intervention Procedure and Indication for Procedure

Group	Procedure	Index Level	Procedure	Indication for Procedure
Simplify®	Removal	C6/7	Staged procedure involving explant of the Simplify® Cervical Artificial Disc at C6/C7, C7 corpectomy, anterior spinal fusion of C6-T1, and posterior spinal fusion at C6-T2.	Esophageal perforation and deep wound infection localized to cervical surgical site.
Simplify®	Removal	C6/7	C6/C7 Simplify® Cervical Artificial Disc explanted, ACDF performed at C6/C7	Recurrent stenosis with worsening disc degeneration status
Simplify®	Supplemental Fixation	C6/7	Anterior cervical corpectomy at C6 with PEEK interbody spacer, anterior plating at C4-C7, and fusion exploration	Symptomatic pseudarthrosis at C5/C6 (adjacent level)
Simplify®	Reoperation	C6/7	C6/C7 foraminotomy for decompression	Radiculopathy at C7
ACDF	Removal	C5/6	Removal of implant at C5/C6 and total disc replacement at C6/C7	Radiculopathy
ACDF	Removal	C6/7	Removal of implant at C6/C7 and application of anterior cervical plate at C5-C7	Adjacent segment degeneration

Group	Procedure	Index Level	Procedure	Indication for Procedure
ACDF	Removal	C5/6	Removal of the implant at C5/C6 and supplemental fixation of C5/C6 using an interbody bone graft and titanium anterior cervical plate and screws	Subsidence of graft
ACDF	Removal	C5/6	Removal of implant at C5/C6 revised to total disc replacement at C5/C6	Symptomatic pseudarthrosis at C5/C6
ACDF	Revision	C5/6	Removal of anterior plate at C5/C6. Placement of a 9 x 7mm spacer with plate to the ventral surface of the vertebral bodies at C6/C7	Adjacent segment degeneration at C6/C7
ACDF	Removal	C5/6	Removal of the fusion implant and re-do of cervical fusion at C5/C6	Symptomatic pseudarthrosis at C5/C6

Neurological Status

Neurological success was defined as maintenance or improvement in neurologic status at Month 24. The CEC reviewed investigator assigned neurologic status (stable/ improved/ deteriorated) at Month 24 for all subjects to confirm or reclassify neurologic status. As evidenced by **Table 24**, at Month 24, one (1) Simplify® Cervical Artificial Disc subject was considered a neurological failure (0.7% - 1/139) and five (5) historical ACDF control subjects were considered neurological failures (5.3% - 5/95).

Table 24: Neurological Status at Month 24 - (Primary Analysis Population)

	Simplify® Cervical Artificial Disc			ACDF		
	N	n	%	N	n	%
Improved	139	111	79.9%	95	52	54.7%
Maintained		27	19.4%		38	40.0%
Deteriorated		1	0.7%		5	5.3%

The one (1) Simplify® Cervical Artificial Disc subject was classified as 'deteriorated' based on decline in sensory status at Month 24. Of the five (5) historical ACDF control subjects who were classified as 'deteriorated', two were based on decline in sensory status, two based on decline in motor function and one based on decline in sensory status and motor function at Month 24.

Effectiveness Results

Primary Overall Success Analysis

The success measurement was developed to measure safety and effectiveness of the Simplify® Cervical Artificial Disc when compared to ACDF. A subject was considered a study success at the Month 24 if he/she met all of the following criteria:

- Improvement in NDI of at least 15 percentage-points (out of 100) as compared to baseline at Month 24,
- Maintenance or improvement in neurologic status as compared to baseline at Month 24 (as determined by the CEC),
- No device failures within 24 months of index procedure,
- No SSI at the index level within 24 months of index procedure (as determined by the CEC), and
- No major AEs within 24 months of index procedure (as determined by the CEC).

For overall success, the proportion of subjects meeting the success criteria in each group was determined and the difference (Simplify® Cervical Artificial Disc minus ACDF) and the one-sided 90% confidence interval for the difference between treatment groups was calculated. The one-sided 90% lower confidence interval was greater than the non-inferiority margin (-10%); consequently, the primary endpoint was met. Additionally, the one-sided 95% confidence interval for the difference between treatment groups was calculated. The one-sided 95% lower confidence interval was greater than the superiority margin (0%), and as a result, the Simplify® Cervical Artificial Disc group is confirmed to be superior to the historical ACDF control group. The primary overall success outcomes are presented in **Table 25**.

Table 25: Overall Efficacy (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
Outcome	**N**	**n**	**%|**	**N**	**n**	**%|**	**p**	**Δ**	**90% LB**	**95% LB**
Implanted	150	148	99.5%	117	117	100.0%				
No secondary surgical intervention‡	**148**	**144**	**97.1%**	**117**	**112**	**97.1%**	**0.979**	**-0.1%**	**-3.6%**	**-4.3%**
No removals‡	148	146	98.6%	117	113	98.0%				
No revisions§	148	148	100.0%	117	116	100.0%				
No reoperations‡	148	147	99.3%	117	117	100.0%				
No supplemental fixations‡	148	147	99.3%	117	117	100.0%				
No device failure†§	**137**	**137**	**100.0%**	**90**	**83**	**92.2%**				
No device condition failure†§	137	137	100.0%	92	85	92.4%				
No device migration failure†§	137	137	100.0%	90	90	100.0%				
NDI 15-point Responder†	**138**	**135**	**97.9%**	**96**	**83**	**88.0%**	**0.009**	**9.9%**	**3.2%**	**1.9%**
No Neurological Deterioration (CEC)†	**139**	**138**	**99.6%**	**95**	**90**	**94.1%**	**0.015**	**5.6%**	**1.0%**	**0.2%**
No Major Adverse Event (CEC)†§	**150**	**150**	**100.0%**	**117**	**117**	**100.0%**				
Composite Clinical Success (CCS)¶	**150**	**--**	**93.0%**	**117**	**--**	**73.6%**	**<.001**	**19.4%**	**10.9%**	**9.3%**
CCS: Observed data only	142	132	93.0%	96	68	71.3%	<.001	21.6%	12.4%	10.7%
CCS: Best-Case	150	140	93.3%	117	68	58.8%	<.001	34.5%	25.4%	23.6%
CCS: Worst-Case	150	132	88.1%	117	89	76.4%	0.025	11.7%	3.3%	1.8%

*Device group differences and 90% and 95% LB adjusting for propensity score (PS) subclass using two-way generalized linear model;
|Equally weighted PS adjusted within group proportion. This will not equal n/N which is the observed data;
† Subjects censored at Index level secondary surgical interventions;
‡ Propensity Score treated as continuous variable to promote convergence;
§ Not estimable due to zero cell. Unadjusted within group rate shown;
¶ A Fully Conditional Specification (FCS) approach was used to produce 20 multiply imputed completed data sets. The FCS approach accommodates non-monotonicity in the pattern of missing data and requires regression models to be specified for each variable with missing values needing imputation. All models included the PS subclass and treatment group. NDI responder status and secondary surgical interventions over time were sequentially added to account for longitudinal temporality. The resulting completed datasets were combined using Rubin's Rules.
Source: Tables Overall Efficacy.sas; Analyzed: 27AUG2020

Using multiple imputation to account for missing data, the adjusted success rate was 93.0% for Simplify® Cervical Artificial Disc cohort and 73.6% for historical ACDF control cohort. The adjusted difference between groups was 19.4%. The lower-bound of the 1-sided 90% confidence interval for the group difference controlling for PS subclass was 10.9%. Since 10.9% is greater than -10%, the results from this comparison demonstrate that the study success criterion for non-inferiority has been achieved. Further, the 1-sided 95% confidence interval for the group difference controlling for PS subclass was 9.3%. Since 9.3% is greater than 0%, the results from this comparison demonstrate that the study success criterion for superiority has been achieved.

Sensitivity analyses were performed to evaluate the composite success measurement using observed data only, best case evaluation and worst-case evaluation. All sensitivity analyses demonstrate that the study success criterion for non-inferiority has been achieved. Further, the sensitivity analyses confirm the superiority of the Simplify® Cervical Artificial Disc group as compared to the historical ACDF control group.

Secondary Effectiveness Analyses

This section focuses on secondary clinical endpoints from a number of relevant domains (i.e., NDI, VAS, SF-12v2, Dysphagia Handicap Index (DHI), medication usage, neurological assessments, work status, and Radiographic Measurements), which were assessed at preoperative (baseline) and at prescribed clinical intervals throughout the follow-up period. In addition, Odom's criteria, treatment satisfaction, and time to recovery, were assessed postoperatively at Month 24. Overall, subjects treated with the Simplify® Cervical Artificial Disc exhibited improvement and numerically favorable rates of success as compared to the historical ACDF control cohort across the broad spectrum of secondary analyses. The secondary effectiveness outcomes at Month 24 compared to baseline are shown in **Table 26**.

Table 26: Secondary Effectiveness Subject Outcomes at Month 24 Compared to Baseline (Primary Analysis Population)

Secondary Effectiveness Endpoint	Simplify® Cervical Artificial Disc (N=150)	ACDF (N=117)
NDI Improvement ≥ 15 percentage-points (out of 100)	135/138 (97.8%)	83/96 (86.5%)
VAS Neck and Arm Pain Improvement ≥ 20mm	134/139 (96.4%)	83/95 (87.4%)
SF-12 PCS Maintenance or Improvement	129/138 (93.5%)	-
SF-12 MCS Maintenance or Improvement	105/138 (76.1%)	-
Treatment Satisfaction (Very Satisfied)	122/138 (88%)	67/96 (70%)
Odom's Criteria (Excellent or Good)	133/139 (95.8%)	82/95 (86.3%)
Narcotic Use (No. of Subjects Using)	15/139 (10.8%)	35/95 (36.8%)

Neck Disability Index (NDI)

Table 27 and **Table 28** present the NDI percentage-points for all treated subjects. NDI is scored on a 50-point scale (10 questions with a score of 0-5 for each) that is then normalized to a scale of 100%. Higher NDI is representative of greater symptomatology. The following outcomes reflect NDI percentage-points out of 100%. NDI data are censored following intraoperative deviation or SSI.

Table 27: NDI percentage-points over time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	150	63.3	12.5	61.0	40.0	94.0	117	62.4	12.6	64.0	40.0	90.0	0.950	0.1	-3.3	3.5
Week 06	146	23.1	17.8	20.0	0.0	86.0	112	33.7	19.5	32.0	0.0	78.0	<.001	-11.3	-16.5	-6.2
Month 03	145	17.3	16.7	14.0	0.0	84.0	111	25.9	19.5	24.0	0.0	74.0	<.001	-9.5	-14.5	-4.5
Month 06	144	16.8	16.6	12.0	0.0	86.0	101	23.0	20.3	22.0	0.0	78.0	0.009	-7.0	-12.2	-1.8
Month 12	143	16.5	17.4	14.0	0.0	88.0	100	22.8	21.3	17.0	0.0	78.0	0.022	-6.4	-11.9	-0.9
Month 24	138	13.6	14.3	10.0	0.0	84.0	96	23.0	19.8	19.0	0.0	72.0	<.001	-11.0	-15.9	-6.1

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

Table 27 shows the mean NDI percentage-points for the Primary Analysis Population at preoperative, 6-week, 3-month, 6-month, 12-month, and 24-month timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups. Preoperative percentage-point was numerically greater in the Simplify® Cervical Artificial Disc group; however, the difference in percentage-points was not statistically significant (p=0.950). The mean preop NDI score for the Simplify® Cervical Artificial Disc cohort was 63.3, which improved to a mean NDI score of 13.6 at Month 24. Similarly, the mean preop NDI score for the historical ACDF control cohort was 62.4, which improved to a mean NDI score of 23.0 at Month 24. The difference in NDI percentage-points between groups was statistically significant at Week 6 through Month 24, in favor of the Simplify® Cervical Artificial Disc group ($p<0.05$).

Table 28: NDI change in percentage-points from preoperative (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	146	-40.3	20.0	-43.0	-78.0	14.0	112	-28.5	19.4	-28.0	-78.0	8.0	<.001	-11.7	-17.2	-6.2
Month 03	145	-46.3	18.6	-50.0	-86.0	6.0	111	-36.5	19.8	-36.0	-76.0	6.0	<.001	-9.8	-15.1	-4.6
Month 06	144	-46.6	17.8	-48.0	-86.0	8.0	101	-39.1	19.8	-40.0	-82.0	6.0	0.005	-7.6	-12.9	-2.3
Month 12	143	-47.2	19.2	-50.0	-94.0	8.0	100	-39.3	20.5	-40.0	-78.0	8.0	0.011	-7.4	-13.0	-1.7
Month 24	138	-49.4	16.8	-50.0	-92.0	4.0	96	-38.9	20.6	-38.0	-78.0	10.0	<.001	-11.9	-17.3	-6.5

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

Table 28 presents the mean change in NDI percentage-points from preoperative for the Primary Analysis Population at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups. Similar to the trends seen in mean score, the difference in NDI percentage-points change from preoperative was statistically significant at all timepoints, in favor of the Simplify® Cervical Artificial Disc group ($p<0.05$). Of interest, there was a greater change at the Week 6 visit (-40.3 vs. -28.5, $p<0.001$) in the Simplify® Cervical Artificial Disc group that was sustained through the study. The historical ACDF control group mean change was significantly smaller with the plateau seen at the Month 6 visit, presumably when the fusion was generally healed. This speaks to the clinical meaning of the acute response seen with reconstructing the disc space with a motion-permitting device versus a fusion that requires months to heal.

Table 29: NDI Improved/ Stable/ Deteriorated Status (Primary Analysis Population)

	Week 06				Month 03				Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Improved [-100, -15]	127	87%	86	77%	139	96%	90	81%	138	96%	92	91%	133	93%	84	84%	135	98%	83	86%
Stable (-15, 0]	14	10%	18	16%	3	2%	18	16%	3	2%	7	7%	6	4%	13	13%	2	1%	10	10%
Deteriorated (0, 100]	5	3%	8	7%	3	2%	3	3%	3	2%	2	2%	4	3%	3	3%	1	1%	3	3%

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

Table 29 presents the number and percentage of subjects who demonstrated improvement (NDI decrease >15 percent), number and percentage of subjects who were stable (NDI decrease 0-15 percent), and number and percentage of subjects who deteriorated (any increase) relative to preoperative at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints. As shown above, majority of subjects demonstrated improvement in both groups.

Table 30: NDI 15 Percentage-Point Responder (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Week 06	146	127	87.0%	112	86	76.8%	0.080	9.4%	-0.8%	19.7%
Month 03	145	139	95.9%	111	90	81.1%	0.002	14.0%	5.3%	22.6%
Month 06	144	138	95.8%	101	92	91.1%	0.283	3.7%	-3.1%	10.4%
Month 12	143	133	93.0%	100	84	84.0%	0.064	8.4%	-0.4%	17.3%
Month 24	138	135	97.8%	96	83	86.5%	0.009	9.9%	1.9%	17.9%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

Table 30 presents the number and percentage of subjects showing an improvement in NDI greater than 15 percentage-points as compared to all subjects in the study at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups. A numerically greater percentage of Simplify® Cervical Artificial Disc subjects achieved 15 percent-point improvement in NDI at all timepoints as compared to the historical ACDF control group, with 97.8% (135/138) of subjects in the Simplify® Cervical Artificial Disc Group meeting achieving this level of improvement in NDI at Month 24. This difference was statistically significant at Month 3 and Month 24 ($p<0.05$).

VAS Neck and Arm

Table 31 shows the VAS score for combined Neck and Arm pain for the Primary Analysis Population at preoperative, postoperative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 31: VAS (Neck, Arm) values over time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	150	81.6	12.4	84.0	41.0	100.0	117	77.6	13.5	79.0	42.0	100.0	0.717	0.6	-2.7	4.0
Post-Op	146	32.6	28.6	23.5	0.0	100.0	114	37.8	27.4	30.5	0.0	100.0	0.269	-4.3	-12.0	3.4
Week 06	146	22.9	24.5	13.0	0.0	99.0	113	27.6	24.9	19.0	0.0	100.0	0.052	-6.7	-13.4	0.1
Month 03	144	18.2	21.5	10.0	0.0	90.0	111	25.0	25.0	15.0	0.0	91.0	0.024	-7.4	-13.8	-1.0
Month 06	144	17.9	22.2	7.5	0.0	93.0	101	23.9	23.4	15.0	0.0	79.0	0.028	-7.3	-13.8	-0.8
Month 12	142	17.7	21.3	9.0	0.0	81.0	100	22.3	23.6	13.0	0.0	88.0	0.169	-4.5	-10.8	1.9
Month 24	139	15.6	20.2	7.0	0.0	90.0	95	23.3	24.3	15.0	0.0	92.0	<.001	-11.9	-18.1	-5.6

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 31**, mean preoperative score was numerically greater in the Simplify® Cervical Artificial Disc group (81.6) as compared to the historical ACDF control group (77.6), though the difference was not statistically significant ($p=0.717$). The difference in mean VAS score for combined Neck and Arm pain between groups was statistically significant at Months 3, 6, and 24, in favor of the Simplify® Cervical Artificial Disc group ($p<0.05$), with a mean VAS score of 15.6 for the Simplify® Cervical Artificial Disc group at Month 24, as compared to a mean VAS score of 23.3 for the historical ACDF control group at Month 24.

Table 32 presents the change in VAS score from preoperative for combined Neck and Arm pain for the Primary Analysis Population at postoperative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 32: VAS (Neck, Arm) change from preoperative (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Post-Op	146	-49.1	29.6	-52.0	-96.0	26.0	114	-39.7	31.3	-46.5	-100.0	39.0	0.235	-5.0	-13.2	3.3
Week 06	146	-58.8	25.5	-63.5	-99.0	19.0	113	-49.8	27.5	-52.0	-100.0	55.0	0.041	-7.5	-14.8	-0.3
Month 03	144	-63.7	22.7	-68.5	-97.0	14.0	111	-52.7	26.6	-59.0	-100.0	13.0	0.015	-8.4	-15.1	-1.6
Month 06	144	-64.0	24.2	-71.5	-100.0	17.0	101	-53.6	25.0	-57.0	-99.0	4.0	0.016	-8.6	-15.6	-1.6
Month 12	142	-64.5	23.1	-70.5	-99.0	0.0	100	-54.8	26.9	-59.5	-100.0	14.0	0.066	-6.6	-13.6	0.5
Month 24	139	-66.4	21.8	-71.0	-100.0	14.0	95	-53.7	26.6	-56.0	-100.0	16.0	<.001	-13.9	-20.9	-6.9

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

Similar to the trends seen in mean score presented in **Table 32**, the mean difference in VAS combined Neck and Arm pain score change compared to preoperative was statistically significant at 6-week, 3-month, 6-month, and 24-month timepoints ($p<0.05$), in favor of the Simplify® Cervical Artificial Disc group. At Month 24, the change in mean VAS score as compared to preop was -66.4 for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the change in mean VAS score at Month 24 as compared to preop was -53.7.

Table 33 presents the number and percentage of subjects showing an improvement in VAS combined Neck and Arm pain greater than 20 points as compared to baseline at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 33: VAS Neck and Arm 20-Point Responder (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Post-Op	146	114	78.1%	114	82	71.9%	0.577	3.3%	-7.9%	14.6%
Week 06	146	133	91.1%	113	97	85.8%	0.073	8.0%	-0.6%	16.7%
Month 03	144	136	94.4%	111	94	84.7%	0.059	7.3%	-0.5%	15.2%
Month 06	144	136	94.4%	101	91	90.1%	0.268	4.2%	-3.2%	11.5%
Month 12	142	132	93.0%	100	87	87.0%	0.300	4.2%	-3.8%	12.3%
Month 24	139	134	96.4%	95	83	87.4%	0.008	10.9%	2.6%	19.1%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 33**, a numerically greater percentage of Simplify® Cervical Artificial Disc subjects achieved 20-point improvement at VAS combined Neck and Arm pain as compared to the historical ACDF control group at all timepoints with a statistically significant difference at Month 24 in favor of the Simplify® Cervical Artificial Disc group ($p=0.008$). A total of 96.4% (134/139) of the Simplify® Cervical Artificial Disc subjects achieved at least a 20-point improvement in VAS combined Neck and Arm pain at Month 24, as compared to 87.4% (83/95) of the historical ACDF control subjects at the same evaluation timepoint.

Short-Form 12 (SF-12) – Physical Component Score (PCS)

Table 34 includes the PCS of the SF-12 for all subjects in the Simplify® Cervical Artificial Disc group at preoperative, Month 6, Month 12, and Month 24 timepoints. SF-12 scores are normalized to the US general population (not age/gender based). At preop, the mean PCS of the Simplify® Cervical Artificial Disc subjects was 31.1, which improved to a mean PCS of 50.7 at Month 24.

Table 34: SF-12 (Physical Component Score – PCS) values over time (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Pre-Op	150	31.1	7.4	30.3	11.2	56.1
Month 06	143	48.7	9.0	50.3	17.4	64.4
Month 12	143	49.7	8.6	51.8	16.5	62.2
Month 24	138	50.7	8.7	53.5	16.5	66.3

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 34**, the mean SF-12 PCS score increased from the preoperative timepoint through the Month 24 timepoint, indicating continued improvement in SF-12 PCS.

Table 35 includes the change in PCS from preoperative for all subjects in the Simplify® Cervical Artificial Disc group at 6-month, 12-month, and 24-month timepoints. At Month 6, the mean PCS improvement of the Simplify® Cervical Artificial Disc subjects was 17.5, which increased to a mean PCS improvement of 19.3 at Month 24.

Table 35: SF-12 (Physical Component Score - PCS) change from preoperative (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Month 06	143	17.5	9.3	18.7	-20.7	35.3
Month 12	143	18.4	9.9	19.2	-7.8	40.9
Month 24	138	19.3	10.4	21.6	-10.1	43.6

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 35**, the magnitude of change in SF-12 PCS increased through Month 24.

Table 36 includes the number and percentage of subjects achieving maintenance or improvement in SF-12 PCS score.

Table 36: SF-12 PCS – Subjects Achieving Maintenance or Improvement (Primary Analysis Population)

	Simplify Disc		
	N	n	%
Month 06	143	138	96.5%
Month 12	143	134	93.7%
Month 24	138	129	93.5%

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas;
Analyzed: 14MAY2020

As shown above, a high rate of subjects achieved maintenance or improvement in SF-12 PCS at all postoperative timepoints.

Short-Form 12 (SF-12) – Mental Component Score (MCS)

Table 37 includes the MCS of the SF-12 for all subjects in the Simplify® Cervical Artificial Disc group at preoperative, 6-month, 12-month, and 24-month timepoints. SF-12 scores are normalized to the US general population (not age/ gender based). At preop, the mean MCS of the Simplify® Cervical Artificial Disc subjects was 42.4, which increased to a mean MCS of 52.2 at Month 24.

Table 37: SF-12 (Mental Component Score – MCS) values over time (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Pre-Op	150	42.4	12.2	42.3	15.6	67.5
Month 06	143	52.5	9.4	56.4	18.9	67.0
Month 12	143	52.3	9.1	55.6	14.5	67.5
Month 24	138	52.2	8.8	54.9	23.1	63.5

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 37**, the mean SF-12 MCS increased postoperatively and was maintained through Month 24, indicating continued improvement in SF-12 MCS.

Table 38 includes the change in MCS from preoperative for all subjects in the Simplify® Cervical Artificial Disc group in the study at 6-month, 12-month, and 24-month timepoints. At Month 6, the mean MCS improvement of the Simplify® Cervical Artificial Disc subjects was 10.1, which decreased to a mean MCS improvement of 9.5 at Month 24.

Table 38: SF-12 (Mental Component Score - MCS) change from preoperative (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Month 06	143	10.1	12.2	10.0	-17.4	44.5
Month 12	143	10.0	12.1	9.5	-26.1	44.5
Month 24	138	9.5	12.1	8.4	-21.2	41.5

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 38**, the magnitude of change in SF-12 MCS was maintained through the Month 24 timepoint.

Table 39 includes the number and percentage of subjects achieving maintenance or improvement in SF-12 MCS score.

Table 39: SF-12 MCS – Subjects Achieving Maintenance or Improvement (Primary Analysis Population)

	Simplify Disc		
	N	n	%
Month 06	143	111	77.6%
Month 12	143	109	76.2%
Month 24	138	105	76.1%

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As shown above, a high rate of subjects achieved maintenance or improvement in SF-12 MCS at all postoperative timepoints. However, health-related quality of life data was not collected for the historical ACDF control group; therefore, no comparative analysis could be performed.

Treatment Satisfaction

Table 40 presents the subject responses for both the Simplify® Cervical Artificial Disc and historical ACDF control groups to the survey question, “How does the subject rate satisfaction with the treatment received?” The response options included “Very Satisfied,” “Satisfied,” “Somewhat Satisfied,” “Somewhat Dissatisfied,” “Dissatisfied,” and “Very Dissatisfied.” A total of 88% (122/138) of Simplify® Cervical Artificial Disc subjects reported that they were “Very Satisfied” at Month 24, as compared to a total of 70% (67/96) of this historical ACDF control subjects. Less than 1% of subjects in either group reported being “Dissatisfied” or “Very Dissatisfied” at Month 24.

Table 40: Treatment Satisfaction: "How does the subject rate satisfaction with the treatment received?" (Primary Analysis Population)

	Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%
Very Satisfied	118	83%	66	66%	122	88%	67	70%
Satisfied	17	12%	20	20%	12	9%	20	21%
Somewhat Satisfied	5	4%	11	11%	2	1%	5	5%
Somewhat Dissatisfied	0	0%	2	2%	2	1%	3	3%
Dissatisfied	1	1%	1	1%	0	0%	1	1%
Very Dissatisfied	1	1%	0	0%	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 40**, a greater percentage of subjects in the Simplify® Cervical Artificial Disc group reported "Very Satisfied" in terms of treatment satisfaction at Month 12 and Month 24 than the historical ACDF control group.

Table 41 presents the subject responses to the survey question, "If you could go back in time, would you choose to have the same treatment that you received for your neck condition?" The response options included "Definitely Yes," "Probably Yes," "Maybe," "Probably Not," and "Definitely Not." A total of 90% (124/138) of Simplify® Cervical Artificial Disc subject indicated that they would have the same procedure again when asked at Month 24, as compared to 70% (67/96) of historical ACDF control subjects.

Table 41: Treatment Satisfaction: "If you could go back in time, would you choose to have the same treatment that you received for your neck condition?" (Primary Analysis Population)

	Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%
Definitely Yes	122	86%	66	67%	124	90%	67	70%
Probably Yes	10	7%	16	16%	6	4%	16	17%
Maybe	8	6%	10	10%	7	5%	7	7%
Probably Not	2	1%	5	5%	1	1%	4	4%
Definitely Not	0	0%	2	2%	0	0%	2	2%

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 41**, a greater percentage of subjects in the Simplify® Cervical Artificial Disc group reported "Definitely Yes" when asked if the subject would choose the same treatment for their neck condition again after treatment at Month 12 and Month 24 than the historical ACDF control group.

Odom's Criteria

Odom's criteria data are censored following intraoperative deviation or SSI. Simplify® Cervical Artificial Disc and historical ACDF control subjects were categorized by the physician according to Odom's criteria as described below.

Excellent	Improvement in most (at least 80%) of the preoperative signs and symptoms, with little deterioration (not more than 10%)
Good	Improvement in some (at least 70%) of the preoperative signs and symptoms, with some deterioration (not more than 15%)
Fair	Improvement in half (at least 50%) of the preoperative signs and symptoms, with some deterioration (not more than 20%)
Poor	Improvement in few (less than 50%) of the preoperative signs and symptoms, or significant deterioration (more than 20%)

Table 42. Odom's Criteria (Primary Analysis Population)

	Post-Op				Week 06				Month 03			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%
Excellent	92	62%	55	49%	100	69%	66	58%	113	78%	66	59%
Good	38	26%	38	34%	37	26%	35	31%	24	17%	27	24%
Fair	15	10%	15	13%	5	3%	12	11%	6	4%	13	12%
Poor	3	2%	4	4%	3	2%	1	1%	1	1%	6	5%
	Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%
Excellent	124	86%	65	63%	118	83%	62	63%	121	87%	64	67%
Good	17	12%	25	24%	17	12%	19	19%	12	9%	18	19%
Fair	3	2%	8	8%	7	5%	14	14%	5	4%	8	8%
Poor	1	1%	5	5%	1	1%	4	4%	1	1%	5	5%

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As shown above in **Table 42**, a greater percentage of Simplify® Cervical Artificial Disc subjects were classified as 'Excellent' at all follow-up timepoints. At Month 24, 87% (121/139) of Simplify® Cervical Artificial Disc subjects were classified as "Excellent", as compared to 67% (64/95) of historical ACDF control subjects.

Medication Usage

Table 43 presents self-reported narcotic use at baseline and follow-up timepoints. As shown below, the PS adjusted group difference is not statistically significant at baseline; however, the difference between groups is statistically significant at all follow-up timepoints with a greater percentage of historical ACDF control subjects using narcotics.

Table 43: Narcotic Use (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Pre-Op	147	61	41.5%	117	64	54.7%	0.838	-1.5%	-14.9%	12.0%
Month 06	145	28	19.3%	103	42	40.8%	0.010	-16.8%	-29.0%	-4.5%
Month 12	144	22	15.3%	100	39	39.0%	0.002	-19.6%	-31.6%	-7.5%
Month 24	139	15	10.8%	95	35	36.8%	<.001	-25.8%	-37.8%	-13.9%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Medication and Cons Therapy.sas; Analyzed: 23JUN2020

Other Performance Outcomes

Other evaluations of effectiveness included dysphagia handicap index (DHI), return to work status, and time to recovery.

Dysphagia Handicap Index (DHI)

Table 44 includes the DHI score for all subjects in the Simplify® Cervical Artificial Disc group at preoperative, postoperative, 6-month, 12-month, and 24-month timepoints. At preop, the mean DHI score for subjects in the Simplify® Cervical Artificial Disc group was 6.2, which increased to 7.0 at week 6, and then gradually fell to 3.8 at Month 6, where it appeared to plateau thereafter (4.1 at Month 12; 4.0 at Month 24).

Table 44: DHI scores over time (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Pre-Op	150	6.2	8.8	3.0	0.0	50.0
Week 06	146	7.0	11.0	2.0	0.0	78.0
Month 03	145	4.2	7.6	2.0	0.0	50.0
Month 06	144	3.8	7.4	0.0	0.0	44.0
Month 12	143	4.1	8.3	0.0	0.0	72.0
Month 24	138	4.0	7.6	2.0	0.0	58.0

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 44**, there was an increase in mean DHI at Week 6, followed by a decrease at Month 3 that was maintained through Month 24.

Table 45 includes the change in DHI score from preoperative for all subjects in the Simplify® Cervical Artificial Disc group at 6-week, 3-month, 6-month, 12-month, and 24-month timepoints.

Table 45: DHI score change from preoperative (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Week 06	146	0.7	10.9	0.0	-50.0	70.0
Month 03	145	-2.2	8.9	-2.0	-50.0	28.0
Month 06	144	-2.6	8.6	-2.0	-42.0	36.0
Month 12	143	-2.3	9.2	-2.0	-48.0	42.0
Month 24	138	-2.3	8.6	-2.0	-48.0	28.0

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

As demonstrated in **Table 45**, there was an increase in mean change in DHI from preoperative at Week 6, followed by a maintained decrease Month 3 through Month 24.

The incidence and severity of dysphagia as evaluated during neurologic exam over time is presented in **Table 46**. No incidences of dysphagia were categorized as severe at any evaluation timepoint. The highest incidences of mild dysphagia occurred at week 6 (26% - 38/110) and Month 3 (29% - 34/77), but these events gradually declined over time, with only 3% (4/139) of subjects observed to have mild dysphagia at Month 24.

Table 46. Dysphagia Over Time – Safety Analysis Set

	Preop		Postop		Week 06		Month 03		Month 06		Month 12		Month 24	
	I		I		I		I		I		I		I	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Absent	149	99%	113	97%	110	74%	77	66%	129	89%	97	84%	139	97%
Mild	1	1%	4	3%	38	26%	34	29%	14	10%	16	14%	4	3%
Moderate	0	0%	0	0%	0	0%	5	4%	2	1%	2	2%	1	1%
Severe	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Neurological.sas; Analyzed: 14MAY2020

DHI scores are provided below by timepoint for the eight (8) Simplify® Cervical Artificial Disc subjects who reported dysphagia AEs. DHI was not collected in the historical study; therefore, these data are not available for the three (3) historical ACDF control subjects reporting dysphagia AEs.

Table 47. DHI Scores in Simplify® Cervical Artificial Disc Subjects Reporting Dysphagia

Subject	Preop	Week 6	Month 3	Month 6	Month 12	Month 24
01	0	2	14	14	0	0
02	0	12	6	0	0	0
02	10	18	12	14	8	6
04	4	6	4	12	6	22
05	2	6	0	0	26	26
06	0	2	4	0	4	4
07	4	2	14	8	12	4
08	2	28	30	16	4	2

According to Silbergleit et al., patient perceived severity of dysphagia correlated to the following DHI scores: normal = 7.89 ± 7.75, mild = 15.69 ± 9.77, moderate = 34.86 ± 16.02, and severe =

63.20 ± 23.38.[5] As shown in **Table 47**, majority of Simplify® Cervical Artificial Disc subjects reported DHI scores corresponding to normal to mild severity. DHI scores were not collected for the historical ACDF control group; therefore, no comparative analysis could be performed.

Work Status

Work status data are censored following intraoperative deviation or SSI. As shown in **Table 48**, 80% of the Simplify® Cervical Artificial Disc group was employed preoperatively and 89% were employed at Month 24. 70% of the historical ACDF control group was employed preoperatively and 68% were employed at Month 24. Please note: the one (1) subject reporting 'N/A' at Month 6 is a stay-at-home mom. 'Other' employment included student and homemaker.

Table 48: Work Status (Primary Analysis Population)

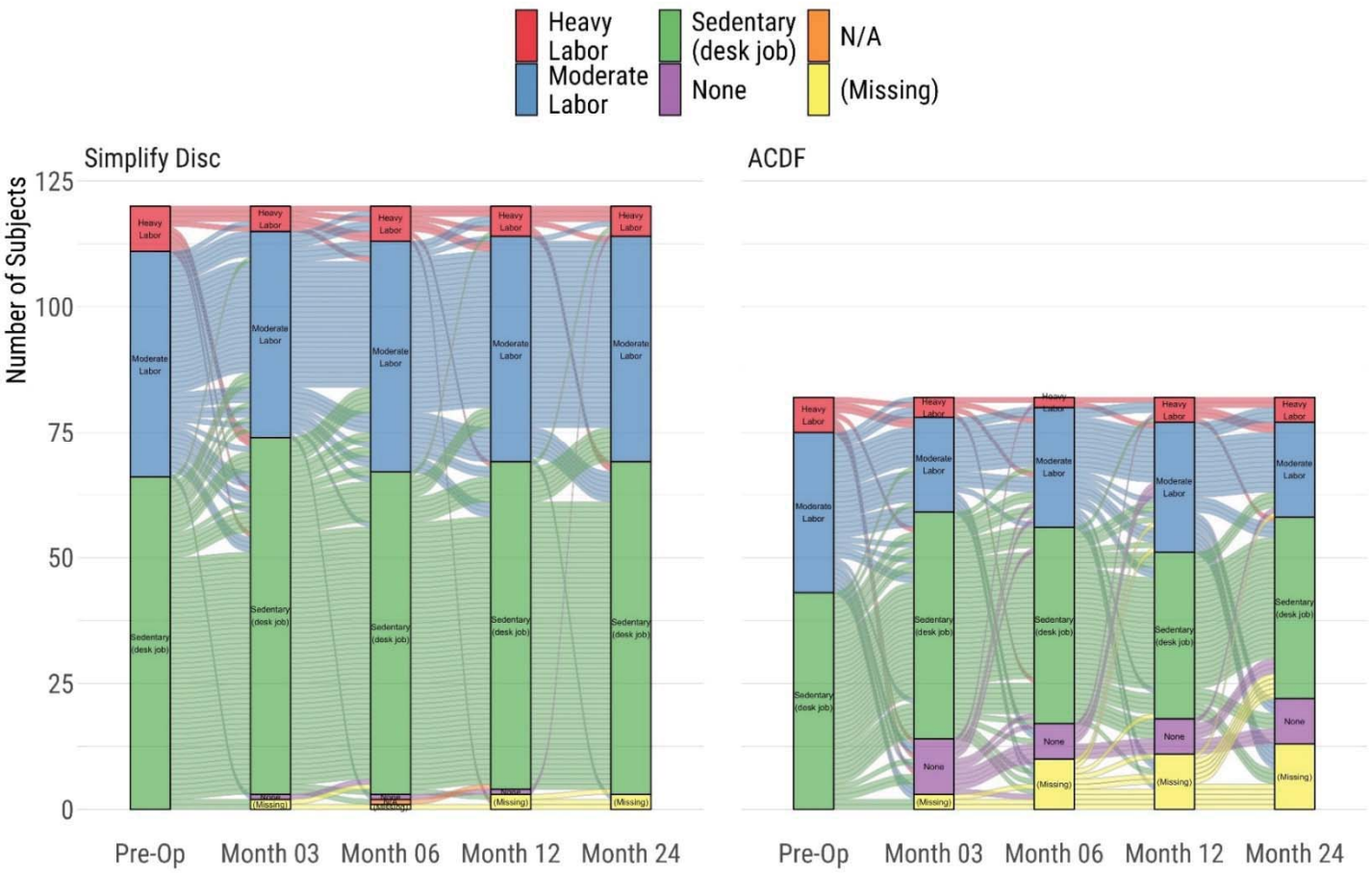
	Pre-Op				Month 03				Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Employed	120	80%	82	70%	117	81%	74	66%	123	85%	74	72%	124	86%	69	69%	124	89%	65	68%
Short-term disability	4	3%	6	5%	7	5%	12	11%	3	2%	4	4%	3	2%	3	3%	1	1%	4	4%
Long-term disability	3	2%	9	8%	2	1%	8	7%	2	1%	9	9%	2	1%	10	10%	2	1%	11	11%
Unemployed	10	7%	8	7%	10	7%	8	7%	8	6%	6	6%	4	3%	11	11%	6	4%	6	6%
Retired	0	0%	0	0%	0	0%	0	0%	0	0%	2	2%	0	0%	0	0%	0	0%	3	3%
Other	13	9%	12	10%	9	6%	10	9%	8	6%	8	8%	11	8%	7	7%	6	4%	7	7%
N/A	0	0%	0	0%	0	0%	0	0%	1	1%	0	0%	0	0%	0	0%	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Clinical Follow-up.sas; Analyzed: 14MAY2020

Figure 2 is an Alluvial plot showing the Normal employment type at Preop through Month 24 in all subjects who were Employed at baseline. The lines within each plot denote one subject's longitudinal Normal employment journey following their index procedure. In general, in the Simplify® Cervical Artificial Disc arm, it is observed that large proportions of subjects maintained their previous Normal employment type, with only one subject reporting None as their Normal employment type at Month 3 to Month 6, and none by Month 24. In the ACDF arm, 14% of those previously employed subjects reported "None" as their Normal employment at Month 3, with fractions not returning to Normal employment through Month 24 and another fraction restarting and re-stopping previous employment types.

[5] Silbergleit, A.K., Schultz, L., Jacobson, B., Beardsley, T. and Johnson, A. (2012) The Dysphagia Handicap Index: Development and Validation. Dysphagia, 27, 46-52.

Figure 2: Alluvial Diagram of Employment status among subjects employed at baseline



Note: These data are not censored after SSI to show the entire trajectory of subjects. Therefore, a fraction the "(Missing)" in ACDF is made up of previously re-operated subjects. Please note: Table 48 above reports Work Status and the Figure 2 reports Employment type.

Time to Recovery

Time to recovery data are censored following intraoperative deviation or SSI. Time to recovery is defined as time to first 15-point improvement in NDI. At Week 6, 87.0% (127/146) of the Simplify® Cervical Artificial Disc subjects and 76.8% (86/112) of historical ACDF control subjects achieved recovery defined as an improvement of at least 15 percentage-points. By Month 3, 95.9% (139/145) of Simplify® Cervical Artificial Disc and 81.1% (90/111) of historical ACDF control subjects achieved recovery.

Radiographic Assessments

Average Disc Height – Superior Adjacent Level

Table 49 describes the average disc height above the index level at preoperative, postoperative, 6-week, 3-month, 6-month, 12-month and 24-month timepoint.

Table 49: Average Disc Height (Above the Index Level) [mm] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	150	3.82	0.75	3.80	1.70	6.20	115	3.89	0.71	3.80	2.30	6.10	0.519	-0.07	-0.27	0.14
Post-Op	147	3.82	0.77	3.80	1.60	6.40	112	3.86	0.70	3.85	2.30	5.40	0.815	-0.02	-0.23	0.18
Week 06	144	3.79	0.77	3.80	1.60	6.20	112	3.86	0.72	3.80	2.20	6.20	0.505	-0.07	-0.28	0.14
Month 03	144	3.80	0.77	3.75	1.60	6.20	107	3.87	0.71	3.90	2.20	5.80	0.661	-0.05	-0.26	0.16
Month 06	143	3.83	0.82	3.80	1.50	6.60	100	3.89	0.68	3.90	1.90	5.40	0.689	-0.04	-0.27	0.18
Month 12	142	3.82	0.78	3.80	1.60	6.30	95	3.94	0.66	4.00	2.40	5.70	0.231	-0.13	-0.35	0.08
Month 24	137	3.82	0.77	3.80	1.70	6.30	92	3.83	0.75	3.85	1.30	6.20	0.773	-0.03	-0.26	0.19

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Radiography - Quantitative.sas; Analyzed: 14MAY2020

Mean disc height at the level above the index level was relatively unchanged as compared to preoperative in both arms of the study. There were no statistically significant differences in adjacent (above) disc height at any timepoint.

Table 50 describes the change in average disc height above the index level at postoperative, 6-week, 3-month, 6-month, 12-month and 24-month timepoint as compared to preoperative.

Table 50: Average Disc Height (Above the Index Level) [mm] Change from Preoperative (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Post-Op	147	0.01	0.16	0.00	-0.50	0.40	111	-0.01	0.16	0.00	-0.50	0.40	0.587	0.01	-0.03	0.06
Week 06	144	-0.02	0.15	0.00	-0.40	0.40	111	-0.04	0.13	0.00	-0.50	0.30	0.475	0.01	-0.03	0.05
Month 03	144	-0.02	0.15	0.00	-0.70	0.40	106	-0.03	0.14	0.00	-0.50	0.30	0.289	0.02	-0.02	0.06
Month 06	143	0.01	0.22	0.00	-0.50	1.70	99	-0.03	0.16	0.00	-0.80	0.20	0.147	0.04	-0.01	0.10
Month 12	142	0.01	0.22	0.00	-0.50	1.10	94	-0.03	0.20	0.00	-0.80	0.40	0.334	0.03	-0.03	0.09
Month 24	137	0.00	0.23	0.00	-0.90	1.10	91	-0.05	0.40	0.00	-1.40	2.80	0.638	0.02	-0.07	0.11

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Radiography - Quantitative.sas; Analyzed: 14MAY2020

There were no statistically significant differences in mean change in adjacent (above) disc height between groups at any timepoint.

Average Disc Height – Index Level

Table 51 describes the average disc height at the index level at preoperative, postoperative, 6-week, 3-month, 6-month, 12-month and 24-month timepoint.

Table 51: Average Disc Height (Index Level) [mm] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	148	3.31	0.74	3.30	1.10	5.70	115	3.27	0.79	3.20	1.40	5.20	0.813	-0.03	-0.23	0.18
Post-Op	144	4.72	0.88	4.80	2.20	6.80	112	5.41	1.09	5.45	3.10	9.30	<.001	-0.63	-0.90	-0.36
Week 06	142	4.45	0.92	4.55	1.50	6.80	112	5.07	1.14	5.05	2.80	9.30	<.001	-0.56	-0.85	-0.28
Month 03	143	4.40	0.87	4.50	1.90	6.60	107	4.94	1.14	4.90	2.50	9.30	<.001	-0.48	-0.76	-0.21
Month 06	142	4.35	0.88	4.40	1.90	6.60	100	4.83	1.20	4.85	2.30	9.20	0.006	-0.42	-0.71	-0.12
Month 12	141	4.29	0.91	4.40	1.90	6.50	95	4.78	1.24	4.80	1.70	9.10	0.003	-0.47	-0.77	-0.16
Month 24	136	4.24	0.94	4.35	1.70	6.50	92	4.79	1.24	4.85	1.90	9.10	0.002	-0.50	-0.82	-0.19

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Radiography - Quantitative.sas; Analyzed: 14MAY2020

As shown in **Table 51**, mean index disc height increased in both groups postoperatively; however, there was a greater increase in disc height in the historical ACDF control group, resulting in a statistically significant difference in index disc height between groups postoperatively through Month 24.

Table 52 describes the change in average disc height at the index level at postoperative, 6-week, 3-month, 6-month, 12-month and 24-month timepoint as compared to preoperative.

Table 52: Average Disc Height (Index Level) [mm] Change from Preoperative (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Post-Op	143	1.42	0.79	1.40	-0.70	3.10	111	2.15	1.08	2.20	-0.30	5.20	<.001	-0.62	-0.87	-0.36
Week 06	141	1.17	0.84	1.20	-1.70	3.00	111	1.82	1.16	1.80	-0.70	4.80	<.001	-0.53	-0.81	-0.26
Month 03	141	1.13	0.81	1.10	-1.30	2.90	106	1.68	1.16	1.70	-0.80	4.60	0.002	-0.44	-0.71	-0.17
Month 06	141	1.07	0.83	1.00	-1.30	3.00	99	1.54	1.19	1.60	-1.00	4.70	0.013	-0.36	-0.64	-0.08
Month 12	140	1.01	0.86	0.90	-1.30	3.10	94	1.45	1.19	1.50	-1.40	4.80	0.024	-0.34	-0.63	-0.05
Month 24	135	0.94	0.88	0.90	-1.30	3.10	91	1.46	1.24	1.50	-1.40	4.40	0.006	-0.44	-0.74	-0.13

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Radiography - Quantitative.sas; Analyzed: 14MAY2020

Similar to trends seen in mean scores, **Table 52** shows a statistically significant difference in mean change from preoperative between groups at all timepoints with greater change in the historical ACDF control group.

Average Disc Height – Inferior Adjacent Level

Table 53 describes the average disc height below the index level at preoperative, postoperative, 6-week, 3-month, 6-month, 12-month and 24-month timepoint.

Table 53: Average Disc Height (Below Index Level) [mm] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	119	3.93	0.70	4.00	2.00	6.00	75	4.24	0.69	4.30	2.80	6.60	<.001	-0.44	-0.66	-0.21
Post-Op	113	3.95	0.73	4.00	1.90	6.20	74	4.23	0.72	4.20	2.80	6.70	<.001	-0.42	-0.66	-0.18
Week 06	113	3.87	0.77	3.90	1.40	6.10	74	4.19	0.71	4.20	2.70	6.50	<.001	-0.50	-0.74	-0.25
Month 03	113	3.89	0.73	3.90	1.90	6.00	73	4.22	0.73	4.30	2.60	6.50	<.001	-0.46	-0.70	-0.22
Month 06	110	3.89	0.74	3.90	1.90	5.90	64	4.21	0.71	4.20	2.70	6.70	<.001	-0.46	-0.71	-0.21
Month 12	109	3.84	0.73	3.90	1.90	5.60	62	4.22	0.75	4.20	2.50	6.60	<.001	-0.57	-0.83	-0.32
Month 24	109	3.86	0.76	3.90	2.00	5.90	60	4.14	0.81	4.05	2.50	6.80	0.001	-0.45	-0.72	-0.19

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Radiography - Quantitative.sas; Analyzed: 14MAY2020

As shown in **Table 53**, the mean average disc height of the inferior adjacent level was significantly lower in the Simplify® Cervical Artificial Disc group at preoperative and all follow-up timepoints as compared to the historical ACDF control group (p=0.001).

Table 54 describes the change in average disc height below the index level at postoperative, 6-week, 3-month, 6-month, 12-month and 24-month timepoint as compared to preoperative.

Table 54: Average Disc Height (Below Index Level) [mm] Change from Preoperative (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Post-Op	112	0.02	0.16	0.00	-0.40	0.50	73	0.00	0.16	0.00	-0.30	0.50	0.538	0.02	-0.04	0.07
Week 06	110	-0.05	0.30	0.00	-2.60	0.50	73	-0.03	0.16	0.00	-0.40	0.30	0.302	-0.04	-0.13	0.04
Month 03	111	-0.03	0.23	0.00	-1.60	0.40	72	-0.01	0.20	0.00	-0.50	0.60	0.386	-0.03	-0.10	0.04
Month 06	106	-0.02	0.16	0.00	-0.50	0.50	63	-0.03	0.21	0.00	-0.60	0.50	0.848	0.01	-0.06	0.07
Month 12	105	-0.04	0.26	0.00	-1.60	0.50	61	-0.09	0.25	-0.10	-0.70	0.50	0.793	0.01	-0.08	0.10
Month 24	106	-0.08	0.31	-0.10	-1.60	0.50	59	-0.07	0.26	0.00	-0.70	0.40	0.344	-0.05	-0.15	0.05

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Radiography - Quantitative.sas; Analyzed: 14MAY2020

Differences in mean change from preoperative were not statistically significant between groups at any follow-up timepoint.

Device Migration

Device migration assesses significant movement of the implant and was evaluated as follows:

0. None: No evidence of migration of the implant >3mm relative to the initial position of the implant at PostOp.
1. Present: Presence of device migration >3mm relative to the initial position of the implant at PostOp.
    a. Anterior: Device has migrated anteriorly.
    b. Posterior: Device has migrated posteriorly.
    c. Left: Device has migrated laterally to the left.
    d. Right: Device has migrated laterally to the right.

Migration was evaluated relative to the first available postoperative visit. A threshold of >3mm of implant motion was used to define significance. This represents approximately 20% of the AP

dimension of a typical cervical vertebra. If a notable implant slip occurs that does not meet the threshold, it may be documented in the reviewer's comments for subsequent evaluation. Presence of Left or Right migration was only evaluated in the Simplify® Cervical Artificial Disc group.

Table 55 presents the number and percentage of subjects with radiographic confirmation of device migration a 6-week, 3-month, 6-month, 12-month and 24-month timepoints.

Table 55: Device Migration (Primary Analysis Population)

	Week 06				Month 03				Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
None	145	100%	109	96%	144	99%	108	97%	144	99%	95	94%	142	100%	90	92%	137	99%	90	95%
Anterior	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Posterior	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Left	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Right	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Unable to assess	0	0%	5	4%	1	1%	3	3%	1	1%	6	6%	0	0%	8	8%	2	1%	5	5%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Radiography - Qualitative.sas; Analyzed: 14MAY2020

Device migration was not observed in Simplify® Cervical Artificial Disc or historical ACDF control subjects through Month 24.

Flexion/Extension Rotation

Table 56 describes the amount of rotation at the index level at preoperative, postoperative, Month 3, Month 6, Month 12, and Month 24 timepoint.

Table 56: Rotation (Index Level) [degrees] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	143	7.29	4.22	6.40	0.00	21.40	110	7.27	4.36	6.75	-0.80	19.00	0.588	-0.33	-1.54	0.87
Month 03	139	8.64	5.06	8.20	0.30	22.10	107	1.74	1.21	1.40	0.00	5.10	<.001	7.11	6.01	8.21
Month 06	140	9.54	5.55	8.70	0.10	23.40	101	1.51	1.42	1.10	-0.20	6.80	<.001	8.15	6.89	9.41
Month 12	138	9.44	5.90	9.10	0.00	22.60	95	1.08	1.19	0.80	0.00	7.50	<.001	8.57	7.22	9.93
Month 24	134	9.61	6.30	9.15	0.00	23.60	95	0.72	0.75	0.50	-0.20	4.10	<.001	9.04	7.60	10.48

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Radiography - Quantitative.sas; Analyzed: 14MAY2020

The mean degree of rotation at the index level was not significantly different between groups at preoperative. Postoperatively, rotation increased in the Simplify® Cervical Artificial Disc group and decreased in the historical ACDF control group. The mean rotation was significantly different between groups at all postoperative timepoints ($p<0.001$). This outcome is expected due to the motion sparing design of the Simplify® Cervical Artificial Disc treatment versus the ACDF treatment.

Table 57 describes the mean change in rotation at the index level over time at postoperative, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to preoperative.

Table 57: Rotation (Index Level) Change from Preoperative [degrees] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Month 03	135	1.54	4.85	1.50	-16.70	11.20	100	-5.47	4.22	-4.65	-16.90	2.00	<.001	7.46	6.12	8.81
Month 06	137	2.33	5.18	1.90	-13.80	16.90	95	-5.82	4.30	-5.00	-17.60	0.60	<.001	8.63	7.19	10.08
Month 12	134	2.38	5.35	2.25	-12.00	13.30	89	-6.28	4.47	-5.70	-17.60	1.90	<.001	9.23	7.70	10.75
Month 24	130	2.41	6.00	2.05	-12.10	16.90	90	-6.76	4.35	-6.05	-18.40	0.80	<.001	9.68	8.03	11.32

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Radiography - Quantitative.sas; Analyzed: 14MAY2020

As expected, the mean change in rotation at the index level as compared to preoperative was significantly greater in the Simplify® Cervical Artificial Disc group as compared to the historical ACDF control group ($p<0.001$).

Device Condition

Device Condition assesses the condition of the device using the following device specific grading scales:

Simplify® Cervical Artificial Disc Device

0. Intact: No evidence of dislocation or fracture of the device components.
1. Failed Superior Component: Fracture or deformation of the superior endplate.
2. Failed Core: Fracture or other failure of the core.
3. Failed Inferior Component: Fracture or deformation of the inferior endplate.
4. Disassembled: Dislocation or permanent subluxation of the articulating components of the implant. (Permanent subluxation is defined as severe (i.e. >50%) misalignment of the device components that does not reduce in flexion-extension or lateral bending.) There is little or no motion across the implant in the plane of the subluxation or dislocation.

ACDF:

0. Intact: No failed graft, loose screws or fractured hardware. The graft and hardware are intact and stable.
1. Failed Graft: Presence of visible gaps, fracture or disintegration of the graft material within the interbody space
2. Failed Screw: Fracture, deformation, migration, pull-out or loosening of one or more screws
3. Failed Plate: Fracture, deformation or disassembly of the plate from the screw(s)

Table 58 reports the number and percentage of subjects with radiographic confirmation of the condition of the device and the status of the Simplify® Cervical Artificial Disc device (Intact, Failed Superior Component, Failed Core, Failed Inferior Component, Disassembled, Indeterminate, or Unable to assess) at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 58: Device Condition (Primary Analysis Population)

	Week 06		Month 03		Month 06		Month 12		Month 24	
	Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc	
	n	%	n	%	n	%	n	%	n	%
Intact	145	100%	144	99%	144	99%	142	100%	137	99%
Failed Superior Component	0	0%	0	0%	0	0%	0	0%	0	0%
Failed Core	0	0%	0	0%	0	0%	0	0%	0	0%
Failed Inferior Component	0	0%	0	0%	0	0%	0	0%	0	0%
Disassembled	0	0%	0	0%	0	0%	0	0%	0	0%
Unable to assess	0	0%	1	1%	1	1%	0	0%	2	1%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Radiography - Qualitative.sas; Analyzed: 14MAY2020

As shown above, all evaluated Simplify® Cervical Artificial Discs were observed to be intact at latest timepoint. No device condition observations were reported at any timepoint.

Table 59 reports the number and percentage of subjects with radiographic confirmation of the condition of the device and the status of the device specific to fusion materials (Intact, Failed Graft, Failed Screw, Failed Plate, Disassembled, Indeterminate, or Unable to assess) at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 59: Device Condition ACDF (Primary Analysis Population)

	Week 06		Month 03		Month 06		Month 12		Month 24	
	ACDF		ACDF		ACDF		ACDF		ACDF	
	n	%	n	%	n	%	n	%	n	%
Intact	106	93%	96	86%	75	74%	74	76%	83	87%
Failed Graft	0	0%	1	1%	13	13%	13	13%	7	7%
Failed Screw	1	1%	5	5%	1	1%	2	2%	1	1%
Failed Plate	0	0%	0	0%	0	0%	0	0%	0	0%
Unable to assess	7	6%	9	8%	12	12%	9	9%	4	4%

As shown in **Table 59**, 7% of subjects were reported to have a failed graft and 1% of subjects were reported to have a failed screw at the latest timepoint.

Device Failure

Device failure is defined as any device condition evaluation other than ‘intact’ and/or any device migration evaluation other than ‘none’ at any time through Month 24. Subsidence or failure of the allograft was not counted as a device failure in the historical ACDF control group. **Table 60** and **Figure 3** show a survival analysis and product-limit estimates of freedom from device failure.

The ‘N Start’, shown in **Table 60**, reports the number of subjects not yet terminal failures or censored and therefore are at risk for device failure in the current interval. That is, ‘N Start’ is the number of subjects at the end of the previous interval. ‘N Start’ is calculated based on prior interval ‘N start’ minus failures within the preceding interval (‘F’) and censored subjects (‘C’). Subjects shown as ‘censored’ (‘C’) are unevaluable for the following interval but are not a failure (i.e., loss to follow-up, intraoperative deviation). One hundred forty-five (145) Simplify® Cervical Artificial Disc subjects remain at risk for device failure at the start of the 24-month interval.

As shown below, no Simplify® Cervical Artificial Disc subjects exhibited postoperative device failure; therefore, there were no secondary surgeries related to a device performance issue. Seven (7) screw failures were identified in the historical ACDF control group.

Table 60. Device Failure Survival Analysis (Primary Analysis Population)

	Simplify® Cervical Artificial Disc (N= 150)								ACDF (N= 117)								Group Difference	
	N	Within Interval†			Cumulative*				N	Within Interval†			Cumulative*				Δ	Log-Rank
End Interval	Start	F	C	Surv.	F	%	LB	UB	Start	F	C	Surv.	F	%	LB	UB		p-value
Treatment	150	--	--	100.0%	0	--	--	--	117	--	--	100.0%	0	--	--	--	--	
Month 03	150	0	4	100.0%	0	100.0%	--	--	117	1	7	99.1%	1	99.1%	97.4%	100.0%	0.9%	
Month 06	146	0	0	100.0%	0	100.0%	--	--	109	4	10	96.3%	5	95.5%	91.6%	99.4%	4.5%	0.002
Month 12	146	0	1	100.0%	0	100.0%	--	--	95	1	4	98.9%	6	94.5%	90.2%	98.8%	5.5%	
Month 24	145	0	145	100.00	0	100.0%	--	--	90	1	89	98.9%	7	93.4%	88.7%	98.2%	6.6%	

Notes:
† Within Interval: F = failures within interval (visit), C = censored within interval, survival for that interval. These reflect within interval lifetable estimates;
* Cumulative: F = cumulative number of events, % is Kaplan-Meier (product-limit) estimate with 95% lower bound (LB) and upper bound (UB) based on log-log approach. The definitive product limit estimates cannot be recovered from lifetable estimates.

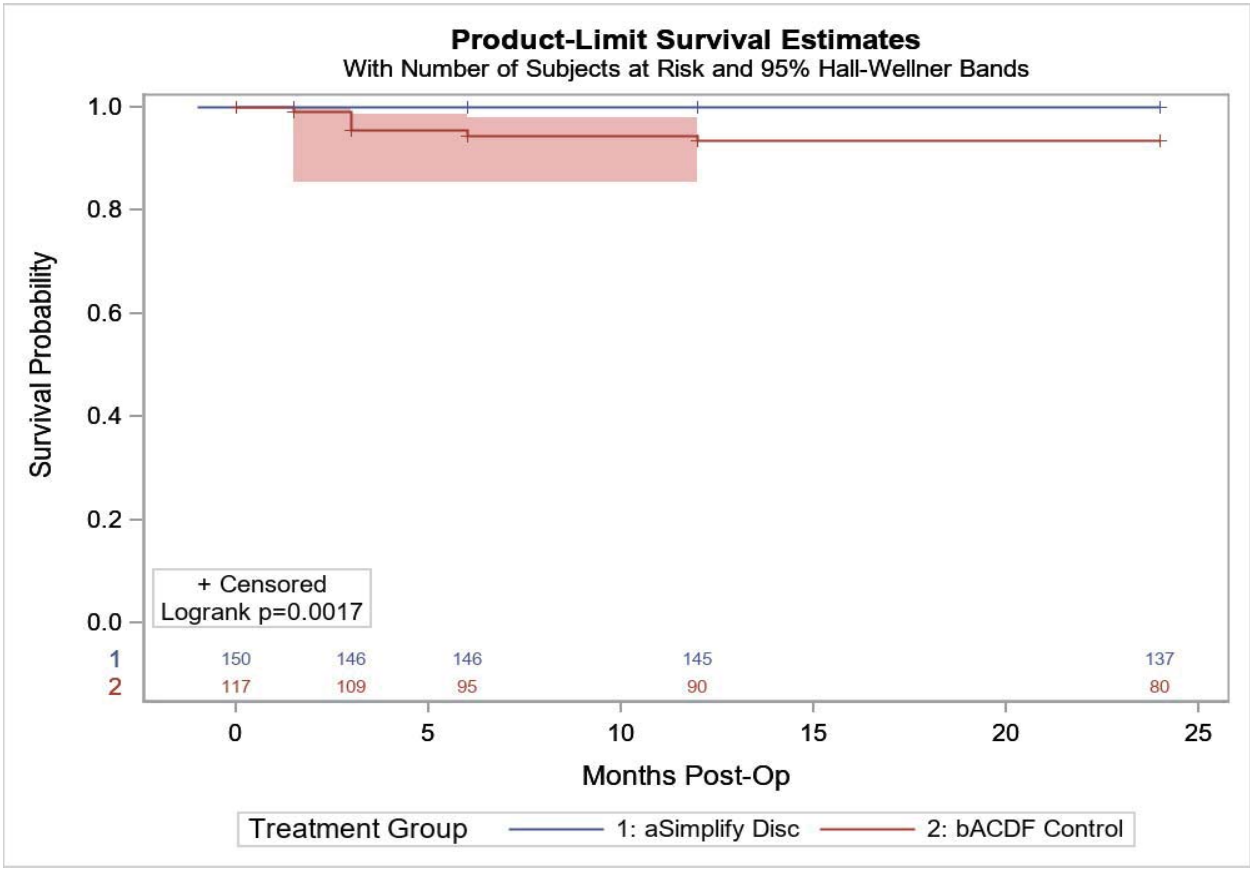


Figure 3: Device Failure Survival Analysis (Primary Analysis Population)

Adjacent Level Disc Degeneration (Derived)

Disc degeneration at the adjacent levels are graded in accordance with the following definitions:

1. None: Negligible disc space narrowing, no osteophyte formation, no endplate sclerosis.
2. Mild: <33% disc space narrowing, mild osteophyte formation, no endplate sclerosis.
3. Moderate: 33% - 66% disc space narrowing, moderate osteophyte formation, mild to moderate endplate sclerosis
4. Severe: >66% disc space narrowing, severe osteophyte formation or fusion, severe endplate sclerosis.

Superior Adjacent Level

Table 61 reports the number and percentage of subjects with adjacent level disc degeneration (ALDD) above the index level at preoperative, Month 3, Month 6, Month 12 and Month 24 timepoints.

Table 61: Adjacent Level Disc Degeneration (Above Index Level) (Primary Analysis Population)

	Pre-Op				Month 03				Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
None	104	69%	56	48%	100	69%	45	41%	99	68%	35	35%	92	65%	23	23%	87	63%	15	16%
Mild	28	19%	22	19%	26	18%	26	23%	26	18%	26	26%	29	20%	26	27%	26	19%	22	23%
Moderate	17	11%	27	23%	16	11%	29	26%	17	12%	30	30%	18	13%	32	33%	20	14%	36	38%
Severe	1	1%	9	8%	1	1%	10	9%	1	1%	10	10%	1	1%	15	15%	3	2%	20	21%
Unable to assess	0	0%	3	3%	2	1%	1	1%	2	1%	0	0%	2	1%	2	2%	3	2%	2	2%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Radiography - Qualitative.sas; Analyzed: 14MAY2020

As shown in **Table 61**, the trend of ALDD at the superior adjacent level in the Simplify® Cervical Artificial Disc group was nearly constant from preop through 24 months. Conversely, adjacent level disc degeneration at the superior adjacent level continued to progress from preop to 24 months in the historical ACDF control group.

Inferior Adjacent Level

Table 62 reports the number and percentage of subjects with ALDD below the index level at preoperative, Month 3, Month 6, Month 12 and Month 24 timepoints.

Table 62: Adjacent Level Disc Degeneration (Below Index Level) (Primary Analysis Population)

	Pre-Op				Month 03				Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
None	121	81%	39	33%	112	77%	32	29%	115	79%	30	30%	106	75%	20	20%	95	68%	14	15%
Mild	11	7%	12	10%	16	11%	13	12%	12	8%	10	10%	17	12%	15	15%	15	11%	15	16%
Moderate	7	5%	24	21%	8	6%	23	21%	9	6%	23	23%	10	7%	21	21%	16	12%	23	24%
Severe	1	1%	3	3%	0	0%	7	6%	0	0%	6	6%	1	1%	7	7%	2	1%	10	11%
Unable to assess	10	7%	39	33%	9	6%	36	32%	9	6%	32	32%	8	6%	35	36%	11	8%	33	35%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Radiography - Qualitative.sas; Analyzed: 14MAY2020

As shown above, the progression of inferior ALDD was minimal in the Simplify® Cervical Artificial Disc group, with 78% of subjects with “None” or “Mild” at 24 months compared to 88%

at preop. In the historical ACDF control group, 43% had “None” to “Mild” at preop while 31% had the same categorization at 24 months.

Changes in Derived Adjacent Level Disc Degeneration

Change in adjacent level disc degeneration (ALDD) was derived from the assessment of adjacent level disc degeneration relative to preoperative and graded in accordance with the following definitions:

0. No change in derived ALDD since preoperative.
1. One Grade Progression: One grade change in derived ALDD since preoperative.
2. Two Grade Progression: Two grade change in derived ALDD since preoperative
3. Three Grade Progression: Three grade change in derived ALDD since preoperative
4. Decrease: One or more grade decrease in derived ALDD since preoperative

Superior Adjacent Level

Table 63 reports the number and percentage of subjects with changes in ALDD above the index level at the Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 63: Change in Adjacent Level Disc Degeneration (Above Index Level) (Primary Analysis Population)

	Month 03				Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
No Change	137	94%	94	85%	134	92%	82	81%	124	87%	64	65%	114	82%	49	52%
One Grade Progression	3	2%	10	9%	6	4%	12	12%	13	9%	21	21%	14	10%	25	26%
Two Grade Progression	0	0%	3	3%	0	0%	4	4%	0	0%	8	8%	6	4%	13	14%
Three Grade Progression	0	0%	1	1%	0	0%	1	1%	0	0%	2	2%	0	0%	6	6%
Decrease	3	2%	0	0%	3	2%	0	0%	3	2%	0	0%	2	1%	0	0%
Unable to assess	2	1%	3	3%	2	1%	2	2%	2	1%	3	3%	3	2%	2	2%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Radiography - Qualitative.sas; Analyzed: 14MAY2020

A higher percentage of historical ACDF control subjects demonstrated progression in ALDD at the superior index level than investigational subjects at Month 24 (14% of Simplify® Cervical Artificial Disc subjects had any grade progression vs 46% of ACDF subjects), despite having less margin to progress since there was more preoperative superior ALDD.

Inferior Adjacent Level

Table 64 reports the number and percentage of subjects with changes in ALDD below the index level at the Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 64: Change in Adjacent Level Disc Degeneration (Below Index Level) (Primary Analysis Population)

	Month 03				Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
No Change	129	89%	65	59%	129	89%	54	53%	119	84%	41	42%	100	72%	32	34%
One Grade Progression	5	3%	4	4%	5	3%	5	5%	11	8%	15	15%	21	15%	16	17%
Two Grade Progression	0	0%	0	0%	0	0%	1	1%	0	0%	1	1%	3	2%	5	5%
Three Grade Progression	0	0%	2	2%	0	0%	2	2%	0	0%	2	2%	0	0%	2	2%
Decrease	1	1%	0	0%	0	0%	0	0%	1	1%	0	0%	1	1%	0	0%
Unable to assess	10	7%	40	36%	11	8%	39	39%	11	8%	39	40%	14	10%	40	42%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Radiography - Qualitative.sas; Analyzed: 14MAY2020

As shown in **Table 64**, "No Change" in inferior level ALDD progression was seen in 72% of the Simplify® Cervical Artificial Disc group versus 34% of the historical ACDF control group at Month 24.

Facet Degeneration

Facet degeneration was assessed using MRI and graded in accordance with the following definitions:[6,7]

0. None: Normal facet joint space.
1. Mild: Narrowing of the facet joint space and/or small osteophytes and/or mild hypertrophy of the articular process.
2. Moderate: Narrowing of the facet joint space and/or moderate osteophytes and/or moderate hypertrophy of the articular process and/or mild subarticular bone erosions.
3. Severe: Narrowing of the facet joint space and/or large osteophytes and/or severe hypertrophy of the articular process and/or severe subarticular bone erosions and/or subchondral cysts.

This measurement was performed in the Simplify® Cervical Artificial Disc group only.

Table 65 presents the number and percentage of subjects with evidence of facet degeneration at the index level at the preoperative and 24-month timepoints. At preop, 36% (52/148) of Simplify® Cervical Artificial Disc subjects were identified to have some degree of facet degeneration, while similarly 37% (52/139) were found to have evidence of facet degeneration at Month 24.

[6] Weishaupt D, Zanetti M, Boos N, Hodler J. MR imaging and CT in osteoarthritis of the lumbar facet joints. Skeletal Radiology 28:215-219. (1999) 28:215-219. 1999.
[7] Fujiwara A, Tamai K, Yamato M, An HS, Yoshida H, Saotome K, Kurihashi A. The relationship between facet joint osteoarthritis and disc degeneration of the lumbar spine: an MRI study. Eur Spine J 8:396-401. 1999.

Table 65: Facet Degeneration over time (Primary Analysis Population)

	Pre-Op		Month 24	
	Simplify Disc		Simplify Disc	
	n	%	n	%
None	92	62%	80	58%
Mild	47	32%	42	30%
Moderate	4	3%	9	6%
Severe	1	1%	1	1%
Unable to Assess	4	3%	7	5%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Radiography - Qualitative.sas; Analyzed: 14MAY2020

Similar percentages of facet degeneration were seen in the Simplify® Cervical Artificial Disc group at preoperative and Month 24, indicating a lack of progression of facet degeneration during the 2 year follow-up.

Heterotopic Ossification

Heterotopic ossification was measured in the investigational group using the following definitions:

0. None (Grade 0): No evidence of osteophyte formation or heterotopic ossification.

1. Mild (Grade 1): HO is detectable in the front or sides or the vertebral body, or as islands of bone in the adjacent soft tissue, but is not in the intervertebral disc space. Bone is not present between the planes formed by the two vertebral endplates.

2. Moderate (Grade 2): HO is growing into the disc space. Bone is present between the planes formed by the two adjacent endplates but is not significantly blocking or articulating between adjacent vertebral endplates or osteophytes.

3. Severe (Grade 3): The range of motion of the vertebral endplates is likely blocked by the formation of HO and/ or postoperative osteophytes on the radiographs, but some movement of the prosthesis may remain.

4. Bridging (Grade 4): HO is causing bony ankylosis. An apparent continuous connection of bridging bone exists between the adjacent vertebral endplates with little or no motion occurring across the treated segment.

Table 66 presents heterotopic ossification grades of the index level for all treated subjects at preoperative, Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 66: Heterotopic Ossification (Index Level) (Primary Analysis Population)

	Pre-Op		Month 03		Month 06		Month 12		Month 24	
	Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc	
	n	%	n	%	n	%	n	%	n	%
None (Grade 0)	100	68%	81	56%	58	40%	36	25%	20	14%
Mild (Grade 1)	26	18%	43	30%	41	28%	23	16%	16	12%
Moderate (Grade 2)	21	14%	18	12%	42	29%	74	52%	80	58%
Severe (Grade 3)	1	1%	2	1%	2	1%	7	5%	11	8%
Bridging (Grade 4)	0	0%	0	0%	1	1%	2	1%	10	7%
Unable to Assess	0	0%	1	1%	1	1%	0	0%	2	1%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Radiography - Qualitative.sas; Analyzed: 14MAY2020

As shown above, “moderate” or lower grade heterotopic ossification was observed in the majority of subjects (58% - 80/139) at the latest timepoint. Few Simplify® Cervical Artificial Disc subjects experienced Grade 3 (11 subjects, 8% - 11/139) or Grade 4 (7% - 10/139) heterotopic ossification at Month 24.

All subjects with Grade 4 heterotopic ossification and bridging bone reached clinical success at 24 months according to the primary endpoint criteria (100% CCS).

Fusion

Fusion was assessed in the control subjects. Fusion was defined as:

- <3 mm translational motion;
- <5° angular motion;
- Evidence of bridging bone; and
- Radiolucent lines <50%

Fusion was observed in 88.4% (84/95) of the control subjects through 24 months.

5. Conclusions Drawn from the Clinical Study

The valid scientific evidence presented in the preceding sections provides reasonable assurance that the Simplify® Cervical Artificial Disc is a safe and effective disc replacement in skeletally mature patients for reconstruction of the disc from C3-C7 following discectomy at one level for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and manifested by at least one of the following conditions confirmed by radiographic imaging (e.g., X-rays, computed tomography (CT), magnetic resonance imaging (MRI)): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels.

Based on the clinical study results, it is reasonable to conclude that the clinical benefits of the use of the Simplify® Cervical Artificial Disc in terms of improvement in pain and disability, and the potential for motion preservation, outweigh the risks, both in terms of the risks associated with the Simplify® Cervical Artificial Disc and surgical procedure when used in the indicated population

in accordance with the directions for use, and as compared to the historical ACDF control treatment in the same indicated population.

B. Two-Level IDE Study (G150206)

1. Study Design

Subjects in the Simplify® Cervical Artificial Disc two-level pivotal study ("Simplify® Cervical Artificial Disc IDE study") were treated between April 2017 and November 2018. The database for this PMA reflects data collected through October 2020 and included 182 Simplify® Cervical Artificial Disc subjects (200 including training subjects) at 18 sites and 188 historical ACDF control subjects treated at 30 sites. Control subjects were treated between June 2006 and November 2007 in a prior IDE study that supported an FDA marketing application.

The prospective, non-randomized, historically controlled, multi-center study was performed in the United States under IDE #G150206 combined with a historical control ACDF data from a previous multi-center, prospective, randomized concurrently-controlled cervical disc IDE study performed in the United States. The previous study incorporated a similar study design, indications for use, study entry criteria, study endpoints, and data collected. The two studies were not identical, and differences were identified in some categories and are discussed below. A Clinical Events Committee (CEC) adjudicated all historical AEs, secondary surgeries, neurological data, and protocol deviations to ensure consistency with the Simplify® Cervical Artificial Disc study.

A statistical plan utilizing propensity score (PS) modeling was developed to incorporate the historical control and to match the baseline covariates to the Simplify® Cervical Artificial Disc group. The resultant PS Selected study cohort used for the primary analysis population thus included all investigational Simplify® Cervical Artificial Disc subjects (excluding training subjects) and historical control subjects (excluding trimmed subjects) and is termed the "Primary Analysis Set."

Clinical Inclusion and Exclusion Criteria

To be eligible for the Simplify® Cervical Artificial Disc IDE study, subjects had to be eligible for a fusion procedure using the anterior approach and meet all of the inclusion criteria and none of the exclusion criteria:

Table 67: Study Inclusion/Exclusion Criteria

Study Inclusion Criteria	Study Exclusion Criteria
• Has cervical degenerative disc disease at two (2) adjacent cervical levels (from C3 C7) requiring surgical treatment and involving intractable radiculopathy, myelopathy, or both; • Has a herniated disc and/or osteophyte formation at each level to be treated that is producing symptomatic nerve root and/or spinal cord compression. The condition is documented by patient history (e.g., neck pain with arm pain, functional deficit and/or neurological deficit), and	• Has a cervical spinal condition other than symptomatic cervical DDD requiring surgical treatment at the involved levels; • Has documented or diagnosed cervical instability relative to adjacent segments at either level, defined by dynamic (flexion/extension) radiographs showing: o Sagittal plane translation >3.5 mm, or o Sagittal plane angulation >20°;

Study Inclusion Criteria	Study Exclusion Criteria
the requirement for surgical treatment is evidenced by radiographic studies (e.g., CT, MRI, x-rays, etc.); • Has been unresponsive to non-operative treatment for at least six weeks or has the presence of progressive symptoms or signs of nerve root/spinal cord compression in the face of continued non-operative management; • Has no previous surgical intervention at the involved levels or any subsequent planned/staged surgical procedure at the involved or adjacent level(s); • Must be at least 18 years of age and be skeletally mature at the time of surgery; • Has a preoperative Neck Disability Index (NDI) ≥30; • Has a preoperative neck pain score ≥8 based on the preoperative Neck and Arm Pain Questionnaire; • If a female of childbearing potential, patient is non-pregnant, non-nursing, and agrees not to become pregnant during the study period; • Is willing to comply with the study plan and sign the Patient Informed Consent Form.	• Has more than two cervical levels requiring surgical treatment; • Has a fused level (or artificial disc replacement) adjacent to the levels to be treated; • Has severe pathology of the facet joints of the involved vertebral bodies; • Has had previous surgical intervention at either one or both of the involved levels or at adjacent levels; • Axial neck pain only (no radicular or myelopathy symptoms); • Has been previously diagnosed with osteopenia or osteomalacia; • Has any of the following that may be associated with a diagnosis of osteoporosis (if "Yes" to any of the below risk factors, a DEXA Scan will be required to determine eligibility): o Postmenopausal non-black female over 60 years of age who weighs less than 140 pounds; o Postmenopausal female who has sustained a non-traumatic hip, spine, or wrist fracture; o Male over the age of 70; o Male over the age of 60 who has sustained a non-traumatic hip or spine fracture. o If the level of bone mineral density is a T score of -1.5 or lower (i.e., -1.6, -1.7, etc.), then the patient is excluded from the study • Has presence of spinal metastases; • Has overt or active bacterial infection, either local or systemic; • Has insulin-dependent diabetes; • Has chronic or acute renal failure or prior history of renal disease; • Known PEEK, ceramic, titanium allergy; • Is mentally incompetent (if questionable, obtain psychiatric consult); • Is a prisoner; • Is pregnant[1]; • Is currently an alcohol and/or drug abuser or currently undergoing treatment for alcohol and/or drug abuse; • Is involved with current or pending litigation regarding a spinal condition; • Has received drugs that may interfere with bone metabolism within two weeks prior to the planned date of spinal surgery (e.g., steroids or methotrexate), excluding routine perioperative anti-inflammatory drugs; • Has a history of an endocrine or metabolic disorder known to affect osteogenesis (e.g., Paget's Disease, renal osteodystrophy, Ehlers-Danlos Syndrome, or osteogenesis imperfecta);

Study Inclusion Criteria	Study Exclusion Criteria
	• Has a condition that requires postoperative medications that interfere with the stability of the implant, such as steroids. (This does not include low-dose aspirin for prophylactic anticoagulation and routine perioperative anti-inflammatory drugs); • Has received treatment with an investigational therapy within 28 days prior to implantation surgery or such treatment is planned during the 16 weeks following implantation. NOTE: If a patient did not meet the entry criteria during the initial enrollment, the patient was not re-evaluated for entry into the study at a later time.

[1] Pregnancy during participation in this study should also be discouraged, since pregnancy may prohibit exposure to X-rays during necessary follow-up timeframes.

Control

Control subjects received ACDF. The historical control was collected from the control arm of a previously completed multi-center, prospective, randomized non-inferiority clinical trial. Comparison of the data collected from the Simplify® Cervical Artificial Disc Pivotal IDE study and historical ACDF control demonstrated that the cohorts were comparable, though not identical.

- A detailed comparison of the indications and inclusion/exclusion criteria of the historical ACDF cohort and the Simplify® Cervical Artificial Disc IDE study protocol was conducted to determine if the historical data were adequate to serve as comparator and support a PMA Supplement application. The protocol and case report forms were reviewed and discussed with FDA. It was determined that the historical study was similar to the IDE study in its Indications for Use and Inclusion/Exclusion criteria.
- The historical study collected the parameters used to calculate overall success, success of the individual components of the composite primary endpoint, secondary endpoints, and safety assessments per the defined assessments in the Simplify® Cervical Artificial Disc IDE study protocol.

A PS method was used to address selection bias in the observational study design when pooling data from the historical control and actively enrolled Simplify® Cervical Artificial Disc group. The objective of the observational design was to select from the candidate pool of historical controls those subjects whose baseline covariate distribution was approximately the same as Simplify® Cervical Artificial Disc subjects within PS subclasses. The final Primary Analysis set included all 182 Simplify® Cervical Artificial Disc subjects (200 including training subjects) and 170 of 188 historical control subjects. Rigorous statistical criteria and graphical analyses demonstrated that within PS subclasses, Simplify® Cervical Artificial Disc subjects and PS-selected historical controls had approximately the same multivariate baseline covariate distribution.

Postoperative Care
Following completion of the procedure, recommended postoperative care regimen was implemented.

Subjects were encouraged to return to normal activity with the following guidelines:

- Use of a soft collar (at the discretion of the surgeon)
- Ambulation on day of surgery progressing to aerobic walking over the course of 6 weeks
- Gradually increase cervical range of motion
- No heavy lifting (greater than 20 lbs) for 6 weeks and then progress to more resistive exercise
- No impact sports for 3 months

Follow-up Schedule
All subjects were evaluated preoperatively, at treatment/discharge (prior to the subject being discharged from the hospital) and postoperatively at 6 weeks (±2 weeks), 3 months (±2 weeks), 6 months (±1 month), 1 year (±2 months), 2 years (±2 months), 3 years (±2 months) and annually thereafter (±3 months). The following parameters **(Table 68)** were measured throughout the study:

Table 68: Simplify® Cervical Artificial Disc IDE Study Assessment Schedule

Timepoint	Pre-op	Tx/ Discharge	6W	3M	6M	12M	24M	Post 24M
Informed Consent	X							
DDD assessment (MRI, CT or X-ray)	X							
Medical History & Physical Examination	X							
DXA	X							
AP & Lateral X-rays	X	X	X	X	X	X	X	X
Flexion & Extension X-rays	X		X	X	X	X	X	X
Lateral bending X-rays	X				X	X	X	X
MRI (or CT at Pre-op only); Investigational group only at 24M	X						X	
Radiographic Core Lab Assessments	X	X	X	X	X	X	X	X
Preoperative Patient Survey	X							
Dysphagia Handicap Index	X		X	X	X	X	X	X
NDI	X		X	X	X	X	X	X
SF-36 Health Survey	X				X	X	X	X
Neck and Arm Pain Questionnaires	X		X	X	X	X	X	X
Foraminal Compression Test	X		X	X	X	X	X	X
Physician Perception of Results			X	X	X	X	X	X
Neurologic Exam	X	X	X	X	X	X	X	X
Gait Assessment	X		X	X	X	X	X	X
Medications	X		X	X	X	X	X	X
Work Status	X		X	X	X	X	X	X
Treatment Assessments		X						
Postoperative Subject Survey			X	X	X	X	X	X
Health Economic Data		As available						
AE Assessment	N/A	As needed						
Study Completion/ Termination	N/A	N/A	As needed					

Clinical Endpoints

The effectiveness of the Simplify® Cervical Artificial Disc was assessed using a composite endpoint, as described below. Effectiveness was evaluated by assessing improvement in the Neck Disability Index (NDI), neck and arm pain questionnaires, and quality of life using the short-form questionnaire (SF-36), work status, as well as patient satisfaction of the Simplify® Cervical Artificial Disc group compared to the historical ACDF control group. Similar criteria were used to measure success in both groups.

The safety of the Simplify® Cervical Artificial Disc was assessed by comparison to the historical ACDF control group with respect to the nature and frequency of AEs (overall and in terms of severity and relationship to the implant), subsequent index level surgical procedures and maintenance or improvement in neurological status.

Primary Endpoints

The study hypothesis was that the Month 24 (i.e., 24 months post-operatively) composite clinical success (CCS) rate of the two-level Simplify® Cervical Artificial Disc would be no worse than conventional two-level ACDF when success is evaluated at Month 24 in patients with intractable radiculopathy (arm pain and/or a neurological deficit) with neck pain or myelopathy due to abnormalities localized to the levels of the two contiguous disc spaces at two contiguous levels from C3 to C7 that is unresponsive to conservative management or have presence of progressive symptoms or signs of nerve root/spinal cord compression.

Individual success for both the investigational and control groups was defined as:

- Neck Disability Index (NDI) score improvement of at least 15 points (out of 100) from as compared to baseline at month 24;
- Maintenance or improvement in neurological status at Month 24[8];
- No serious adverse event (SAE) classified as implant associated or implant/surgical procedure associated within 24 months of index procedure; and
- No additional surgical procedure classified as a “failure” within 24 months of index procedure.

Device failure was defined as breakage, migration, or mechanical failure of the components.

Overall success was determined based on data collected during the initial 24 months of follow-up. Each element of the neurological study exam was evaluated for maintenance or improvement.

All secondary index surgeries were classified as failures.

[8] Maintenance or improvement in neurological status was based on motor, sensory, and myelopathic gait assessments.

Per the FDA Guidance for the Preparation of IDEs for Spinal Systems, the following definitions applied:

- Reoperation - any surgical procedure at the index level(s) that *does not involve* modification, addition or removal of any components of the device and is not considered a removal, revision, or supplemental fixation.
- Revision – any procedure in the postoperative or follow-up period that adjusts or in any way modifies either one or both of the original implant configurations (e.g., adjusting the position of the original configuration, removal with replacement with same type of study implant).
- Removal – a procedure that removes one or more components of the original implant configuration without replacement with the same type of trial implant.
- Supplemental fixation – a procedure at the index level(s) in which additional spinal devices not approved as part of the protocol are placed.
- Other – any additional surgical procedure not classified as a removal, revision, supplemental fixation, or reoperation.

Secondary Endpoints

Secondary endpoints, measured in both groups (except as noted), included:

- Clinically significant improvement in one or more radicular symptoms or myelopathy at each post-operative timepoint compared to baseline for the investigational two-level Simplify® Cervical Artificial Disc and the two-level historical ACDF control group. The data collected reflected the number of patients who improved (numbers were stratified to reflect clinical improvement), who remain unchanged, and who deteriorated at each study timepoint.
- These endpoints were graded and defined as follows:
    - Pain questionnaires were used to evaluate each of the following pain locations:
        - Neck pain
        - Arm pain
        - Left arm pain (investigational group only);
        - Right arm pain (investigational group only);
    - Motor status - A change of one or more grade levels in muscle strength was regarded as clinically significant.
    - Sensory status - Sensation was graded as normal or abnormal (diminished or absent). Any changes from abnormal to normal or absent to diminished were regarded as clinically significant improvement.[9]
- Time to recovery (earliest time at which a minimum 15-point (out of 100) NDI improvement is reached).

[9] Hacker *et al.*, *supra* note 7, at 2648; Aids to the Investigation of Peripheral Nerve Injuries (UK Medical Research Council, War Memorandum No. 7 (2d ed. Rev. 1943).

- Disc height at each post-operative timepoint compared to baseline (6 weeks). Both levels had to be a disc height success to claim success for overall disc height. Disc height success for each level is based on either the anterior or posterior measurements meet the following criterions:

  Postoperative Height – 6 Week Postoperative Height ≥-2mm

- Adjacent level deterioration at 24 months compared to baseline for the investigational group.
- Displacement or migration of the device for the investigational group; only a change of >3 mm was considered significant due to the margin of error in radiographic determination of displacement distances.
- Return to work status post-operatively.
- Patient satisfaction and perceived effect at each applicable postoperative timepoint. Success for each of the three satisfaction questions was defined as either a "Definitely True" or "Mostly True" response. Success for the perceived effect question was defined as either a "Completely Recovered," "Much Improved," or "Slightly Improved" response.
- Health Survey (SF-36) at each applicable postoperative timepoint compared to baseline. Success was expressed in terms of the PCS (physical component summary) and MCS (mental component summary) scores and was defined as a maintenance or improvement in status postoperatively as compared to the preoperative condition. To be classified as a success for each component summary, the following criteria must be met:

  PCSPostop - PCSPreop ≥0
  MCSPostop - MCSPreop ≥0

- Dysphagia Handicap Index (DHI scale) at each applicable postoperative timepoint compared to baseline for the investigational group.
- Facet deterioration at 24 months compared to baseline for the investigational group.
- Adjacent Level Motion (Stability) was compared at each applicable postoperative timepoint to baseline.
- Results at each applicable postoperative timepoint were categorized by the physician's perception of the subject's condition (excellent, good, fair, or poor).
- Gait assessment at each applicable timepoint compared to baseline. This was based on Nurick's classification. Success was defined as maintenance or improvement in the postoperative status as compared to the preoperative condition:

  Preoperative Score – Postoperative Score ≥0

2. Accountability of PMA Cohort

One-hundred eighty-two (182) subjects were enrolled in the Simplify® Cervical Artificial Disc population. An additional 18 Simplify® Cervical Artificial Disc subjects were training subjects for total 200 investigational subjects. The historical ACDF control population included 188 subjects.

The 370 available subjects (182 Simplify® Cervical Artificial Disc (excluding training subjects) and 188 historical ACDF control) were assessed via the PS sub-classification sequential model-building process. After applying a sequential heuristic for PS modeling, all 182 randomized Simplify® Cervical Artificial Disc and 170 historical ACDF control subjects were retained in the final PS designed sample.[10] Inclusion into a PS subclass is the observational study analogue to randomized treatment allocation. When accounting for the PS design, there was excellent balance across all considered baseline covariates. For subjects at Month 24, the follow-up rates for expected due subjects was 97% for Simplify® Cervical Artificial Disc subjects and 84% for the PS Selected historical ACDF control subjects. With regards to CCS evaluable follow up, there were 173 Simplify® Cervical Artificial Disc subjects and 145 historical ACDF control subjects at 24 months, resulting in an overall follow-up rate of 95.1% (173/182) and 85.3% (145/170) for the Simplify® Cervical Artificial Disc and historical ACDF control subjects, respectively.

The subject accountability for Month 12 and Month 24 clinical evaluations is presented in **Table 69** and **Figure 4**.

[10] Maislin G and Rubin DB. Design of Non-Randomized Medical Device Trials Based on Sub-Classification Using Propensity Score Quintiles, Topic Contributed Session on Medical Devices. Proceedings of the Joint Statistical Meetings 2010, pg 2182-2196.

Table 69: Subject Accounting Summary (Primary Analysis Population)

	Month 12		Month 24	
	I	C	I	C
Accounting				
(1) Theoretical follow-up	182	170	181	170
(2) Cumulative Death	0	0	2	1
(3a) Intra-Op Deviations	1	4	1	4
(3b) Cumulative SSI Failures	2	11	4	14
(4) Not Yet Overdue	0	0	0	0
(5) Deaths+SSI failures+Intra-Op Deviations among theoretically due	3	15	7	19
(6) Expected Due [(6)=(1)-(4)-(5)]	179	155	174	151
(7) SSI failures+Intra-Op Deviations among theoretically due	3	15	5	18
(8) Expected due+SSI failures+Intra-Op Deviations among theoretically Due [(8)=(6)+(7)]	182	170	179	169
All Evaluated Accounting (Actual[B]) Among Expected Due Procedures				
(9) Procedures with any clinical data in interval†	177	136	168	127
(10) Visit Compliance (%)	99%	88%	97%	84%
(11) Change in NDI	177	136	168	127
(12) Neuro evaluations	177	136	166	127
(13) Composite Clinical Success (CCS)			168	127
(14) Actual[B] %Follow-up for CCS			97%	84%
Within Window Accounting (Actual[A]) Among Expected Due Procedures				
(15) Procedures with any clinical data in interval†	173	129	158	109
(16) Visit Compliance (%)	97%	83%	91%	72%
(17) Change in NDI	173	129	158	109
(18) Neuro evaluations	173	129	157	109
(19) Composite Clinical Success (CCS)			158	109
(20) Actual[A] %Follow-up for CCS			91%	72%
Composite Study Success				
(21) Composite Clinical Success (CCS)			173	145
(22) %Follow-up for CCS			95.1%	85.3%

†Defined as Change in NDI or available Neuro motor status.
Source: Tables Follow-up Compliance.sas; Analyzed: 09NOV2020

Actual[A]: Patients with complete data for each endpoint, within window.

Actual[B]: Patients with any follow-up data reviewed or evaluated by investigator ("all evaluated" accounting).

(1) Theoretical follow-up: The theoretical follow-up is the number of devices at two levels that would have been examined if all patients returned on the exact anniversary of their respective initial surgery dates. The date of database closure for these analyses was November 3, 2020. All subjects were theoretically due for Month 12 and Month 24 follow-up at the date of database closure, with the exception of one subject that was theoretically due on November 12, 2020 and missed the 24 Month visit.

(2) Cumulative deaths: Cumulative deaths up to the date of the exact anniversary defining the current interval. Deaths occurring after the exact anniversary are recorded in the next interval.

(3a) Intra-Op Deviations: Subjects who were to be treated with Simplify® Cervical Artificial Disc but converted to alternate treatment intra-operatively. Intra-operative deviation subjects are

considered a treatment failure in the CCS primary endpoint calculation and censored at day 0 for SSI and device survivorship. In the Simplify® Cervical Artificial Disc population, there was one subject who was enrolled to be treated with Simplify® Cervical Artificial Disc, but at time of surgery, the surgeon identified a large flowing osteophyte at one level that prevented adequate placement of a TDR as too much bone had to be removed. The surgeon proceeded with a fusion at that level and a commercially available TDR at the other level. In the control study, four subjects received a different fusion device. In one case, the patient was very small in stature and the control plate was too wide; in the other three cases, the investigators deviated from the protocol requirements. Since these intra-op deviations do not meet the definition of an SSI, they are accounted for separately. These five subjects were recorded as intra-operative deviations and are accounted for in Figure 4.

(3b) Cumulative SSI Failures: Failures are defined as any result that removes the patient from further evaluation of effectiveness, that is, these Failures are "***terminal failures***". As per FDA Guidance (2004), failure includes SSIs categorized as reoperations, revisions, removals, or supplemental fixation. It also includes other severe AEs or other parameters that would define the device as ineffective or unsafe from that point on. Failures are counted up to the date of the exact anniversary defining the current interval. Terminal failures occurring after the exact anniversary are recorded in the next interval. Terminal failures on this row do not include radiographic failure since radiographic failure does not remove a subject from the study. It also does not include clinical failures determined on the basis of clinical scores such NDI, Neck and Arm Pain Questionnaire, or deteriorating neurological status because these types of failure do not remove the patient from further follow-up. Although the cumulative number of failures is recorded on this row, only failures among devices that are theoretically due for that interval are subtracted from theoretically due to determine the number expected due for clinical indices.

(4) Not Yet Overdue: Includes subjects whose surgical anniversary has occurred; however, clinical data has not yet been collected (i.e., NDI or Neck and Arm Pain Questionnaire is currently unavailable) but the subject is still in the protocol specified follow-up window. Such subjects may not yet be observed and so follow-up compliance estimates account for this by removing such subjects from the denominator as well as from the numerator when determining compliance ratios. There are no subjects Not Yet Overdue for Month 24 at the time of this database lock.

(5) Deaths + SSI Failures + Intra-Op Deviations among theoretically due: This row records the sum of deaths, SSI Failures, and Intra-Op Deviations among those theoretically due for follow-up according to the exact anniversary of the scheduled follow-up visit. Only deaths, SSI Failures, and Intra-Op Deviations among procedures that are theoretically due for that interval are subtracted from theoretically due to determine the number expected due for clinical index evaluation.

(6) Expected Due for clinic visit: This row is the number of subjects expected for a given time interval. These include the theoretical number of subjects who are due to be evaluated, less the number of subjects who died or who were considered failures by that time interval and less the subjects in the "Not yet overdue" category. **Expected = Theoretical - [Deaths + Failures + Not yet overdue]** where the counts of the numbers of Deaths, Failures, and Not yet overdue are determined from among the theoretically due subjects. At the time of database lock, no subjects are Not Yet Overdue. This row serves as denominator for evaluation % follow-up for clinical indices (e.g., NDI). The Expected row includes subjects lost to follow-up, and major protocol violations are included in the expected group for all timepoints.

(7) SSI Failures + Intra-Op Deviations among theoretical due: SSI failures and intra-op deviations among theoretically due is the count of theoretically due Failures that need to be "added back" to the number of expected due to serve as the correct denominator for CCS counts when determining CCS follow-up compliance.

(8) Expected due + SSI Failures + Intra-Op Deviations among theoretical due: Expected due plus theoretical due Failures is computed by adding expected due in row **(6)** to the number of cumulative Failures among theoretically due devices in row **(7)**. This row serves as the denominator for composite clinical success (CCS) outcomes since CCS status is known for subjects with a Failure as defined in row **(3)**.

(9) and (15) Procedures with any clinical data in interval: These rows indicate the number of subjects with any clinical data that report a change in NDI or neurological status for all evaluated subjects among expected due subjects **(9)** and for all subjects that are within window among expected due subjects **(15)**.

(10) and (16) Visit Compliance (%): These rows indicate the percentage of subjects compliant with the specified visit scheduled for all evaluated subjects among expected due subjects **(10)** and for all subjects that are within window among expected due subjects **(16)**.

(11) and (17) Change in NDI: These rows indicate the number of subjects reporting a change in NDI for all evaluated subjects among expected due procedures **(11)** and for all subjects that are within window among expected due procedures **(17)**.

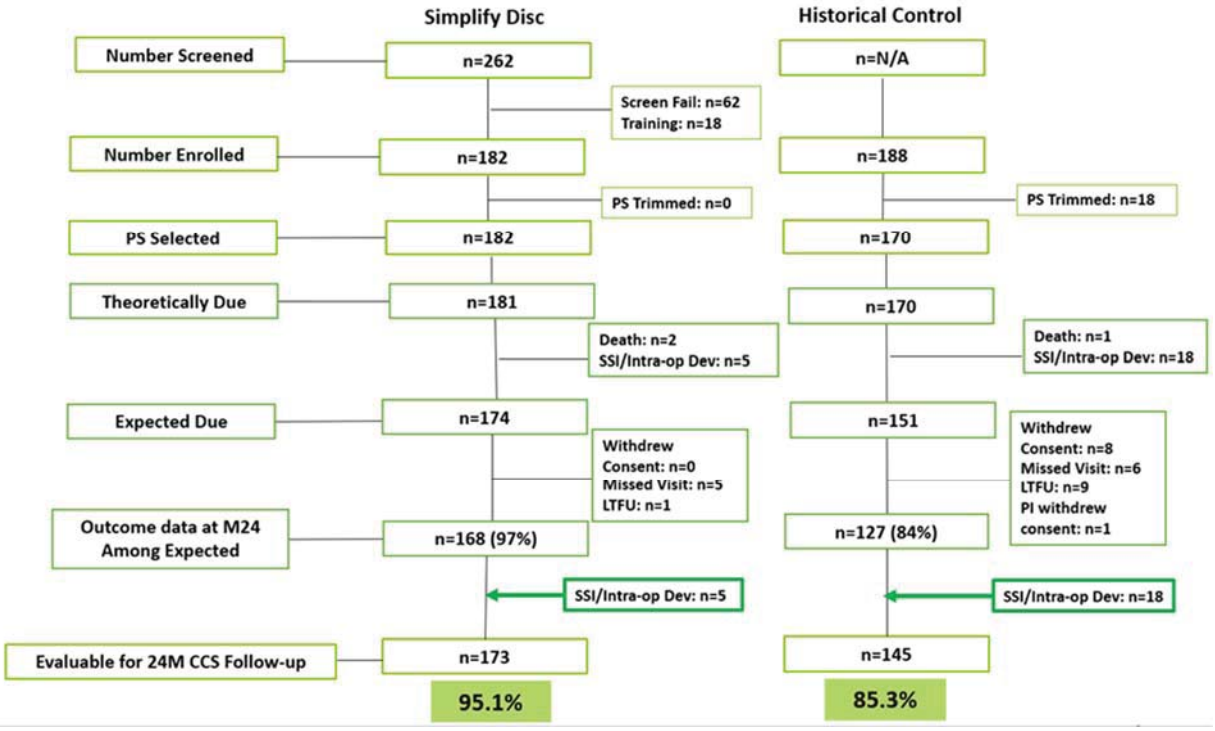
(12) and (18) Neuro evaluations: These rows indicate the number of subjects reporting a change in neurological status for all evaluated subjects among expected due procedures **(12)** and for all subjects that are within window among expected due procedures **(18)**.

(13) and (19) Composite Clinical Success: These rows indicate the number of subjects meeting clinical composite success for all evaluated subjects among expected due procedures **(13)** and for all subjects that are within window among expected due procedures **(19)**.

(14) and (20) Actual Follow-up for CCS: These rows indicate the percentage of subjects with follow-up data available used to evaluate CCS for all evaluated subjects among expected due procedures **(14)** and for all subjects that are within window among expected due procedures **(20)**.

(21) and (22) Composite Clinical Success (CCS): These rows indicate the number **(21)** and percentage (**22)** of subjects with observed data available to evaluate CCS among all PS Selected subjects in the Primary Analysis group

Figure 4: Subject Accountability Tree



3. Study Population Demographics and Baseline Parameters

After adjusting for PS subclass, demographic data showed that the treatment groups were well-balanced and no statistically significant differences were noted in the demographic characteristics and categorical values. The mean baseline pre-operative assessments for NDI, Neck and Arm Pain Questionnaire, SF-36 and baseline radiographic parameters were also similar between treatment groups. There was no significant difference between groups for all clinical baseline parameters (**Table 70** through **Table 72**).

Table 70: Summary of Demographic and Baseline Continuous Variables (Clinical) (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
All																
Age (years)	182	49.25	9.39	49.17	25.14	71.54	170	47.45	7.89	48.00	25.00	69.00	0.943	-0.07	-2.10	1.95
BMI (kg/m^2)	182	29.30	6.04	28.81	19.00	56.88	170	28.44	4.97	28.06	17.97	43.40	0.990	0.01	-1.31	1.33
Height (inches)	182	67.32	3.95	67.00	57.00	76.00	170	67.61	4.01	67.00	60.00	78.00	0.753	-0.15	-1.11	0.80
Weight (lbs)	182	188.97	41.11	185.00	98.00	311.00	170	185.21	37.37	185.00	106.00	300.00	0.828	-1.03	-10.41	8.34
Male																
Age (years)	87	51.01	10.08	50.52	29.49	71.54	81	48.12	7.84	49.00	29.00	66.00	0.683	0.66	-2.50	3.81
BMI (kg/m^2)	87	29.15	4.98	28.24	20.36	45.61	81	28.59	4.35	28.69	17.97	39.58	0.605	0.44	-1.23	2.11
Height (inches)	87	70.51	2.61	71.00	63.00	76.00	81	70.83	2.63	71.00	64.00	78.00	0.847	0.09	-0.84	1.02
Weight (lbs)	87	206.03	35.83	200.00	130.00	300.00	81	203.96	32.99	200.00	140.00	300.00	0.599	3.28	-9.02	15.58
Female																
Age (years)	95	47.63	8.44	48.01	25.14	68.79	89	46.84	7.93	47.00	25.00	69.00	0.834	-0.28	-2.91	2.35
BMI (kg/m^2)	95	29.43	6.90	29.26	19.00	56.88	89	28.30	5.50	27.25	18.48	43.40	0.857	-0.18	-2.20	1.83
Height (inches)	95	64.41	2.43	64.00	57.00	72.00	89	64.67	2.51	65.00	60.00	70.00	0.755	-0.13	-0.95	0.69
Weight (lbs)	95	173.34	39.53	172.00	98.00	311.00	89	168.13	32.77	165.00	106.00	260.00	0.722	-2.13	-13.92	9.66
Clinical Scores																
Neck Disability Index	182	58.65	14.31	58.00	30.00	88.00	170	53.65	14.52	54.00	30.00	92.00	0.699	0.64	-2.61	3.89
Neck Pain	173	16.91	2.54	17.00	8.00	20.00	170	16.33	2.63	17.00	8.00	20.00	0.610	0.16	-0.45	0.76
Neck Pain Frequency	173	8.97	1.46	10.00	3.00	10.00	170	8.68	1.57	9.00	3.00	10.00	0.768	0.05	-0.31	0.41
Neck Pain Intensity	173	7.95	1.60	8.00	2.00	10.00	170	7.65	1.74	8.00	2.00	10.00	0.608	0.10	-0.29	0.50
Arm Pain	173	15.68	3.48	16.00	2.00	20.00	170	14.66	3.92	15.00	0.00	20.00	0.718	0.16	-0.71	1.02
Arm Pain Frequency	173	8.16	1.96	9.00	1.00	10.00	170	7.69	2.27	8.00	0.00	10.00	0.865	0.04	-0.45	0.54
Arm Pain Intensity	173	7.51	1.83	8.00	1.00	10.00	170	6.98	2.19	7.00	0.00	10.00	0.632	0.12	-0.36	0.59
SF36 PCS	173	31.41	7.65	30.76	11.28	58.90	170	32.97	7.13	33.15	14.00	52.43	0.916	-0.09	-1.84	1.65
SF36 MCS	173	41.22	12.31	41.01	10.41	72.13	170	43.15	12.29	44.70	14.54	66.67	0.186	-2.00	-4.97	0.97

*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Baseline Demo.sas; Analyzed: 25AUG2020

Table 71: Summary of Baseline Categorical Variables (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Any Narcotic (weak or strong)	173	56	32.4%	170	69	40.6%	0.193	-7.7%	-18.6%	3.2%
Neurological Sensory Deficit	179	84	46.9%	170	61	35.9%	0.675	2.6%	-8.8%	14.0%
Neurolgoical Motor Deficit	182	59	32.4%	170	75	44.1%	0.727	2.1%	-9.2%	13.4%
Work Status = Employed	173	112	64.7%	170	103	60.6%	0.588	3.2%	-7.8%	14.2%

*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Baseline additional.sas; Analyzed: 18FEB2021

** Narcotic data presented is within the past 8 hours of preop visit.

Table 72 summarizes the available race and ethnicity data. Please note, complete race and ethnicity data were not collected in the historical ACDF control arm.

Table 72: Summary of Baseline Categorical Variables – Race and Ethnicity (Primary Analysis Population)

	Simplify Disc			ACDF			
	N	n	%	N	n	%	p*
Race	182			170			0.931
Caucasian		170	93.4%		157	92.4%	
Black		6	3.3%		6	3.5%	
Asian		1	0.6%		3	1.8%	
Hispanic					3	1.8%	
Other		5	2.8%		1	0.6%	
Ethnicity	182						
Hispanic or Latino		5	2.7%				
Not Hispanic or Latino		177	97.3%				

*p-value adjusted for PS subclass using two-way analysis of variance with race dichotomized as Caucasian vs. Non-Caucasian.
Source: Tables Baseline Demo.sas; Analyzed: 27OCT2020

The radiographic findings used to qualify a subject for enrollment are provided with post-hoc nominal measures of significance in **Table 73**.

Table 73: Summary of Baseline Variables – Radiographic Data (Primary Analysis Population)

		Simplify Disc			ACDF		
		N	n	%	N	n	%
Superior Level	Herniated Disc	182	161	88.5%	170	142	83.5%
	Osteophyte Formation	182	113	62.1%	170	121	71.2%
Inferior Level	Herniated Disc	182	158	86.8%	170	143	84.1%
	Osteophyte Formation	182	115	63.2%	170	113	66.5%

Source: Radiographic Inclusion.sas; Analyzed 26OCT2020

Table 74 provides a summary of the operative variables of operative time, blood loss, and length of hospital stay.

Table 74: Summary of Operative Continuous Variables (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Operative Time (minutes)	182	100.62	26.84	98.50	48.00	180.00	170	100.02	44.44	93.50	39.00	296.00	0.868	0.73	-7.92	9.38
Blood loss (cc)	182	44.66	44.36	25.00	0.00	300.00	170	56.29	46.99	50.00	0.00	250.00	0.169	-7.62	-18.49	3.26
Length of hospital stay	182	0.59	0.77	1.00	0.00	7.00	170	1.31	0.95	1.00	0.00	8.00	<.001	-0.80	-1.01	-0.60

*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Intra-op details.sas; Analyzed: 19FEB2021

The mean, standard deviations from the mean, median, minimum, and maximum values are presented for each variable. There were no significant differences between groups in operative time or blood loss. A statistically significant difference was seen between the two groups for length of hospital stay favoring the investigational group ($p<0.001$); however, this difference in length of hospital stay is likely attributable to the fact that a majority of the investigational group procedures were performed at out-patient sites. Due to the differences in surgical sites between the

investigational group and historical ACDF control arm, no clinical meaningful benefit can be derived from the length of hospital stay.

Table 75 through **Table 77** provides a summary of additional intraoperative surgical variables for subjects treated in the study for both the investigational and Control groups, where applicable. Variables summarized include operative level, status of the posterior ligament, and device size used.

Table 75. Summary of Index Level

	Simplify		ACDF	
	n	%	n	%
C3/4-C4/5	5	3%	2	1%
C4/5-C5/6	44	24%	40	24%
C5/6-C6/7	133	73%	128	75%
Source: Tables Intra-op details.sas; Analyzed: 25AUG2020				

Table 76: Summary of Posterior Ligament Cut (Simplify Subjects Only)

	Superior		Inferior	
	n	%	n	%
No	2	1%	2	1%
Yes	180	99%	180	99%
Source: Tables Intra-op details.sas; Analyzed: 25AUG2020				

Table 77: Summary of Device Size (Simplify Subjects Only)

	Superior		Inferior	
	n	%	n	%
SM-4	35	19%	23	13%
SM-5S	4	2%	4	2%
SM-6S	1	1%	1	1%
MD-4	71	39%	65	36%
MD-5	11	6%	12	7%
MD-5L	14	8%	20	11%
MD-6	1	1%	1	1%
LG-5	20	10%	15	9%
LG-5L	19	10%	33	18%
LG-6	3	2%	6	3%
LG-6L	2	1%	1	1%
Source: Tables Intra-op details.sas; Analyzed: 23OCT2020				

*S indicates small core if small and large core options were available; L indicates lordotic

As shown in **Table 75**, majority of subjects in both groups were treated at C5/C6 and C6/C7 levels. Additionally, as shown in **Table 76**, a majority of subjects in the investigational group also had their posterior longitudinal ligament cut. **Table 77** summarizes the device size used for the investigational subjects. The smallest device height, 4mm height, accounted for 54% of the devices implanted in Simplify® Cervical Artificial Disc subjects.

4. Safety and Effectiveness Results

Safety Results

Please note: There are potential differences in AE data reporting and collection between historical ACDF and prospective Simplify® Cervical Artificial Disc study arms, which may account for group differences in the AE rates exhibited between the Simplify® Cervical Artificial Disc and ACDF cohorts.

Table 78 presents a summary of AE rates between the Simplify® Cervical Artificial Disc cohort and the historical ACDF control cohort. It is important to note that implant associated events were determined to only have potential for causal relationship to implant, and vice versa for procedure associated events. Implant/procedure associated events were used in cases where it was undetermined if the event was implant or procedure associated, or it was determined it was both. Lastly, treatment associated is the sum of all implant associated, procedure associated and implant / procedure associated events. Overall, the Simplify® Cervical Artificial Disc cohort experienced a numerically lower number of AEs (250 events in 121 subjects) than the historical ACDF control group (574 events in 155 subjects).

Table 78: Comparisons of Summary AE Rates between Simplify® Cervical Artificial Disc and ACDF Groups (Primary Analysis Set through Day 790)

	Simplify Disc (N= 182)			ACDF (N= 170)		
	Events	Subjs	%|	Events	Subjs	%|
Adverse Events						
All	250	121	66.5%	574	155	91.2%
Treatment Associated	32	28	15.4%	91	61	35.9%
Implant Associated	8	7	3.8%	6	6	3.5%
Procedure Associated	18	16	8.8%	62	40	23.5%
Implant/Procedure Associated	6	6	3.3%	23	22	12.9%
Serious Adverse Events						
All	41	32	17.6%	85	62	36.5%
Treatment Associated	8	8	4.4%	26	22	12.9%
Implant Associated	2	2	1.1%	1	1	0.6%
Procedure Associated	2	2	1.1%	14	13	7.6%
Implant/Procedure Associated	4	4	2.2%	11	11	6.5%
AE by Severity						
Mild	47	39	21.4%	157	90	52.9%
Moderate	159	87	47.8%	336	134	78.8%
Severe	38	30	16.5%	76	52	30.6%
Life Threatening	6	6	3.3%	5	5	2.9%
SAE by Severity						
Mild	0	0	0.0%	2	2	1.2%
Moderate	4	4	2.2%	15	14	8.2%
Severe	31	24	13.2%	63	47	27.6%
Life Threatening	6	6	3.3%	5	5	2.9%
Death						
All	2	2	1.1%	1	1	0.6%

|Percentage of subjects experiencing specific event;
Source: Tables Safety - AE Summary.sas; Analyzed: 17DEC2020

Counts and percentages of subjects with specific AEs are presented in **Table 79** and counts of AEs by timecourse are presented in **Table 80**. The most commonly occurring events reported to have occurred in the Simplify® Cervical Artificial Disc cohort include cervical radiculopathy (14.3% - 26/182), lumbar radiculopathy (13.7% - 25/182), and pain with no narcotic given (12.6% - 23/182). In the historical ACDF control cohort, the most commonly reported AEs include accidental trauma (22.9% - 39/170), cervical radiculopathy (20% - 34/170), and pain with no narcotic given (20% - 34/170).

Table 79: Counts and Percentages of Subjects with Specific AEs – (Primary Analysis Population through Day 790)

	Simplify Disc (N= 182)			ACDF (N= 170)		
	Events	Subjs	%|	Events	Subjs	%|
All Events	250	121	66.5%	574	155	91.2%
Soft tissue damage	4	3	1.6%	2	1	0.6%
Death	2	2	1.1%	1	1	0.6%
Infection localized to cervical surgical site	2	2	1.1%	3	3	1.8%
Hoarseness	3	3	1.6%	1	1	0.6%
Embolism	1	1	0.5%	1	1	0.6%
Dental Pain	2	2	1.1%	3	3	1.8%
Thoracic Radiculopathy	1	1	0.5%	2	2	1.2%
Drug allergy (administered)	2	2	1.1%	2	2	1.2%
Cardiac Event	2	2	1.1%	3	3	1.8%
Dysphonia	1	1	0.5%	2	2	1.2%
Compressive Neuropathy	12	12	6.6%	18	18	10.6%
Lumbar Radiculopathy	26	25	13.7%	30	29	17.1%
Cancer	1	1	0.5%	3	3	1.8%
Psychological Illness	1	1	0.5%	9	8	4.7%
Hypertension	3	3	1.6%	5	5	2.9%
Infection (all other infections-NOT at cervical surgical site)	19	15	8.2%	22	19	11.2%
Difficulty with urination	2	2	1.1%	6	5	2.9%
Nonunion/pseudoarthrosis	1	1	0.5%	12	12	7.1%
Other	8	8	4.4%	15	14	8.2%
Dermatitis/Skin allergy	2	2	1.1%	10	10	5.9%
Cervical Radiculopathy	30	26	14.3%	39	34	20.0%
Pain (narcotic given)	6	6	3.3%	14	13	7.6%
Spasm	3	3	1.6%	13	11	6.5%
Gastrointestinal complications including ileus, nausea and vomiting	7	7	3.8%	22	17	10.0%
Headache	9	9	4.9%	24	23	13.5%
Development of DDD at adjacent levels	1	1	0.5%	10	10	5.9%
Inflammation	23	21	11.5%	35	31	18.2%
Numbness - increased from pre-op or prior visit	4	4	2.2%	14	14	8.2%
Dysphagia	7	7	3.8%	17	17	10.0%
Low back pain (no narcotic given)	1	1	0.5%	14	14	8.2%
Appendicular arthritis	7	6	3.3%	34	27	15.9%
Low back pain (narcotic given)	1	1	0.5%	13	13	7.6%
Pain (no narcotic given)	25	23	12.6%	39	34	20.0%
Accidental trauma	21	19	10.4%	46	39	22.9%
Hematoma or seroma	4	4	2.2%	0	0	0.0%
Vertebral fracture	2	2	1.1%	0	0	0.0%
Blood loss (greater than 500ml)	1	1	0.5%	0	0	0.0%
Otitis Media	1	1	0.5%	0	0	0.0%
Surgery at a location other than the spine	1	1	0.5%	0	0	0.0%
Delayed wound healing	1	1	0.5%	0	0	0.0%
Neck Stiffness	0	0	0.0%	9	9	5.3%
Sleep apnea	0	0	0.0%	9	8	4.7%
Non-Infectious pulmonary disorder	0	0	0.0%	8	8	4.7%
Allergic Rhinitis	0	0	0.0%	6	6	3.5%
Pneumonia	0	0	0.0%	5	5	2.9%
Sore throat	0	0	0.0%	5	5	2.9%
Diabetes	0	0	0.0%	5	5	2.9%
Swelling (edema)	0	0	0.0%	4	4	2.4%
Implant/Joint Noise	0	0	0.0%	3	3	1.8%
Anemia	0	0	0.0%	3	3	1.8%
Renal dysfunction	0	0	0.0%	3	3	1.8%
Sleep disorder (excluding sleep apnea)	0	0	0.0%	3	3	1.8%
Altered mental status/altered level of consciousness	0	0	0.0%	3	3	1.8%
Thoracic Disc Disease	0	0	0.0%	3	3	1.8%
Gait disturbance	0	0	0.0%	2	2	1.2%
Thrombosis	0	0	0.0%	2	2	1.2%
Weakness - increased from pre-op or prior visit	0	0	0.0%	2	2	1.2%
Myelopathy	0	0	0.0%	2	2	1.2%
Cerebrospinal fluid leakage	0	0	0.0%	1	1	0.6%
Coordination abnormalities	0	0	0.0%	1	1	0.6%
Dural injury	0	0	0.0%	1	1	0.6%
Implant breakage	0	0	0.0%	1	1	0.6%
Implant collapse or subsidence	0	0	0.0%	1	1	0.6%
Lymphadenopathy	0	0	0.0%	1	1	0.6%
Spondylosis acquista	0	0	0.0%	1	1	0.6%
Tingling - increased from pre-op or prior visit	0	0	0.0%	1	1	0.6%
Vocal cord paralysis	0	0	0.0%	1	1	0.6%
Stroke	0	0	0.0%	1	1	0.6%
Atelectasis	0	0	0.0%	1	1	0.6%
Injury to muscles or organs	0	0	0.0%	1	1	0.6%
Opioid Dependency	0	0	0.0%	1	1	0.6%

|Percentage of subjects experiencing specific event;
Source: Tables Safety - All AEs.sas; Analyzed: 17DEC2020

Table 80: Counts of Specific AEs by Time of Occurrence – (Primary Analysis Population through Day 790) (I = Simplify® Cervical Artificial Disc, C = ACDF)

	Days Post-Op																	
	Missing		0-2		2-30		30-90		90-180		180-365		365-730		730-790		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
All Events	0	0	12	45	30	72	28	76	38	92	71	105	70	155	1	29	250	574
Cervical Radiculopathy	0	0	0	4	3	11	3	7	6	6	10	5	8	6	0	0	30	39
Lumbar Radiculopathy	0	0	0	0	2	3	2	5	2	6	8	4	12	11	0	1	26	30
Pain (no narcotic given)	0	0	2	2	2	2	4	5	4	6	7	12	5	11	1	1	25	39
Inflammation	0	0	0	0	2	4	4	7	3	6	9	10	5	7	0	1	23	35
Accidental trauma	0	0	0	0	4	8	3	4	3	3	5	7	6	20	0	4	21	46
Infection (all other infections-NOT at cervical surgical site)	0	0	1	2	3	4	1	2	3	3	8	6	3	4	0	1	19	22
Compressive Neuropathy	0	0	0	1	1	3	0	1	2	3	4	1	5	8	0	1	12	18
Headache	0	0	0	2	2	4	0	6	3	3	2	3	2	3	0	3	9	24
Other	0	0	0	2	0	0	0	1	2	1	4	5	2	6	0	0	8	15
Dysphagia	0	0	2	4	2	1	0	5	0	1	1	1	2	4	0	1	7	17
Gastrointestinal complications including ileus, nausea and vomiting	0	0	0	4	1	2	1	1	2	2	0	2	3	9	0	2	7	22
Appendicular arthritis	0	0	0	0	0	2	1	1	1	7	3	11	2	12	0	1	7	34
Pain (narcotic given)	0	0	0	2	0	3	2	0	0	5	1	2	3	1	0	1	6	14
Hematoma or seroma	0	0	1	0	3	0	0	0	0	0	0	0	0	0	0	0	4	0
Numbness - increased from pre-op or prior visit	0	0	0	1	0	1	1	5	2	5	0	1	1	1	0	0	4	14
Soft tissue damage	0	0	0	0	0	0	0	0	0	0	1	0	3	1	0	1	4	2
Hoarseness	0	0	2	1	0	0	0	0	1	0	0	0	0	0	0	0	3	1
Spasm	0	0	0	1	0	4	0	2	0	2	2	1	1	1	0	2	3	13
Hypertension	0	0	0	1	0	0	0	0	0	0	2	2	1	2	0	0	3	5
Vertebral fracture	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	2	0
Cardiac Event	0	0	0	0	0	0	0	0	0	0	1	2	1	1	0	0	2	3
Difficulty with urination	0	0	2	2	0	2	0	0	0	1	0	0	0	0	0	1	2	6
Death	0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	2	1
Infection localized to cervical surgical site	0	0	0	0	1	2	1	0	0	1	0	0	0	0	0	0	2	3
Dermatitis/Skin allergy	0	0	0	2	1	2	0	0	0	1	1	1	0	3	0	1	2	10
Drug allergy (administered)	0	0	1	0	0	0	0	0	0	0	0	0	1	2	0	0	2	2
Dental Pain	0	0	0	0	2	0	0	0	0	1	0	0	0	2	0	0	2	3
Blood loss (greater than 500ml)	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Cancer	0	0	0	0	0	0	0	1	1	0	0	0	0	2	0	0	1	3
Development of DDD at adjacent levels	0	0	0	0	0	1	0	2	1	1	0	2	0	4	0	0	1	10
Dysphonia	0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	1	2
Otitis Media	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
Surgery at a location other than the spine	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Embolism	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	1	1
Psychological illness	0	0	0	1	0	0	0	1	0	0	0	1	1	5	0	1	1	9
Low back pain (narcotic given)	0	0	0	1	0	2	1	1	0	3	0	2	0	2	0	2	1	13
Low back pain (no narcotic given)	0	0	0	0	0	0	0	4	0	3	1	4	0	3	0	0	1	14
Nonunion/pseudoarthrosis	0	0	0	0	0	1	0	2	0	8	1	1	0	0	0	0	1	12
Thoracic Radiculopathy	0	0	0	0	1	0	0	0	0	0	0	0	0	2	0	0	1	2
Delayed wound healing	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
Cerebrospinal fluid leakage	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Coordination abnormalities	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Dural injury	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Gait disturbance	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	2
Implant breakage	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Implant collapse or subsidence	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Lymphadenopathy	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1
Pneumonia	0	0	0	2	0	1	0	0	0	0	0	1	0	1	0	0	0	5
Spondylosis acquista	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Thrombosis	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	2
Tingling - increased from pre-op or prior visit	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1
Vocal cord paralysis	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Weakness - increased from pre-op or prior visit	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	2
Implant/Joint Noise	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	1	0	3
Swelling (edema)	0	0	0	0	0	1	0	0	0	0	0	1	0	2	0	0	0	4
Stroke	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1
Atelectasis	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Injury to muscles or organs	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
Sore throat	0	0	0	0	0	1	0	3	0	0	0	0	0	1	0	0	0	5
Myelopathy	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	2
Sleep apnea	0	0	0	1	0	0	0	0	0	3	0	3	0	2	0	0	0	9
Anemia	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	0	0	3
Renal dysfunction	0	0	0	0	0	1	0	0	0	0	0	1	0	1	0	0	0	3
Sleep disorder (excluding sleep apnea)	0	0	0	1	0	0	0	0	0	0	0	1	0	1	0	0	0	3
Allergic Rhinitis	0	0	0	0	0	1	0	1	0	0	0	0	0	4	0	0	0	6
Altered mental status/altered level of consciousness	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	1	0	3
Diabetes	0	0	0	1	0	0	0	0	0	0	0	1	0	2	0	1	0	5
Non-Infectious pulmonary disorder	0	0	0	2	0	1	0	1	0	1	0	3	0	0	0	0	0	8
Neck Stiffness	0	0	0	0	0	0	0	2	0	4	0	1	0	2	0	0	0	9
Opioid Dependency	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1
Thoracic Disc Disease	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	0	3

Source: Tables Safety-AllAEs.sas; Analyzed: 17DEC2020

Implant-Associated AEs

There were eight events in seven subjects in the Simplify® Cervical Artificial Disc group and six events in six subjects in the historical ACDF control group that were determined to be implant associated. In the Simplify® Cervical Artificial Disc group, the implant-associated AE rate was 3.8% (7/182), with events categorized as dysphagia, cervical radiculopathy, pain, and hematoma or seroma. In the historical ACDF control group, the implant-associated AE rate was 3.5% (6/170), with the events categorized as dysphagia, cervical radiculopathy, implant/joint noise, implant breakage, and nonunion/pseudoarthrosis. Additional details regarding the implant-associated AEs are presented in **Table 81** below.

Table 81: Counts and Percentages of Subjects with Specific Implant Associated AE– (Primary Analysis Population through Day 790)

	Simplify Disc (N= 182)			ACDF (N= 170)		
	Events	Subjs	%	Events	Subjs	%
All Events	8	7	3.8%	6	6	3.5%
Dysphagia	4	4	2.2%	1	1	0.6%
Cervical Radiculopathy	1	1	0.5%	1	1	0.6%
Pain (no narcotic given)	2	2	1.1%	0	0	0.0%
Hematoma or seroma	1	1	0.5%	0	0	0.0%
Implant/Joint Noise	0	0	0.0%	2	2	1.2%
Implant breakage	0	0	0.0%	1	1	0.6%
Nonunion/pseudoarthrosis	0	0	0.0%	1	1	0.6%

|Percentage of subjects experiencing specific event;
Source: Tables Safety - Implant Associated.sas; Analyzed: 17DEC2020

Table 82 includes a timecourse of implant-associated AEs for all subjects in the study through post-operative day 790 by day of occurrence. As shown below, the majority of implant-associated events occurred between 0-30 days and 730-790 days for both groups.

Table 82: Implant Associated AEs (Timecourse) by Code (Primary Analysis Population through Day 790)

	Days Post-Op																	
	Missing		0-2		2-30		30-90		90-180		180-365		365-730		730-790		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
All Events	0	0	2	0	4	4	0	0	0	0	1	0	1	0	0	2	8	6
Dysphagia	0	0	2	0	2	0	0	0	0	0	0	0	0	0	0	1	4	1
Pain (no narcotic given)	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	2	0
Hematoma or seroma	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Cervical Radiculopathy	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1
Implant breakage	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Implant/Joint Noise	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	2
Nonunion/pseudoarthrosis	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1

Source: Tables Safety - Implant Associated.sas; Analyzed: 17DEC2020

Table 83 includes implant-associated AEs by severity for subjects in the Simplify® Cervical Artificial Disc group through post-operative day 790. As shown below, two events were mild in severity, four events were moderate, and two events were severe.

Table 83: All Implant-Associated AEs (Severity) by Code – (Simplify® Cervical Artificial Disc Group, N=182)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	2	25.0%	4	50.0%	2	25.0%	0	0.0%	8
Dysphagia	2	50.0%	0	0.0%	2	50.0%	0	0.0%	4
Pain (no narcotic given)	0	0.0%	2	100.0%	0	0.0%	0	0.0%	2
Hematoma or seroma	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Cervical Radiculopathy	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1

*Percentage of total events.

Source: Tables Safety - Implant Associated.sas; Analyzed: 17DEC2020

Table 84 includes implant-associated AEs by severity for subjects in the historical ACDF control group through post-operative day 790. As shown below, three events were mild in severity, two events were moderate, and one event was severe.

Table 84: All Implant-Associated AEs (Severity) by Code – (Historical ACDF Control Group, N=170)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	3	50.0%	2	33.3%	1	16.7%	0	0.0%	6
Implant/Joint Noise	1	50.0%	1	50.0%	0	0.0%	0	0.0%	2
Dysphagia	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Implant breakage	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Nonunion/pseudoarthrosis	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1
Cervical Radiculopathy	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1

*Percentage of total events.

Source: Tables Safety - Implant Associated.sas; Analyzed: 17DEC2020

Surgical Procedure-Associated AEs

Table 85 through **Table 88** present AEs that were determined by the CEC to be associated to the procedure.

Table 85 includes procedure-associated AEs by code for all subjects in the study through post-operative day 790. As shown below, sixteen (16) subjects in the Simplify® Cervical Artificial Disc group and 40 subjects in the historical ACDF control group had procedure-associated events. The most commonly occurring AEs categorized as procedure-associated in the Simplify® Cervical Artificial Disc cohort were hematoma/seroma (1.6% - 3/182), pain with no narcotic given (1.6% - 3/182), and infection (all other infections-NOT at cervical surgical site) (1.6% - 3/182). In the historical ACDF control cohort, the most commonly occurring AEs categorized as procedure-associated were dysphagia (5.3% - 9/170), cervical radiculopathy (3.5% - 6/170), pain with no narcotic given (2.4% - 4/170), and headache (2.4% - 4/170).

Table 85: Procedure Associated AEs by Code (Primary Analysis Population through Day 790)

	Simplify Disc (N= 182)			ACDF (N= 170)		
	Events	Subjs	%|	Events	Subjs	%|
All Events	18	16	8.8%	62	40	23.5%
Infection localized to cervical surgical site	2	2	1.1%	2	2	1.2%
Infection (all other infections-NOT at cervical surgical site)	3	3	1.6%	2	2	1.2%
Hoarseness	2	2	1.1%	1	1	0.6%
Dermatitis/Skin allergy	1	1	0.5%	2	2	1.2%
Pain (no narcotic given)	3	3	1.6%	4	4	2.4%
Dysphonia	1	1	0.5%	2	2	1.2%
Difficulty with urination	1	1	0.5%	2	2	1.2%
Hematoma or seroma	3	3	1.6%	0	0	0.0%
Drug allergy (administered)	1	1	0.5%	0	0	0.0%
Delayed wound healing	1	1	0.5%	0	0	0.0%
Dysphagia	0	0	0.0%	9	9	5.3%
Cervical Radiculopathy	0	0	0.0%	7	6	3.5%
Headache	0	0	0.0%	4	4	2.4%
Numbness - increased from pre-op or prior visit	0	0	0.0%	3	3	1.8%
Pain (narcotic given)	0	0	0.0%	3	3	1.8%
Pneumonia	0	0	0.0%	3	3	1.8%
Gastrointestinal complications including ileus, nausea and vomiting	0	0	0.0%	3	3	1.8%
Spasm	0	0	0.0%	2	2	1.2%
Cerebrospinal fluid leakage	0	0	0.0%	1	1	0.6%
Spondylosis acquista	0	0	0.0%	1	1	0.6%
Vocal cord paralysis	0	0	0.0%	1	1	0.6%
Weakness - increased from pre-op or prior visit	0	0	0.0%	1	1	0.6%
Other	0	0	0.0%	1	1	0.6%
Swelling (edema)	0	0	0.0%	1	1	0.6%
Atelectasis	0	0	0.0%	1	1	0.6%
Hypertension	0	0	0.0%	1	1	0.6%
Sore throat	0	0	0.0%	1	1	0.6%
Appendicular arthritis	0	0	0.0%	1	1	0.6%
Diabetes	0	0	0.0%	1	1	0.6%
Non-Infectious pulmonary disorder	0	0	0.0%	1	1	0.6%
Opioid Dependency	0	0	0.0%	1	1	0.6%

|Percentage of subjects experiencing specific event;
Source: Tables Safety - Procedure Associated.sas; Analyzed: 17DEC2020

Table 86 includes a timecourse of procedure-associated AEs for all subjects in the study through post-operative day 790 by day of occurrence. As shown below, the majority of procedure-associated events occurred between 0-90 days.

Table 86: Procedure Associated AEs (Timecourse) by Code (Primary Analysis Population through Day 790)

	Days Post-Op																	
	Missing		0-2		2-30		30-90		90-180		180-365		365-730		730-790		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
All Events	0	0	8	30	7	14	2	10	0	4	0	3	0	0	1	1	18	62
Hematoma or seroma	0	0	1	0	2	0	0	0	0	0	0	0	0	0	0	0	3	0
Pain (no narcotic given)	0	0	1	2	1	0	0	0	0	1	0	1	0	0	1	0	3	4
Infection (all other infections-NOT at cervical surgical site)	0	0	1	2	2	0	0	0	0	0	0	0	0	0	0	0	3	2
Hoarseness	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	2	1
Infection localized to cervical surgical site	0	0	0	0	1	2	1	0	0	0	0	0	0	0	0	0	2	2
Dysphonia	0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	1	2
Difficulty w ith urination	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	1	2
Dermatitis/Skin allergy	0	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	1	2
Drug allergy (administered)	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Delayed w ound healing	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
Cerebrospinal fluid leakage	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Dysphagia	0	0	0	4	0	1	0	4	0	0	0	0	0	0	0	0	0	9
Headache	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0	1	0	4
Numbness - increased from pre-op or prior visit	0	0	0	1	0	0	0	1	0	1	0	0	0	0	0	0	0	3
Pain (narcotic given)	0	0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0	3
Pneumonia	0	0	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0	3
Spondylosis acquista	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Vocal cord paralysis	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Weakness - increased from pre-op or prior visit	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Other	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Gastrointestinal complications including ileus, nausea and vomiting	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	3
Spasm	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	2
Sw elling (edema)	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Atelectasis	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Hypertension	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Sore throat	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Appendicular arthritis	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Cervical Radiculopathy	0	0	0	1	0	4	0	1	0	0	0	1	0	0	0	0	0	7
Diabetes	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Non-Infectious pulmonary disorder	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Opioid Dependency	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1

Source: Tables Safety - Procedure Associated.sas; Analyzed: 17DEC2020

Table 87 includes procedure-associated AEs by severity for subjects in the Simplify® Cervical Artificial Disc group through post-operative day 790. As shown below, there was one life-threatening procedure-associated event in the Simplify® Cervical Artificial Disc group which was identified as a hematoma or seroma.

Table 87: Procedure Associated AEs (Severity) by Code – (Simplify® Cervical Artificial Disc Group, N=182)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	3	16.7%	13	72.2%	1	5.6%	1	5.6%	18
Hematoma or seroma	1	33.3%	0	0.0%	1	33.3%	1	33.3%	3
Pain (no narcotic given)	1	33.3%	2	66.7%	0	0.0%	0	0.0%	3
Infection (all other infections-NOT at cervical surgical site)	1	33.3%	2	66.7%	0	0.0%	0	0.0%	3
Hoarseness	0	0.0%	2	100.0%	0	0.0%	0	0.0%	2
Infection localized to cervical surgical site	0	0.0%	2	100.0%	0	0.0%	0	0.0%	2
Dysphonia	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Difficulty w ith urination	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Dermatitis/Skin allergy	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Drug allergy (administered)	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Delayed w ound healing	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1

*Percentage of total events.

Source: Tables Safety - Procedure Associated.sas; Analyzed: 17DEC2020

Table 88 includes all procedure-associated AEs by severity for subjects in the historical ACDF control group through post-operative day 790. As shown below, there was one life-threatening procedure-associated event in the historical ACDF control group, which was identified as "Other". This subject had post-operative respiratory depression secondary to narcotic overdose that prolonged hospital stay.

Table 88: Procedure Associated AEs (Severity) by Code – (Historical ACDF Control Group, N=170)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	17	27.4%	36	58.1%	8	12.9%	1	1.6%	62
Dysphagia	5	55.6%	4	44.4%	0	0.0%	0	0.0%	9
Cervical Radiculopathy	0	0.0%	5	71.4%	2	28.6%	0	0.0%	7
Headache	0	0.0%	4	100.0%	0	0.0%	0	0.0%	4
Pain (no narcotic given)	4	100.0%	0	0.0%	0	0.0%	0	0.0%	4
Numbness - increased from pre-op or prior visit	3	100.0%	0	0.0%	0	0.0%	0	0.0%	3
Pain (narcotic given)	0	0.0%	2	66.7%	1	33.3%	0	0.0%	3
Pneumonia	0	0.0%	2	66.7%	1	33.3%	0	0.0%	3
Gastrointestinal complications including ileus, nausea and vomiting	0	0.0%	3	100.0%	0	0.0%	0	0.0%	3
Dysphonia	1	50.0%	1	50.0%	0	0.0%	0	0.0%	2
Spasm	0	0.0%	2	100.0%	0	0.0%	0	0.0%	2
Difficulty w ith urination	0	0.0%	1	50.0%	1	50.0%	0	0.0%	2
Infection localized to cervical surgical site	0	0.0%	2	100.0%	0	0.0%	0	0.0%	2
Infection (all other infections-NOT at cervical surgical site)	1	50.0%	1	50.0%	0	0.0%	0	0.0%	2
Dermatitis/Skin allergy	0	0.0%	2	100.0%	0	0.0%	0	0.0%	2
Cerebrospinal fluid leakage	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1
Hoarseness	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Spondylosis acquista	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1
Vocal cord paralysis	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Weakness - increased from pre-op or prior visit	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Other	0	0.0%	0	0.0%	0	0.0%	1	100.0%	1
Sw elling (edema)	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Atelectasis	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Hypertension	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Sore throat	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Appendicular arthritis	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Diabetes	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Non-Infectious pulmonary disorder	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Opioid Dependency	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1

*Percentage of total events.

Source: Tables Safety - Procedure Associated.sas; Analyzed: 17DEC2020

Implant/Surgical Procedure-Associated AEs

Table 89, Table 90, Table 91 and **Table 92** present AEs associated with the implant/surgical procedure. Implant/procedure AEs were used in cases where it was undetermined if the event was implant- or procedure-associated or it was determined it was both. The implant/surgical procedure-associated AEs are stratified by event type, by day of occurrence (timecourse), and by severity.

Table 89 includes all implant/surgical procedure-associated AEs by code for all patients in the study through post-operative day 790. As shown below, six (6) subjects in the Simplify® Cervical Artificial Disc group and 22 subjects in the historical ACDF control group had implant/surgical procedure AEs. The most commonly occurring events categorized as implant/surgical procedure-associated events in the Simplify® Cervical Artificial Disc cohort were cervical radiculopathy (2.2% - 4/182). In the historical ACDF control cohort, the most commonly occurring AEs

categorized as implant/surgical procedure-associated events were nonunion/pseudoarthrosis (6.5% - 11/170).

Table 89: All Implant/Surgical Procedure-Associated AEs by Code (Primary Analysis Set)

	Simplify Disc (N= 182)			ACDF (N= 170)		
	Events	Subjs	%	Events	Subjs	%
All Events	6	6	3.3%	23	22	12.9%
Cervical Radiculopathy	4	4	2.2%	1	1	0.6%
Development of DDD at adjacent levels	1	1	0.5%	0	0	0.0%
Vertebral fracture	1	1	0.5%	0	0	0.0%
Nonunion/pseudoarthrosis	0	0	0.0%	11	11	6.5%
Pain (narcotic given)	0	0	0.0%	3	3	1.8%
Pain (no narcotic given)	0	0	0.0%	3	3	1.8%
Dysphagia	0	0	0.0%	1	1	0.6%
Implant collapse or subsidence	0	0	0.0%	1	1	0.6%
Headache	0	0	0.0%	1	1	0.6%
Implant/Joint Noise	0	0	0.0%	1	1	0.6%
Spasm	0	0	0.0%	1	1	0.6%
|Percentage of subjects experiencing specific event; Source: Tables Safety - Implant-Procedure Associated.sas; Analyzed: 17DEC2020						

Table 90 includes a timecourse of all implant/surgical procedure-associated AEs for all patients in the study at through post-operative day 790. As shown below, the majority of implant/surgical procedure-associated AEs occurred between 180-365 days for the Simplify® Cervical Artificial Disc group, while the majority of implant/surgical procedure-associated AEs occurred between 90-180 days for the ACDF control group.

Table 90: All Implant/Surgical Procedure-Associated AEs (Timecourse) by Code (Primary Analysis Set)

	Days Post-Op																	
	Missing		0-2		2-30		30-90		90-180		180-365		365-730		730-790		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
All Events	0	0	0	1	0	1	1	5	2	13	2	1	1	2	0	0	6	23
Cervical Radiculopathy	0	0	0	0	0	0	0	0	1	1	2	0	1	0	0	0	4	1
Development of DDD at adjacent levels	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Vertebral fracture	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
Dysphagia	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Implant collapse or subsidence	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
Headache	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Pain (narcotic given)	0	0	0	1	0	0	0	0	0	1	0	0	0	1	0	0	0	3
Pain (no narcotic given)	0	0	0	0	0	0	0	1	0	2	0	0	0	0	0	0	0	3
Implant/Joint Noise	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
Spasm	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Nonunion/pseudoarthrosis	0	0	0	0	0	0	0	2	0	8	0	1	0	0	0	0	0	11
Source: Tables Safety - Implant-Procedure Associated.sas; Analyzed: 17DEC2020																		

Table 91 includes all implant/surgical procedure-associated AEs by severity for all patients in the investigational group. As shown below, there were no life-threatening implant/surgical procedure-associated events in the Simplify® Cervical Artificial Disc group.

Table 91: All Implant/Surgical Procedure-Associated AEs (Severity) by Code – – (Simplify® Cervical Artificial Disc Group, N=182)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	0	0.0%	2	33.3%	4	66.7%	0	0.0%	6
Cervical Radiculopathy	0	0.0%	1	25.0%	3	75.0%	0	0.0%	4
Development of DDD at adjacent levels	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Vertebral fracture	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1

*Percentage of total events.

Source: Tables Safety - Implant-Procedure Associated.sas; Analyzed: 17DEC2020

Table 92 includes all implant/surgical procedure-associated AEs by severity for all patients in the historical ACDF control group. As shown below, there were no life-threatening implant/surgical procedure-associated events in the historical ACDF control group.

Table 92: All Implant/Surgical Procedure-Associated AEs (Severity) by Code – (Historical ACDF Control Group, N=170)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	6	26.1%	6	26.1%	11	47.8%	0	0.0%	23
Nonunion/pseudoarthrosis	0	0.0%	2	18.2%	9	81.8%	0	0.0%	11
Pain (narcotic given)	0	0.0%	2	66.7%	1	33.3%	0	0.0%	3
Pain (no narcotic given)	3	100.0%	0	0.0%	0	0.0%	0	0.0%	3
Dysphagia	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Implant collapse or subsidence	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1
Headache	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Implant/Joint Noise	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Spasm	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1
Cervical Radiculopathy	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1

*Percentage of total events.

Source: Tables Safety - Implant-Procedure Associated.sas; Analyzed: 17DEC2020

Unknown Association AEs

Table 93, Table 94, and **Table 95** present AEs with unknown association. The unknown association AEs are stratified by event type, by day of occurrence (timecourse), and by severity.

Table 93 includes all unknown association AEs by code for all patients in the study through post-operative day 790. As shown below, there were no events with unknown association in the

Simplify® Cervical Artificial Disc group. In the historical ACDF control group there were two events.

Table 93: All Unknown Association AEs by Code (Primary Analysis Set)

	Simplify Disc (N= 182)			ACDF (N= 170)		
	Events	Subjs	%|	Events	Subjs	%|
All Events	0	0	0.0%	2	2	1.2%
Myelopathy	0	0	0.0%	1	1	0.6%
Cervical Radiculopathy	0	0	0.0%	1	1	0.6%

|Percentage of subjects experiencing specific event;
Source: Tables Safety - Unknown Associated.sas; Analyzed: 17DEC2020

Table 94 includes a timecourse of all unknown association AEs for all patients in the study through post-operative day 790. As shown below, the unknown association AEs occurred 2-30 days post-operatively.

Table 94: All Unknown Association AEs (Timecourse) by Code (Primary Analysis Set)

	Days Post-Op																	
	Missing		0-2		2-30		30-90		90-180		180-365		365-730		730-790		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
All Events	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	2
Myelopathy	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Cervical Radiculopathy	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1

Source: Tables Safety - Unknown Associated.sas; Analyzed: 17DEC2020

Table 95 includes all unknown association AEs by severity for all patients in the historical ACDF control group. As shown below, there were no life-threatening events with unknown association.

Table 95: All Unknown Association AEs (Severity) by Code – (Historical ACDF Control Group, N=170)

	Mild		Moderate		Severe		Life Threatening		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
All Events	2	100.0%	0	0.0%	0	0.0%	0	0.0%	2
Myelopathy	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Cervical Radiculopathy	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1

*Percentage of total events.

Source: Tables Safety - Unknown Associated.sas; Analyzed: 17DEC2020

Serious Adverse Events (SAEs)

There were a total of 41 SAEs in 32 subjects in the Simplify® Cervical Artificial Disc group subjects and 85 SAEs in 62 subjects in the historical ACDF control group (**Table 96**). The most commonly occurring events categorized as SAEs in the Simplify® Cervical Artificial Disc cohort were lumbar radiculopathy (4.4% - 8/182), infection at a location other than the cervical surgical site (3.3% - 6/182), and cervical radiculopathy (2.2% - 4/182). In the historical ACDF control

cohort, the most commonly occurring events categorized as SAEs were lumbar radiculopathy (7.6% - 13/170), nonunion/pseudoarthrosis (5.9% - 10/170), and low back pain with no narcotic given (3.5% - 6/170).

Table 96: Counts and Percentages of Subjects with Specific Serious AE– (Primary Analysis Population through Day 790)

	Simplify Disc (N= 182)			ACDF (N= 170)		
	Events	Subjs	%‖	Events	Subjs	%‖
All Events	41	32	17.6%	85	62	36.5%
Infection (all other infections-NOT at cervical surgical site)	7	6	3.3%	2	2	1.2%
Death	2	2	1.1%	1	1	0.6%
Embolism	1	1	0.5%	1	1	0.6%
Pain (no narcotic given)	1	1	0.5%	1	1	0.6%
Pain (narcotic given)	1	1	0.5%	2	2	1.2%
Cancer	1	1	0.5%	2	2	1.2%
Difficulty with urination	1	1	0.5%	2	2	1.2%
Cervical Radiculopathy	4	4	2.2%	5	4	2.4%
Dysphagia	2	2	1.1%	3	3	1.8%
Gastrointestinal complications including ileus, nausea and vomiting	2	2	1.1%	5	5	2.9%
Other	1	1	0.5%	3	3	1.8%
Appendicular arthritis	2	1	0.5%	4	4	2.4%
Accidental trauma	1	1	0.5%	4	4	2.4%
Lumbar Radiculopathy	8	8	4.4%	14	13	7.6%
Low back pain (no narcotic given)	1	1	0.5%	6	6	3.5%
Hematoma or seroma	2	2	1.1%	0	0	0.0%
Vertebral fracture	2	2	1.1%	0	0	0.0%
Blood loss (greater than 500ml)	1	1	0.5%	0	0	0.0%
Hypertension	1	1	0.5%	0	0	0.0%
Nonunion/pseudoarthrosis	0	0	0.0%	10	10	5.9%
Pneumonia	0	0	0.0%	2	2	1.2%
Psychological Illness	0	0	0.0%	2	2	1.2%
Low back pain (narcotic given)	0	0	0.0%	2	2	1.2%
Cerebrospinal fluid leakage	0	0	0.0%	1	1	0.6%
Development of DDD at adjacent levels	0	0	0.0%	1	1	0.6%
Dural injury	0	0	0.0%	1	1	0.6%
Implant collapse or subsidence	0	0	0.0%	1	1	0.6%
Spondylosis acquista	0	0	0.0%	1	1	0.6%
Thrombosis	0	0	0.0%	1	1	0.6%
Cardiac Event	0	0	0.0%	1	1	0.6%
Stroke	0	0	0.0%	1	1	0.6%
Atelectasis	0	0	0.0%	1	1	0.6%
Soft tissue damage	0	0	0.0%	1	1	0.6%
Dermatitis/Skin allergy	0	0	0.0%	1	1	0.6%
Sleep apnea	0	0	0.0%	1	1	0.6%
Renal dysfunction	0	0	0.0%	1	1	0.6%
Inflammation	0	0	0.0%	1	1	0.6%

‖Percentage of subjects experiencing specific event;
Source: Tables Safety - Serious AEs.sas; Analyzed: 17DEC2020

One (1) subject in the historical control group had an implant-associated SAE. Two (2) subjects in the Simplify® Cervical Artificial Disc group had an SAE that was determined by the CEC to be implant-associated. Overall, there were eight (4.4% - 8/182) subjects with a treatment-associated

SAE in the Simplify® Cervical Artificial Disc group and 22 (12.9% - 22/170) subjects with a treatment-associated SAE in the historical control group.

Deaths

Three subject deaths were reported through post-operative day 790: one Simplify® Cervical Artificial Disc subject was killed in an automobile accident (study day 432), one Simplify® Cervical Artificial Disc subject drowned (study day 729), and one historical ACDF control subject died of cardiac arrest (study day 499). These deaths were reviewed by the CEC and determined to be unrelated to study treatment.

Secondary Surgical Intervention (SSIs)

Some AEs resulted in SSIs that were classified as revisions, removals, reoperations, supplemental fixations or other in accordance with FDA's Guidance Document, Clinical Data Presentations for Orthopedic Device Applications (2004) and were reviewed and adjudicated by the CEC.

Based on the results presented in **Table 97**, a total of four (4) SSIs occurred in the Simplify® Cervical Artificial Disc group and fifteen (15) SSIs occurred in the historical ACDF group. Of the ACDF SSIs, one (1) occurred at month 25, in window for the 24-month primary endpoint visit, but after the 24-month visit data was collected. This SSI has been included in the count above but not reflected in the *subject accounting summary* table. The timecourse of these events demonstrates that the majority of SSIs occurred between 6 and 24 months in both groups; however, meaningful conclusions cannot be made with respect to timing due to the low number of SSI events in both groups.

Table 97: Surgical Intervention Timecourse by Treatment Type – (Primary Analysis Set)

Treatment Group	SSI Type	Event Timecourse (months)						Total Events (Subjects)
		<1.5	1.5-3	3-6	6-12	12-24	>24	
Simplify® Cervical Artificial Disc	Removal	-	-	-	2	1	-	3
	Revision	-	-	-	-	-	-	0
	Reoperation				-	1	-	1
	Supplemental Fixation	-	-	-	-	-	-	0
	Other	-	-	-	-	-	-	0
Total Events (Subjects)		**-**	**-**	**-**	**2**	**2**	**-**	**4**
ACDF	Removal	-	1	2	1	1	1	6*
	Revision	1	-	-	-	-	-	1
	Reoperation	-	1	-	1	1	-	3
	Supplemental Fixation	-	-	-	1	-	-	1
	Other	-	-	-	3	1	-	4
Total Events (Subjects)		**1**	**2**	**2**	**6**	**3**	**1**	**15***

**One removal occurred at month 25, in window for the 24M primary endpoint visit, but after 24M visit data was collected. This has been included in the count above but not reflected in the subject accounting summary table.*

The procedure and reason for SSI are detailed below in **Table 98**. Of the four (4) SSIs observed in the Simplify® Cervical Artificial Disc cohort, three (3) resulted in device removal. Of the fifteen (15) SSIs reported in the historical ACDF control cohort, six (6) resulted in device removal.

Table 98: Surgical Intervention Procedure and Indication for Procedure

Group	Procedure	Index Level	Procedure	Indication for Procedure
Simplify®	Removal	C5/C6, C6/7	Removal of TDR C5/C6, C6/C7; ACDF C5-C7	C7 vertebral body fracture with implant subsidence, C6 compression fracture, radiculopathy, kyphosis and stenosis C5-C7
Simplify®	Removal	C4/C5, C5/C6	Removal of TDR C4/C5, C5/C6; ACDF C4-C7, Corpectomy C5 and C6	Radiculopathy, kyphosis C4-C7, subsidence of superior endplate at C5 and C6
Simplify®	Removal	C5/C6, C6/7	Removal of TDR C5/C6, C6/C7; ACDF C4-C7	C6 Radiculopathy, C7 Radiculopathy, foraminal stenosis and degenerative disc disease C4/C5
Simplify®	Reoperation	C5/C6, C6/7	C6-T1 Decompression and Discectomy	Emergent pain in back of scapula due to disc herniation C7-T1
ACDF	Other	C5/C6, C6/7	Bone Growth Stimulator	Headaches and difficulty lifting right arm overhead.
ACDF	Other	C5/C6, C6/7	Bone Growth Stimulator	Axial neck pain, broken screw (C5) indicative of delayed union/non-union
ACDF	Reoperation	C5/C6, C6/7	Laminotomies and Foraminotomy C5/C6, C6/C7; PSF C5-C7	Failed fusion C5/C6, C6/C7 with left sided radiculopathy
ACDF	Other	C4/C5, C5/C6	Bone Growth Stimulator	Pseudarthrosis forming at C5/C6, cervical and arm pain
ACDF	Removal	C4/C5, C5/C6	Hardware removal C5/C6 Corpectomy; C5/C6 PEEK cage fusion; new plate placement C5-C7	Radiculopathy and Spondylosis
ACDF	Supplemental fixation	C5/C6, C6/7	C5-C7 PSF	Pseudarthrosis C5/C6, C6/C7 with neck pain
ACDF	Reoperation	C5/C6, C6/7	C5-C7 posterior exploration of fusion mass	Halo surrounding screw at C5/C6, neck pain
ACDF	Revision	C5/C6, C6/7	Removal and replacement of plate, screws, and C6/C7 allograft	Ruptured disc material C6/C7, neck and radicular pain
ACDF	Removal	C5/C6, C6/7	Removal of plate C5-C7; C4/C5 discectomy, foraminotomy, and placement of interbody arthrodesis; New plate placed from C4-C7	Cervical spondylosis and radiculopathy
ACDF	Reoperation	C5/C6, C6/7	C5-C6 posterior laminoforaminotomy with nerve root decompression; C7-T1 lamino-foraminotomy with nerve root decompression	Foraminal narrowing and bony spur at C7-T1, Subsidence of interbody graft C5/C6 into the vertebral body at C6. Foraminal narrowing at C5/C6

Group	Procedure	Index Level	Procedure	Indication for Procedure
ACDF	Removal	C4/C5, C5/C6	C4-C6 Plate removal with exploration; C6, C7 Partial corpectomy; C6/C7 Cervical disc arthroplasty	C6/C7 disc osteophyte abutting and deforming the spinal cord. Neck, shoulder, and arm pain.
ACDF	Removal	C5/C6, C6/7	Removal of instrumentation and grafts C5-C7; Placement of plate and BMP C5-C7; C5 and C6 partial corpectomies	Pseudarthrosis
ACDF	Removal	C5/C6, C6/7	Removal of Hardware and Implants; Revision with PEEK cages; Superior vertebrectomy C5, C6 and inferior vertebrectomy C4, C5; Placement of long strut graft C6/C7 and small strut graft C5/C6	Pseudarthrosis
ACDF	Other	C5/C6, C6/7	Bone Growth Stimulator	Pseudarthrosis
ACDF	Removal	C5/C6, C6/7	Removal of instrumentation and grafts; Placement of PEEK grafts C5/C6, C6/C7 with plating from C5-C7	Pseudarthrosis

Neurological Status

Neurological success was defined as maintenance or improvement in neurologic status at Month 24. The CEC assigned neurological status (stable/ improved/ deteriorated) at Month 24 as compared to baseline for all but two Simplify® Cervical Artificial Disc subjects. CEC adjudicated Month 12 neurologic status was carried forward for two Simplify® Cervical Artificial Disc subjects to represent the unavailable Month 24 results in the primary endpoint. No Simplify® Cervical Artificial Disc subjects were considered a neurological failure and three (3) historical ACDF control subjects that were considered neurological failures (2.3% - 3/128) as shown in **Table 99**.

Table 99: Neurological Status at 24 Months (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference			
Outcome	**N**	**n**	**%‖**	**N**	**n**	**%‖**	**p**	**Δ**	**90% LB**	**95% LB**
No Neurological Deterioration (CEC)†	**168**	**168**	**100.0%**	**128**	**125**	**97.7%**				

P-value is against the null hypothesis of equality;
‖Equally weighted PS adjusted within group proportion. This will not equal n/N which is the observed data;
† Subjects censored at Index level secondary surgical interventions and intra-operative deviations;
The resulting completed datasets were combined using Rubin's Rules.
Source: Tables Overall Efficacy.sas; Analyzed: 09NOV2020

Table 99 presents the number and percentage of patients with no neurological deterioration, adjudicated by the CEC, as included in the primary CCS endpoint. CEC adjudicated Month 12 neurologic status was carried forward for two Simplify® Cervical Artificial Disc subjects to represent the unavailable Month 24 results in the primary endpoint.

Table 100: Neurological Status at 24 Months – Improved, Maintained, Deteriorated (Primary Analysis Population)

	Month 24			
	Simplify Disc		ACDF	
	n	%	n	%
Improved	140	83%	106	83%
Maintained	28	17%	19	15%
Deteriorated	0	0%	3	2%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Clinical Follow-up addtl.sas; Analyzed: 11DEC2020

Table 100 presents the percentage of subjects categorized as improved, maintained, or deteriorated in neurological status at 24 months. Overall, similar rates were exhibited between the Simplify® Cervical Artificial Disc group and the historical ACDF control group. The historical ACDF control group reporting a 2% deterioration rate compared to 0% in the Simplify® Cervical Artificial Disc group.

Effectiveness Results

Please note: The counts and percentages provided for the Simplify® Cervical Artificial Disc and historical ACDF control groups correspond to the values unadjusted for PS subclass. The device group difference and 95% confidence interval lower bound (LB) and upper bound (UB) are calculated controlling for PS subclass, accounting for why the reported difference does not match the difference between the presented unadjusted percentages.

Primary Overall Success Analysis
The success measurement was developed to measure safety and effectiveness of the Simplify® Cervical Artificial Disc when compared to ACDF. A subject was considered a study success at the Month 24 follow-up if he/she met all of the following criteria:

- Neck Disability Index (NDI) score improvement of at least 15 points (out of 100) from as compared to baseline at Month 24;
- Maintenance or improvement in neurological status as compared to Month 24[11, 12];
- No serious adverse event (SAE) classified as implant associated or implant/surgical procedure associated within 24 months of index procedure; and
- No additional surgical procedure classified as a "failure" within 24 months of index procedure.

Overall success was determined based on data collected during the initial 24 months of follow-up. Each element of the neurological study exam was evaluated for maintenance or improvement.

[11] Maintenance or improvement in neurological status was based on motor, sensory, and myelopathic gait assessments.
[12] Due to COVID-19, not all 24M visits (entire or portion) were able to occur in-person. If a 24M in-person visit did not occur, the 12M result was carried forward to represent unavailable 24M results in the primary endpoint and subsequently adjudicated by the CEC.

All secondary index surgeries were classified as failures.

Per the FDA Guidance for the Preparation of IDEs for Spinal Systems, the following definitions applied:

- Reoperation - any surgical procedure at the index level(s) that *does not involve* modification, addition or removal of any components of the device and is not considered a removal, revision, or supplemental fixation.
- Revision – any procedure in the postoperative or follow-up period that adjusts or in any way modifies either one or both of the original implant configurations (e.g., adjusting the position of the original configuration, removal with replacement with same type of study implant).
- Removal – a procedure that removes one or more components of the original implant configuration without replacement with the same type of trial implant.
- Supplemental fixation – a procedure at the index level(s) in which additional spinal devices not approved as part of the protocol are placed.
- Other – any additional surgical procedure not classified as a removal, revision, supplemental fixation, or reoperation.

Overall success was determined based on data collected during the initial 24 months of follow-up. Each element of the neurological study exam was evaluated for maintenance or improvement. The primary overall success outcomes are presented in **Table 101**.

Table 101: Overall Efficacy (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
Outcome	**N**	**n**	**%‖**	**N**	**n**	**%‖**	**p**	**Δ**	**90% LB**	**95% LB**
Implanted§	182	181	99.5%	170	166	97.6%				
No secondary surgical intervention‡§	**181**	**177**	**97.8%**	**166**	**152**	**91.6%**	**0.083**	**4.5%**	**0.3%**	**-0.5%**
No removals§	181	178	98.3%	166	161	97.0%				
No revisions§	181	181	100.0%	166	165	99.4%				
No reoperations§	181	180	99.4%	166	163	98.2%				
No supplemental fixations§	181	181	100.0%	166	165	99.4%				
No other SSI§	181	181	100.0%	166	162	97.6%				
NDI 15-point Responder†§	**168**	**156**	**92.3%**	**127**	**106**	**85.5%**	**0.094**	**6.8%**	**0.2%**	**-1.1%**
No Neurological Deterioration (CEC)†	**168**	**168**	**100.0%**	**128**	**125**	**97.7%**				
No Serious Adverse Event classified as implant associated or implant/surgical procedure associated (CEC)	**182**	**176**	**96.3%**	**170**	**158**	**94.7%**	**0.520**	**1.6%**	**-2.4%**	**-3.2%**
Composite Clinical Success (CCS) ¶	**182**	**--**	**86.7%**	**170**	**--**	**77.1%**	**0.036**	**9.6%**	**2.1%**	**0.6%**
CCS: Observed data only	173	153	87.5%	145	105	75.7%	0.017	11.8%	3.9%	2.4%
CCS: Best-Case	182	162	88.3%	170	105	63.9%	<.001	24.4%	16.5%	15.0%
CCS: Worst-Case	182	153	83.1%	170	130	78.1%	0.301	5.0%	-2.5%	-3.9%

*Device group differences and 90% and 95% LB adjusting for propensity score (PS) subclass using two-way generalized linear model.
P-value is against the null hypothesis of equality;
‖Equally weighted PS adjusted within group proportion. This will not equal n/N which is the observed data;
† Subjects censored at Index level secondary surgical interventions and intra-operative deviations;
‡ Propensity Score treated as a continuous variable to promote convergence;
§Not estimable due to zero cell. Unadjusted within group rate shown;
¶A Fully Conditional Specification (FCS) approach was used to produce 20 multiply imputed completed data sets. The FCS approach accommodates non-monotonicity in the pattern of missing data and requires regression models to be specified for each variable with missing values needing imputation. All models included the PS subclass and treatment group. NDI responder status and secondary surgical interventions over time were sequentially added to account for longitudinal temporality. The resulting completed datasets were combined using Rubin's Rules.
Source: Tables Overall Efficacy.sas; Analyzed: 09NOV2020

Using multiple imputation to account for missing data, the adjusted success rate was 86.7% for Simplify® Cervical Artificial Disc and 77.1% for the historical ACDF control cohort. The adjusted difference between groups was 9.6%. The lower-bound of the 1-sided 90% confidence interval for the group difference controlling for PS subclass was 2.1%. Since 2.1% is greater than -10%, the results from this comparison demonstrate that the study success criterion for non-inferiority has been achieved. Further, the 1-sided 95% confidence interval for the group difference controlling for PS subclass was 0.6%. Since 0.6% is greater than 0%, the results from this comparison demonstrate that the study success criterion for superiority has been achieved.

Sensitivity analyses were performed to evaluate the composite success measurement using observed data only, best-case evaluation and worst-case evaluation. All sensitivity analyses demonstrate that the study success criterion for non-inferiority has been achieved. Further, the primary, 'observed data', and 'best case' sensitivity analyses met the threshold for superiority of the Simplify® Cervical Artificial Disc group as compared to the historical ACDF control group.

Secondary Effectiveness Analyses

This section focuses on secondary clinical endpoints from a number of relevant domains (i.e., NDI, Neck and Arm Pain, SF-36, Dysphagia Handicap Index (DHI), medication usage, neurological assessments, work status, and Radiographic Measurements), which were assessed at preoperative (baseline) and at prescribed clinical intervals throughout the follow-up period. In addition, physician's perception of results, treatment satisfaction, and time to recovery, were assessed post-operatively at Month 24. Overall, subjects treated with the Simplify® Cervical Artificial Disc exhibited improvement and numerically favorable rates across the broad spectrum of secondary analyses.

Table 102: Secondary Effectiveness Subject Outcomes at Month 24 Compared to Baseline (Primary Analysis Population)

Secondary Effectiveness Endpoint	Simplify® Cervical Artificial Disc (N=182)	ACDF (N=170)
NDI Improvement ≥ 15 percentage-points (out of 100)	156/168 (92.9%)	106/127 (83.5%)
Neck Pain Intensity ≥ 2-point Responder Rate	147/158 (93.0%)	110/127 (86.6%)
Neck Pain Frequency ≥ 2-point Responder Rate	148/158 (93.7%)	117/127 (92.1%)
Arm Pain Intensity ≥ 2-point Responder Rate	142/158 (89.9%)	108/127 (85.0%)
Arm Pain Frequency ≥ 2-point Responder Rate	140/158 (88.6%)	115/127 (90.6%)
SF-36 PCS (Change ≥ 0 from baseline)	146/158 (92.4%)	114/127 (89.8%)
SF-36 MCS (Change ≥ 0 from baseline)	125/158 (79.1%)	94/127 (74.0%)

Neck Disability Index (NDI)

Table 103 and **Table 104** present the NDI percentage-points for all treated subjects. NDI is scored on a 50-point scale (10 questions with a score of 0-5 for each) that is then normalized to a scale of 100%. Higher NDI is representative of greater symptomatology. The following outcomes reflect NDI percentage-points out of 100%. NDI data are censored following intra-operative deviation or SSI.

Table 103: NDI percentage-points over time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	182	58.6	14.3	58.0	30.0	88.0	170	53.6	14.5	54.0	30.0	92.0	0.699	0.6	-2.6	3.9
Week 06	179	23.3	16.4	22.0	0.0	72.0	162	32.9	17.4	32.0	0.0	88.0	<.001	-10.5	-14.6	-6.4
Month 03	177	17.3	16.5	12.0	0.0	78.0	154	23.5	18.0	20.0	0.0	84.0	0.003	-6.6	-10.9	-2.3
Month 06	176	15.1	15.8	12.0	0.0	70.0	148	20.8	19.6	16.0	0.0	86.0	0.049	-4.5	-8.9	0.0
Month 12	177	15.1	17.1	10.0	0.0	70.0	136	18.6	17.5	12.0	0.0	72.0	0.133	-3.3	-7.6	1.0
Month 24	168	14.3	15.9	8.0	0.0	64.0	127	17.2	18.2	12.0	0.0	70.0	0.241	-2.6	-7.0	1.8

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

Table 103 shows the mean NDI percentage-points for the Primary Analysis Population at pre-operative, 6-week, 3-month, 6-month, 12-month, and 24-month timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups. Pre-operative percentage-point was numerically greater in the Simplify® Cervical Artificial Disc group; however, the difference in percentage-points was not statistically significant (p=0.699). The mean pre-op NDI score for the Simplify® Disc cohort was 58.6, which improved to a mean NDI score of 14.3 at Month 24. Similarly, the mean pre-op NDI score for the historical ACDF control cohort was 53.6, which improved to a mean NDI score of 17.2 at Month 24. The difference in NDI percentage-points between groups was statistically significant for all follow-ups except Month 12 and Month 24, in favor of the Simplify® Cervical Artificial Disc group (p<0.05). The difference in NDI percentage

points between groups was still in favor of the Simplify® Cervical Artificial Disc group at Month 24 but was not statistically significant.

Table 104: NDI change in percentage-points from pre-operative (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	179	-35.4	19.5	-34.0	-86.0	18.0	162	-20.8	16.4	-20.0	-60.0	14.0	<.001	-11.2	-15.5	-6.9
Month 03	177	-41.6	19.7	-42.0	-86.0	18.0	154	-29.2	16.4	-28.0	-82.0	4.0	<.001	-8.4	-12.8	-4.0
Month 06	176	-44.0	19.6	-44.0	-88.0	20.0	148	-31.7	18.7	-32.0	-92.0	18.0	0.007	-6.4	-11.0	-1.7
Month 12	177	-43.7	20.5	-44.0	-88.0	24.0	136	-33.2	16.4	-34.0	-82.0	10.0	0.017	-5.6	-10.3	-1.0
Month 24	168	-44.7	19.2	-44.0	-88.0	18.0	127	-34.9	18.4	-36.0	-92.0	12.0	0.050	-4.8	-9.6	0.0

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

Table 104 presents the mean change in NDI percentage-points from pre-operative for the Primary Analysis Population at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups. Similar to the trends seen in mean score, the difference in NDI percentage-points as compared to preoperative was statistically significant at all timepoints, in favor of the Simplify® Cervical Artificial Disc group ($p<0.05$). Of interest, there was a greater change at the Week 6 visit (-35.4 vs. -20.8, $p<0.001$) in the Simplify® Cervical Artificial Disc group that was sustained through the study. The historical ACDF control group mean change was significantly smaller with the plateau seen at the Month 12 visit, presumably when the fusion was generally healed. This speaks to the clinical meaning of the acute response seen with reconstructing the disc space with a motion-permitting device versus a fusion that requires months to heal.

Table 105: NDI Improved/ Stable/ Deteriorated Status (Primary Analysis Population)

	Week 06				Month 03				Month 06				Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Improved [-100, -15]	153	85%	101	62%	160	90%	123	80%	162	92%	123	83%	160	90%	117	86%	156	93%	106	83%
Stable (-15, 0]	21	12%	46	28%	13	7%	27	18%	10	6%	17	11%	15	8%	14	10%	9	5%	17	13%
Deteriorated (0, 100]	5	3%	15	9%	4	2%	4	3%	4	2%	8	5%	2	1%	5	4%	3	2%	4	3%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Clinical Follow-up addtl.sas; Analyzed: 11DEC2020

Table 105 presents the number and percentage of subjects who demonstrated improvement (NDI decrease >15 percent), number and percentage of subjects who were stable (NDI decrease 0-15 percent), and number and percentage of subjects who deteriorated (any increase) relative to baseline at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints. As shown above, majority of subjects demonstrated improvement in both groups.

Table 106: NDI 15 Percentage-Point Responder (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Week 06	179	153	85.5%	162	101	62.3%	0.002	16.5%	6.5%	26.6%
Month 03	177	160	90.4%	154	123	79.9%	0.121	6.7%	-1.5%	14.8%
Month 06	176	162	92.0%	148	123	83.1%	0.325	3.7%	-3.9%	11.2%
Month 12	177	160	90.4%	136	117	86.0%	0.949	0.2%	-7.2%	7.7%
Month 24	168	156	92.9%	127	106	83.5%	0.096	6.9%	-1.1%	14.9%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95%CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

Table 106 presents the number and percentage of subjects showing an improvement in NDI greater than 15 percent-points as compared to all subjects in the study at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups. A numerically greater percentage of Simplify® Cervical Artificial Disc subjects achieved 15 percent-point improvement in NDI at all timepoints as compared to the historical ACDF control group, with 92.9% (156/168) of subjects in the Simplify® Cervical Artificial Disc group meeting this level of improvement in NDI at Month 24. This difference was statistically significant at Week 6 ($p<0.05$).

Neck Pain Intensity

Neck pain intensity was measured by filling in the appropriate circle on a scale of 0 to 10 to represent the intensity of neck pain/discomfort, with 0 being no pain and 10 being pain as bad as it could be. **Table 107** shows the Neck Pain Intensity score for the Primary Analysis Population at pre-operative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 107: Neck Pain Intensity Score over Time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	173	7.9	1.6	8.0	2.0	10.0	170	7.7	1.7	8.0	2.0	10.0	0.608	0.1	-0.3	0.5
Week 06	173	2.5	2.3	2.0	0.0	10.0	162	3.1	2.4	3.0	0.0	10.0	0.138	-0.4	-1.0	0.1
Month 03	173	2.0	2.2	1.0	0.0	9.0	154	2.8	2.4	2.0	0.0	10.0	0.041	-0.6	-1.2	0.0
Month 06	175	1.8	2.2	1.0	0.0	8.0	148	2.5	2.5	2.0	0.0	10.0	0.175	-0.4	-1.0	0.2
Month 12	177	2.0	2.5	1.0	0.0	10.0	136	2.2	2.3	1.0	0.0	8.0	0.980	0.0	-0.6	0.6
Month 24	167	1.8	2.4	1.0	0.0	10.0	127	2.5	2.6	1.0	0.0	10.0	0.138	-0.5	-1.1	0.2

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95%CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 107** , there was a decline in mean Neck Pain Intensity score at Week 6 which is maintained through the Month 24 follow-up for both treatment groups. The mean pre-op Neck Pain Intensity score for the Simplify® Cervical Artificial Disc cohort was 7.9, which improved to a mean Neck Pain Intensity score of 1.8 at Month 24. Similarly, the mean pre-op Neck Pain Intensity score for the historical ACDF control cohort was 7.7, which improved to a mean Neck Pain Intensity score of 2.5 at Month 24. There was a statistically significant difference at Month 3 favoring the investigational group ($p<0.05$).

Table 108 presents the change in Neck Pain Intensity for Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to the baseline for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 108: Neck Pain Intensity Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	170	-5.5	2.6	-6.0	-10.0	1.0	162	-4.5	2.5	-4.0	-10.0	2.0	0.058	-0.6	-1.2	0.0
Month 03	167	-5.9	2.5	-6.0	-10.0	1.0	154	-4.7	2.5	-5.0	-10.0	1.0	0.007	-0.9	-1.5	-0.2
Month 06	166	-6.1	2.6	-7.0	-10.0	0.0	148	-5.0	2.7	-5.0	-10.0	1.0	0.057	-0.6	-1.3	0.0
Month 12	168	-5.9	2.8	-6.0	-10.0	2.0	136	-5.3	2.6	-5.0	-10.0	2.0	0.530	-0.2	-0.9	0.5
Month 24	158	-6.1	2.8	-7.0	-10.0	2.0	127	-5.0	2.8	-5.0	-10.0	4.0	0.052	-0.7	-1.5	0.0

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

Similar to the trends seen in mean scores presented in **Table 107**, the results demonstrated a decline in Neck Pain Intensity score at Week 6 which is maintained through the Month 24 follow-up for both treatment groups. The magnitude of mean change in scores compared to baseline is shown to increase over time for both groups. There was a statistically significant difference at Month 3 favoring the investigational group ($p<0.05$). At Month 24, the change in mean Neck Pain Intensity score as compared to baseline was -6.1 for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the change in mean Neck Pain Intensity score at Month 24 as compared to baseline was -5.0.

Table 109 presents the number and percentage of patients showing improvement in Neck Pain Intensity score of at least 2 points compared to baseline at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 109: Neck Pain Intensity 2-Point Responder (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Week 06	170	155	91.2%	162	143	88.3%	0.613	-1.7%	-8.3%	4.9%
Month 03	167	159	95.2%	154	138	89.6%	0.154	4.3%	-1.9%	10.5%
Month 06	166	157	94.6%	148	130	87.8%	0.547	1.7%	-4.5%	7.9%
Month 12	168	156	92.9%	136	127	93.4%	0.216	-3.5%	-9.1%	2.0%
Month 24	158	147	93.0%	127	110	86.6%	0.371	3.3%	-4.0%	10.6%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 109,** the percentage of 2-point responders remains high in both treatment groups through the Month 24 follow up, with the unadjusted Simplify® Cervical Artificial Disc rate numerically higher than the unadjusted historical ACDF control group rate group at Week 6, Month 3, Month 6, and Month 24. The adjusted group difference was not statistically significant. At Month 24, a total of 93% (147/158) of the Simplify® Cervical Artificial Disc subjects achieved at least a 2-point improvement compared to baseline. For historical ACDF control group, a total

of 86.6% (110/127) achieved at least a 2-point improvement compared to baseline at the same evaluation timepoint.

Neck Pain Frequency

Neck pain frequency was measured by filling in the appropriate circle on a scale of 0 to 10 to represent how often you had neck pain/discomfort, with 0 being none of the time and 10 being all of the time. **Table 110** shows the Neck Pain Frequency score for the Primary Analysis Population at pre-operative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 110: Neck Pain Frequency Score over Time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	173	9.0	1.5	10.0	3.0	10.0	170	8.7	1.6	9.0	3.0	10.0	0.768	0.1	-0.3	0.4
Week 06	173	3.3	2.7	3.0	0.0	10.0	162	4.1	2.8	4.0	0.0	10.0	0.022	-0.8	-1.5	-0.1
Month 03	173	2.5	2.5	2.0	0.0	10.0	154	3.6	2.9	3.0	0.0	10.0	0.005	-1.0	-1.6	-0.3
Month 06	175	2.1	2.5	1.0	0.0	10.0	148	3.1	3.1	2.0	0.0	10.0	0.061	-0.7	-1.4	0.0
Month 12	177	2.3	2.7	1.0	0.0	10.0	136	2.9	2.8	2.0	0.0	10.0	0.532	-0.2	-0.9	0.5
Month 24	167	2.2	2.7	1.0	0.0	10.0	127	2.9	2.8	2.0	0.0	10.0	0.248	-0.4	-1.1	0.3

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 110**, there was a decline in mean Neck Pain Frequency score at Week 6 which is maintained through the Month 24 follow-up for both treatment groups. The mean pre-op Neck Pain Frequency score for the Simplify® Cervical Artificial Disc cohort was 9.0, which improved to a mean Neck Pain Frequency score of 2.2 at Month 24. Similarly, the mean pre-op Neck Pain Frequency score for the historical ACDF control cohort was 8.7, which improved to a mean Neck Pain Frequency score of 2.9 at Month 24. A statistically significant difference was seen at Week 6 and Month 3, both favoring the investigational group ($p<0.05$).

Table 111 presents the change in Neck Pain Frequency score from Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to baseline for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 111: Neck Pain Frequency Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	170	-5.7	2.9	-6.0	-10.0	2.0	162	-4.6	2.8	-5.0	-10.0	3.0	0.019	-0.8	-1.5	-0.1
Month 03	167	-6.5	2.8	-7.0	-10.0	2.0	154	-5.1	2.9	-6.0	-10.0	5.0	0.003	-1.1	-1.8	-0.4
Month 06	166	-6.8	2.8	-7.0	-10.0	2.0	148	-5.5	3.1	-6.0	-10.0	2.0	0.045	-0.7	-1.5	0.0
Month 12	168	-6.6	3.0	-7.0	-10.0	4.0	136	-5.7	3.0	-6.0	-10.0	4.0	0.477	-0.3	-1.0	0.5
Month 24	158	-6.8	3.0	-7.0	-10.0	4.0	127	-5.7	2.7	-6.0	-10.0	1.0	0.167	-0.5	-1.3	0.2

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

Similar to the trends seen in mean scores presented in **Table 110**, the results demonstrate an overall decline in mean Neck Pain Frequency score at Week 6 which is maintained through the Month 24 follow-up for both groups. The magnitude of mean change in score compared to baseline was

maintained through Month 24 for both groups. There was a statistically significant difference at Week 6 through Month 6, favoring the investigational group ($p<0.05$). At Month 24, the change in mean Neck Pain Frequency score as compared to baseline was -6.8 for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the change in mean Neck Pain Frequency score at Month 24 as compared to baseline was -5.7.

Table 112 presents the number and percentage of patients showing improvement in Neck Pain Frequency score of at least 2 points compared to baseline at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 112: Neck Pain Frequency 2-Point Responder (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Week 06	170	152	89.4%	162	135	83.3%	0.120	6.7%	-1.2%	14.7%
Month 03	167	154	92.2%	154	131	85.1%	0.275	4.2%	-3.2%	11.5%
Month 06	166	158	95.2%	148	126	85.1%	0.120	4.9%	-2.0%	11.8%
Month 12	168	154	91.7%	136	121	89.0%	0.510	-1.9%	-8.4%	4.6%
Month 24	158	148	93.7%	127	117	92.1%	0.431	-1.9%	-7.3%	3.5%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95%CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 112**, the percentage of 2-point responders remains high in both treatment groups through the Month 24 follow up, with the unadjusted Simplify® Cervical Artificial Disc rate numerically higher than the unadjusted historical ACDF control group rate at Week 6 through Month 24. The adjusted group difference was not statistically significant. At Month 24, a total of 93.7% (148/158) of the Simplify® Cervical Artificial Disc subjects achieved at least a 2-point improvement compared to baseline. For historical ACDF control group, a total of 92.1% (117/127) achieved at least a 2-point improvement compared to baseline at the same evaluation timepoint.

Arm Pain Intensity

Arm pain intensity was measured by filling in the appropriate circle on a scale of 0 to 10 to represent the intensity of arm pain/discomfort, with 0 being no pain and 10 being pain as bad as it could be. **Table 113** shows the Arm Pain Intensity scores for the Primary Analysis Population at pre-operative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 113: Arm Pain Intensity Score over Time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	173	7.5	1.8	8.0	1.0	10.0	170	7.0	2.2	7.0	0.0	10.0	0.632	0.1	-0.4	0.6
Week 06	173	1.9	2.5	1.0	0.0	10.0	162	2.1	2.5	1.0	0.0	9.0	0.430	-0.2	-0.9	0.4
Month 03	173	1.6	2.4	1.0	0.0	10.0	154	2.0	2.6	1.0	0.0	10.0	0.406	-0.3	-0.9	0.4
Month 06	175	1.6	2.3	0.0	0.0	10.0	148	1.7	2.6	0.0	0.0	10.0	0.760	0.1	-0.5	0.7
Month 12	177	1.8	2.5	1.0	0.0	10.0	136	1.7	2.4	0.0	0.0	9.0	0.816	0.1	-0.5	0.7
Month 24	167	1.8	2.5	1.0	0.0	10.0	127	1.6	2.6	0.0	0.0	10.0	0.544	0.2	-0.5	0.9

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95%CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 113** there was a decline in mean Arm Pain Intensity at Week 6 which is maintained through the Month 24 follow-up for both treatment groups. The mean pre-op Arm Pain Intensity score for the Simplify® Cervical Artificial Disc cohort was 7.5, which improved to a mean Arm Pain Intensity score of 1.8 at Month 24. Similarly, the mean pre-op Arm Pain Intensity score for the historical ACDF control cohort was 7.0, which improved to a mean Arm Pain. Intensity score of 1.6 at Month 24. The Arm Pain Intensity score between the two treatment groups were not statistically significant.

Table 114 presents the change in Arm Pain Intensity score from Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to baseline for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 114: Arm Pain Intensity Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	170	-5.6	2.7	-6.0	-10.0	3.0	162	-4.8	3.1	-5.0	-10.0	4.0	0.283	-0.4	-1.1	0.3
Month 03	167	-5.9	2.7	-6.0	-10.0	3.0	154	-4.8	3.2	-5.0	-10.0	5.0	0.189	-0.5	-1.2	0.2
Month 06	166	-5.9	2.8	-6.0	-10.0	3.0	148	-5.2	3.3	-6.0	-10.0	5.0	0.902	0.0	-0.8	0.7
Month 12	168	-5.7	2.9	-6.0	-10.0	5.0	136	-5.2	2.9	-5.5	-10.0	4.0	0.769	-0.1	-0.8	0.6
Month 24	158	-5.7	3.0	-6.0	-10.0	5.0	127	-5.2	3.2	-6.0	-10.0	3.0	0.994	0.0	-0.8	0.8

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

Similar to the trends seen in mean scores presented in **Table 113**, the results demonstrate a decline in mean Arm Pain Intensity at Week 6 which is maintained through the Month 24 follow-up for both groups. The magnitude of mean change in score compared to baseline is maintained through Month 24 for both treatment groups. At Month 24, the change in mean Arm Pain Intensity score as compared to baseline was -5.7 for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the change in mean Arm Pain Intensity score at Month 24 as compared to baseline was -5.2. The difference in mean Arm Pain Intensity score was not statistically significant between the two treatment groups.

Table 115 presents the number and percentage of patients showing improvement in Arm Pain Intensity score of at least 2 points compared to baseline.

Table 115: Arm Pain Intensity 2-Point Responder (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Week 06	170	155	91.2%	162	139	85.8%	0.255	4.4%	-2.9%	11.7%
Month 03	167	153	91.6%	154	136	88.3%	0.987	-0.1%	-6.7%	6.6%
Month 06	166	152	91.6%	148	128	86.5%	0.591	2.0%	-5.2%	9.3%
Month 12	168	149	88.7%	136	119	87.5%	0.868	0.7%	-7.1%	8.5%
Month 24	158	142	89.9%	127	108	85.0%	0.440	3.4%	-4.9%	11.7%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 115** the percentage of 2-point responders remains high in both treatment groups through the Month 24 follow up, with the unadjusted Simplify® Cervical Artificial Disc

rate numerically higher than the unadjusted historical ACDF control group rate at every timepoint. The adjusted group difference was not statistically significant. At Month 24, a total of 89.9% (142/158) of the Simplify® Cervical Artificial Disc subjects achieved at least a 2-point improvement compared to baseline. For historical ACDF control group, a total of 85.0% (108/127) achieved at least a 2-point improvement compared to baseline at the same evaluation timepoint.

Arm Pain Frequency

Arm pain frequency was measured by filling in the appropriate circle on a scale of 0 to 10 to represent how often you had arm pain/discomfort, with 0 being none of the time and 10 being all of the time. **Table 116** shows the Arm Pain Frequency scores for the Primary Analysis Population at pre-operative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 116: Arm Pain Frequency Scores over Time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	173	8.2	2.0	9.0	1.0	10.0	170	7.7	2.3	8.0	0.0	10.0	0.865	0.0	-0.5	0.5
Week 06	173	2.6	3.2	1.0	0.0	10.0	162	2.6	3.0	1.0	0.0	10.0	0.949	0.0	-0.7	0.8
Month 03	173	2.2	2.9	1.0	0.0	10.0	154	2.3	3.0	1.0	0.0	10.0	0.730	-0.1	-0.9	0.6
Month 06	175	1.6	2.4	0.0	0.0	10.0	148	2.0	3.0	1.0	0.0	10.0	0.737	-0.1	-0.8	0.6
Month 12	177	1.8	2.6	1.0	0.0	10.0	136	1.9	2.8	1.0	0.0	10.0	0.798	-0.1	-0.8	0.6
Month 24	167	2.0	2.8	1.0	0.0	10.0	127	1.8	2.6	0.0	0.0	10.0	0.603	0.2	-0.5	0.9

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 116** there was a decline in mean Arm Pain Frequency score at Week 6 which is maintained through the Month 24 follow-up for both treatment groups. The mean pre-op Arm Pain Frequency score for the Simplify® Cervical Artificial Disc cohort was 8.2, which improved to a mean Arm Pain Frequency score of 2.0 at Month 24. Similarly, the mean pre-op Arm Pain Frequency score for the historical ACDF control cohort was 7.7, which improved to a mean Arm Pain Frequency score of 1.8 at Month 24. The Arm Pain Frequency score between the two treatment groups were not statistically significant.

Table 117 presents the change in Arm Pain Frequency score from Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to the baseline for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 117: Arm Pain Frequency Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	170	-5.5	3.4	-7.0	-10.0	3.0	162	-5.0	3.7	-5.0	-10.0	6.0	0.956	0.0	-0.9	0.8
Month 03	167	-6.0	3.3	-7.0	-10.0	3.0	154	-5.2	3.7	-6.0	-10.0	5.0	0.652	-0.2	-1.1	0.7
Month 06	166	-6.5	3.1	-7.0	-10.0	3.0	148	-5.7	3.5	-6.0	-10.0	3.0	0.736	-0.1	-1.0	0.7
Month 12	168	-6.3	3.2	-7.0	-10.0	5.0	136	-5.6	3.5	-6.0	-10.0	7.0	0.739	-0.1	-1.0	0.7
Month 24	158	-6.1	3.3	-7.0	-10.0	5.0	127	-5.9	3.2	-6.0	-10.0	5.0	0.804	0.1	-0.8	1.0

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

Similar to the trends seen in mean scores presented in **Table 116**, the results demonstrated a decline in mean Arm Pain Frequency score at Week 6 which is maintained through the Month 24 follow-up for both groups. The magnitude of mean change in score compared to baseline is maintained through Month 24 both treatment groups. At Month 24, the change in mean Arm Pain Frequency score as compared to baseline was -6.1 for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the change in mean Arm Pain Frequency score at Month 24 as compared to baseline was -5.9. The difference in mean Arm Pain Frequency score was not statistically significant between the two treatment groups.

Table 118 presents the number and percentage of patients showing improvement in Arm Pain Intensity score of at least 2 points compared to baseline at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 118: Arm Pain Frequency 2-Point Responder (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Week 06	170	139	81.8%	162	134	82.7%	0.488	-3.2%	-11.9%	5.5%
Month 03	167	146	87.4%	154	126	81.8%	0.602	2.3%	-6.1%	10.7%
Month 06	166	154	92.8%	148	126	85.1%	0.352	3.5%	-3.7%	10.7%
Month 12	168	149	88.7%	136	119	87.5%	0.915	0.4%	-7.3%	8.2%
Month 24	158	140	88.6%	127	115	90.6%	0.735	-1.4%	-9.0%	6.2%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95%CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 118** the percentage of 2-point responders remains high in both treatment groups through the Month 24 follow up, with the unadjusted Simplify® Cervical Artificial Disc rate numerically higher than the unadjusted historical ACDF control group rate at Month 3 through Month 24. The adjusted group difference was not statistically significant. At Month 24, a total of 88.6% (140/158) of the Simplify® Cervical Artificial Disc subjects achieved at least a 2-point improvement compared to baseline. For historical ACDF control group, a total of 90.6% (115/127) achieved at least a 2-point improvement compared to baseline at the same evaluation timepoint.

Short-Form 36 (SF-36) – Physical Component Score (PCS)

The SF-36 is composed of eight multi-item scales (Physical functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, Mental Health), with scores of each of these scales ranging from 0 to 100, with 0 representing complete disability and 100 representing no disability. The two summary scores are the Physical Component Summary (PCS) score and the Mental Component Summary (MCS) score, which each range from 0 to 100. PCS and MCS are derived by aggregating individual scores. The PCS and MCS scores for the general population in the United States are each 50.[13] A pre-specified threshold score for clinically meaningful improvement was defined as ≥0 points a priori to study initiation.

[13] Brody, T. (2016). Clinical trials: study design, endpoints and biomarkers, drug safety, and FDA and ICH guidelines. Academic press.

Table 119 shows the PCS for the Primary Analysis Population at pre-operative, Month 6, Month 12, and Month 24 timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 119: SF-36 Physical Component Score over Time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	173	31.4	7.6	30.8	11.3	58.9	170	33.0	7.1	33.2	14.0	52.4	0.916	-0.1	-1.8	1.7
Month 06	175	49.2	9.5	50.9	19.0	65.2	147	46.4	10.4	48.7	22.5	63.3	0.039	2.6	0.1	5.1
Month 12	177	48.7	10.1	51.9	18.9	62.1	135	47.7	10.6	51.6	22.7	65.8	0.228	1.6	-1.0	4.2
Month 24	167	49.2	10.0	52.3	17.6	64.8	127	47.9	10.5	51.7	19.1	68.3	0.153	1.9	-0.7	4.6

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 119**, the mean SF-36 PCS score increased from the pre-operative timepoint to Month 6. This increase was maintained through Month 24 follow-up. A statistically significant difference was seen at Month 6 favoring the investigational group ($p<0.05$). At pre-op, the mean SF-36 PCS of the Simplify® Cervical Artificial Disc group was 31.4, which improved to a mean SF-36 PCS of 49.2 at Month 24. Similarly, the mean SF-36 PCS for the historical ACDF control group was 33.0, which improved to a mean SF-36 PCS of 47.9 at Month 24.

Table 120 presents the change in PCS from Month 6, Month 12, and Month 24 timepoints as compared to the baseline for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 120: SF-36 Physical Component Score Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Month 06	166	17.8	10.3	18.8	-13.0	42.6	147	13.1	10.1	13.0	-6.3	37.8	0.026	2.9	0.4	5.5
Month 12	168	17.2	10.9	17.9	-7.2	41.2	135	14.0	9.7	16.5	-9.7	33.1	0.098	2.3	-0.4	4.9
Month 24	158	17.8	11.0	18.5	-9.8	43.8	127	14.1	10.6	14.8	-13.3	34.5	0.065	2.7	-0.2	5.6

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 120**, magnitude of mean change in score compared to baseline is maintained through Month 24. There was a statistically significant difference at Month 6 favoring the investigational group ($p<0.05$). At Month 24, the change in mean SF-36 PCS as compared to baseline was 17.8 for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the change in mean SF-36 PCS at Month 24 as compared to baseline was 14.1.

Table 121 presents the SF-36 PCS Responder Success (Change ≥0 from baseline) for all patients in the study at Month 6, Month 12, and Month 24 follow-up visits. The responder rate is calculated

as the number of patients with SF-36 PCS change from baseline ≥0 divided by the number of patients with completed surveys.

Table 121: SF-36 Physical Component Score Responder Success (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Month 06	166	159	95.8%	147	129	87.8%	0.062	6.2%	-0.3%	12.8%
Month 12	168	155	92.3%	135	124	91.9%	0.899	-0.4%	-6.8%	6.0%
Month 24	158	146	92.4%	127	114	89.8%	0.668	1.6%	-5.4%	8.6%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As shown above, the responder success rate was high through Month 24 follow-up for the Simplify® Cervical Artificial Disc group (92.4%- 146/158) and for the historical ACDF control group (89.8%- 114/127)

Short-Form 36 (SF-36) – Mental Component Score (MCS)

The SF-36 is composed of eight multi-item scales (Physical functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, role-Emotional, Mental Health), with scores of each of these scales ranging from 0 to 100, with 0 representing complete disability and 100 representing no disability. The two summary scores are the Physical Component Summary (PCS) score and the Mental Component Summary (MCS) score, which each range from 0 to 100. PCS and MCS are derived by aggregating individual scores. The PCS and MCS scores for the general population in the United States are each 50.[13]

Table 122 includes the MCS for the Primary Analysis Population at pre-operative, 6-month, 12-month, and 24-month timepoints for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 122: SF-36 Mental Component Score over Time (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	173	41.2	12.3	41.0	10.4	72.1	170	43.2	12.3	44.7	14.5	66.7	0.186	-2.0	-5.0	1.0
Month 06	175	53.2	9.9	56.3	14.5	66.2	147	49.9	11.1	54.4	15.4	66.6	0.150	1.9	-0.7	4.6
Month 12	177	53.7	9.4	56.6	14.4	64.7	135	50.4	11.1	54.5	14.0	67.9	0.036	2.7	0.2	5.3
Month 24	167	53.2	9.8	56.7	18.9	64.5	127	51.2	10.0	54.7	20.0	64.0	0.258	1.5	-1.1	4.1

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 122**, the mean SF-36 MCS increased from the pre-operative timepoint to Month 6. This increase was maintained through Month 24 follow-up. A statistically significant difference was seen at Month 12 favoring the investigational group ($p<0.05$). At pre-op, the mean SF-36 MCS of the Simplify® Cervical Artificial Disc group was 41.2, which improved to a mean SF-36 MCS of 53.2 at Month 24. Similarly, the mean SF-36 MCS for the historical ACDF control group was 43.2, which improved to a mean SF-36 MCS of 51.2 at Month 24.

Table 123 includes the change in SF-36 MCS score from Month 6, Month 12, and Month 24 timepoints as compared to the baseline for both the Simplify® Cervical Artificial Disc and historical ACDF control groups.

Table 123: SF-36 Mental Component Score Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Month 06	166	11.8	12.9	10.8	-22.9	49.7	147	6.0	12.4	3.7	-24.9	44.9	0.004	4.8	1.6	8.0
Month 12	168	12.4	13.7	12.6	-33.0	46.4	135	6.3	13.3	4.8	-27.0	48.1	0.001	5.7	2.2	9.1
Month 24	158	11.7	13.1	12.3	-20.1	51.4	127	7.8	12.2	5.4	-18.9	44.8	0.034	3.6	0.3	7.0

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 123** the magnitude of mean change in score compared to baseline is maintained over time. There was a statistically significant difference at all timepoints favoring the investigational group ($p<0.05$). At Month 24, the change in mean SF-36 MCS as compared to baseline was 11.7 for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the change in mean SF-36 MCS at Month 24 as compared to baseline was 7.8.

Table 124 presents the SF-36 Mental Component Score Responder Success (Change ≥0 from baseline) for all patients at follow-up. The responder rate is calculated as the number of patients with SF-36 MCS change from baseline ≥0 divided by the number of patients with completed surveys.

Table 124: SF-36 Mental Component Score Responder Success (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Month 06	166	134	80.7%	147	104	70.7%	0.243	6.4%	-3.8%	16.6%
Month 12	168	141	83.9%	135	94	69.6%	0.006	15.1%	4.9%	25.4%
Month 24	158	125	79.1%	127	94	74.0%	0.216	7.1%	-3.6%	17.7%

Subjects censored at Index level secondary surgical interventions.
*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As shown above, the responder success rate was higher in the Simplify® Cervical Artificial Disc group as compared to the historical ACDF control group at all follow-ups. This difference was statistically significant at Month 12 ($p<0.05$). The responder success rate at Month 24 follow-up for the Simplify® Cervical Artificial Disc group was 79.1% (125/158) and 74% (94/127) for the historical ACDF control group.

Treatment Satisfaction

Treatment Satisfaction data are not censored following intra-operative deviation or SSI to account for patient perspective of all patients.

Table 125 presents the subject responses for both the Simplify® Cervical Artificial Disc and historical ACDF control groups to the survey statement, "I am satisfied with the results of my

surgery." The response options included "Definitely True," "Mostly True," "Don't Know," "Mostly False," and "Definitely False."

Table 125: Treatment Satisfaction – 'I am satisfied with the results of my surgery' (All Subjects)

	Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%
Definitely True	128	72%	92	62%	131	76%	99	68%
Mostly True	33	19%	44	30%	26	15%	30	21%
Don't Know	10	6%	10	7%	8	5%	7	5%
Mostly False	2	1%	1	1%	5	3%	4	3%
Definitely False	5	3%	2	1%	2	1%	5	3%

Source: Tables Clinical Follow-up - Satisfaction.sas; Analyzed: 11DEC2020

As demonstrated in **Table 125**, a total of 76% (131/172) of Simplify® Cervical Artificial Disc subjects reported that the statement, "I am satisfied with the results of my surgery" were "Definitely True" at Month 24, as compared to a total of 68% (99/145) of this historical ACDF control subjects.

Table 126 presents the patient responses for both the Simplify® Cervical Artificial Disc and historical ACDF control group to the survey statement, "I was helped as much as I thought I would be by my surgery." The response options included "Definitely True," "Mostly True," "Don't Know," "Mostly False," and "Definitely False."

Table 126: Treatment Satisfaction – 'I was helped as much as I thought I would be by my surgery' (All Subjects)

	Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%
Definitely True	121	68%	93	62%	128	74%	93	64%
Mostly True	41	23%	33	22%	28	16%	31	21%
Don't Know	9	5%	13	9%	6	3%	8	6%
Mostly False	0	0%	7	5%	7	4%	5	3%
Definitely False	7	4%	3	2%	3	2%	8	6%

Source: Tables Clinical Follow-up - Satisfaction.sas; Analyzed: 11DEC2020

As demonstrated in **Table 126**, a total of 74% (128/172) of Simplify® Cervical Artificial Disc subjects reported that the statement, "I was helped as much as I thought I would be by my surgery" were "Definitely True" at Month 24, as compared to a total of 64% (93/145) of the historical ACDF control subjects.

Table 127 presents the patient responses for both the Simplify® Cervical Artificial Disc and historical ACDF control group to the survey statement, "All things considered I would have the

surgery again for the same condition." The response options included "Definitely True," "Mostly True," "Don't Know," "Mostly False," and "Definitely False."

Table 127: Treatment Satisfaction – 'All things considered I would have the surgery again for the same condition' (All Subjects)

	Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%
Definitely True	145	81%	114	76%	140	81%	105	72%
Mostly True	20	11%	19	13%	16	9%	23	16%
Don't Know	5	3%	12	8%	10	6%	7	5%
Mostly False	2	1%	2	1%	2	1%	3	2%
Definitely False	6	3%	3	2%	4	2%	7	5%

Source: Tables Clinical Follow-up - Satisfaction.sas; Analyzed: 11DEC2020

As demonstrated in **Table 127,** a total of 81% (140/172) of Simplify® Cervical Artificial Disc subjects reported that the statement, "All things considered I would have the surgery again for the same condition" were "Definitely True" at Month 24, as compared to a total of 72% (105/145) of the historical ACDF control subjects.

Table 128 presents the subject's perceived effect of surgical treatment for both the Simplify® Cervical Artificial Disc and historical ACDF control group. The response options included "Completely Recovered" "Much Improved," "Slightly Improved," "No Change," "Slightly Worsened,", "Much Worsened," and "Vastly Worsened."

Table 128: Treatment Satisfaction – 'Perceived Effect of Surgical treatment?' (All Subjects)

	Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%
Completely Recovered	73	41%	51	34%	86	50%	56	39%
Much Improved	84	47%	72	48%	67	39%	66	46%
Slightly Improved	11	6%	21	14%	11	6%	13	9%
No Change	4	2%	4	3%	4	2%	3	2%
Slightly Worsened	3	2%	1	1%	1	1%	2	1%
Much Worsened	2	1%	1	1%	3	2%	3	2%
Vastly Worsened	1	1%	0	0%	0	0%	2	1%

Source: Tables Clinical Follow-up - Satisfaction.sas; Analyzed: 11DEC2020

As demonstrated in **Table 128**, a total of 50% (86/172) of Simplify® Cervical Artificial Disc subjects reported that their "perceived effect of surgical treatment" were "Completely Recovered" at Month 24, as compared to a total of 39% (56/145) of the historical ACDF control subjects..

Table 129 presents the percentage of subjects deemed an overall Treatment Satisfaction Success as defined as the percentage of subjects meeting the following requirements for both the Simplify® Cervical Artificial Disc and historical ACDF control group:

- Improved = Completely recovered, much improved, or slightly improved
- No change = no change
- Worsened = Slightly worsened, much worsened, vastly worsened

Table 129: Perceived Effect of Surgical Treatment (Overall Treatment Satisfaction Success) (All Subjects)

	Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%
Improved	168	94%	144	96%	164	95%	135	93%
No Change	4	2%	4	3%	4	2%	3	2%
Worsened	6	3%	2	1%	4	2%	7	5%
Source: Tables Clinical Follow-up - Satisfaction.sas; Analyzed: 11DEC2020								

As demonstrated in **Table 129**, a majority of subjects in both treatment groups were considered "Recovered" based on their perceived effect of surgical treatment. At Month 24, the percentage of subjects meeting the requirements for "Improved" was 95% (164/172) for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the percentage of subjects meeting the requirements for "Improved" was 93% (135/145).

Table 130 presents the physician responses for both the Simplify® Cervical Artificial Disc and historical ACDF control group to the Physician Perception of Results survey. The response options included "Excellent," "Good," "Fair," and "Poor."

Table 130: Physician Perception of Results (All Subjects)

	Month 12				Month 24			
	Simplify Disc		ACDF		Simplify Disc		ACDF	
	n	%	n	%	n	%	n	%
Excellent	134	74%	86	57%	139	82%	85	59%
Good	39	22%	44	29%	26	15%	42	29%
Fair	6	3%	19	13%	3	2%	15	10%
Poor	1	1%	1	1%	2	1%	3	2%
Not Done	0	0%	0	0%	0	0%	0	0%
Source: Tables Clinical Follow-up - Satisfaction.sas; Analyzed: 11DEC2020								

As demonstrated in **Table 130**, a higher rate of physicians in the Simplify® Cervical Artificial Disc group reported "Excellent" when asked how they perceived the results Month 12, and Month 24 compared to the historical ACDF control group. At Month 24, the Physician Perception of Results Survey for "Excellent" was 82% (139/170) for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the Physician Perception of Results Survey for "Excellent" was 59% (85/145) at Month 24.

Table 131 presents the subject responses for the investigational group to the statement, "It is important to me that this treatment may reduce the need for radiation exposure from CT scans if I should have a problem in my cervical spine in the future." The response options included "Definitely True," "Mostly True," "Don't Know," "Mostly False," and "Definitely False."

Table 131: Treatment Satisfaction – 'It is important to me that this treatment may reduce the need for radiation exposure from CT scans if I should have a problem in my cervical spine in the future' (Investigational Group)

	Week 06		Month 03		Month 06		Month 12		Month 24	
	Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc	
	n	%	n	%	n	%	n	%	n	%
Definitely True	105	61%	119	69%	118	67%	116	65%	106	62%
Mostly True	32	19%	29	17%	27	15%	34	19%	39	23%
Don't Know	30	17%	21	12%	26	15%	23	13%	21	12%
Mostly False	3	2%	1	1%	3	2%	4	2%	3	2%
Definitely False	2	1%	3	2%	1	1%	1	1%	3	2%

Source: Tables Clinical Follow-up - Satisfaction.sas; Analyzed: 11DEC2020

As demonstrated in **Table 131**, the majority of patients at all timepoints stated "Definitely True". At Month 24, the response to the survey question answered as "Definitely True" was 62% (106/172).

Medication Usage

Patient-reported Medication usage data were collected at preoperative and follow-up timepoints. *Please note, data were collected on medication usage for neck/arm pain, which may not have been specific to the subject pathology. Medication usage is a patient-reported outcome*

Table 132 presents self-reported use of narcotic medication within the past 8 hours at baseline and follow-up timepoints. As shown below, use of non-narcotics decreased in both treatment groups from baseline to Week 6, and this decrease was maintained through all follow up timepoints. There was a statistically significant difference ($p<0.05$) in narcotic use at Month 6 and Month 24 in favor of the investigational group. This difference in narcotic use may be due to the social healthcare focus on reducing prescriptions of narcotics between the time the control data and the investigational data were collected, reflecting more of a change in standard of care rather than differences in the treatments.

Table 132: Medication Use – Any Narcotics (Primary Analysis Population)

	Simplify Disc			ACDF			Group Difference*			
	N	n	%	N	n	%	p	Δ	LB	UB
Pre-Op	173	56	32.4%	170	69	40.6%	0.193	-7.7%	-18.6%	3.2%
Week 06	172	28	16.3%	162	42	25.9%	0.194	-6.4%	-15.7%	2.9%
Month 03	173	23	13.3%	161	34	21.1%	0.267	-5.0%	-13.6%	3.5%
Month 06	176	14	8.0%	155	30	19.4%	0.036	-8.5%	-16.4%	-0.6%
Month 12	178	14	7.9%	149	26	17.4%	0.052	-7.7%	-15.4%	-0.1%
Month 24	172	10	5.8%	144	27	18.8%	0.008	-10.9%	-18.9%	-2.9%

*Device group differences and 95% CI adjusting for propensity score (PS) subclass using two-way generalized linear model.
Source: Tables Medication and Cons Therapy.sas; Analyzed: 11DEC2020

Other Performance Outcomes

Other evaluations of effectiveness included dysphagia handicap index (DHI), return to work status, and time to recovery.

Dysphagia Handicap Index (DHI) Values

Table 133 includes the DHI score for all subjects in the primary analysis population for Simplify® Cervical Artificial Disc group at pre-operative, Week 6, 6-month, 12-month, and 24-month timepoints.

Table 133: DHI scores over time (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Pre-Op	182	10.8	14.3	4.0	0.0	62.0
Week 06	179	10.3	11.9	6.0	0.0	48.0
Month 03	177	7.4	10.4	4.0	0.0	56.0
Month 06	174	7.2	10.8	2.0	0.0	54.0
Month 12	177	6.3	10.4	2.0	0.0	64.0
Month 24	167	6.9	10.7	2.0	0.0	62.0

Subjects censored at Index level secondary surgical interventions.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 133**, there was a decrease in mean DHI at Week 6 which continues through Month 24. At pre-op, the mean DHI score for subjects in the Simplify® Cervical Artificial Disc group was 10.8, which overall decreased to 6.9 at Month 24.

Table 134 includes the change in DHI score from pre-operative for all subjects in the Simplify® Cervical Artificial Disc group at 6-week, 3-month, 6-month, 12-month, and 24-month timepoints.

Table 134: DHI Score Change from Baseline (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Week 06	179	-0.4	14.7	0.0	-52.0	40.0
Month 03	177	-3.5	13.2	-2.0	-52.0	50.0
Month 06	174	-3.5	13.6	-2.0	-50.0	50.0
Month 12	177	-4.6	14.0	-2.0	-52.0	52.0
Month 24	167	-4.3	13.3	-2.0	-52.0	38.0

Subjects censored at Index level secondary surgical interventions.
Source: Tables Clinical Follow-up.sas; Analyzed: 11DEC2020

As demonstrated in **Table 134**, the magnitude of mean change in score compared to baseline is shown to increase over time through Month 24. At Month 24, the change in mean DHI as compared to baseline was -4.3 for the Simplify® Cervical Artificial Disc group.

There were eight (n=8) subjects with reported dysphagia AEs. The DHI scores for these patients are presented below in **Table 135.**

Table 135: DHI Over Time for Dysphagia Subjects

Subject	Pre Op	Week 06	Month 03	Month 06	Month 12	Month 24
A	18	24	14	32	10	2
B	2	32	46	42	32	8
C	4	22	14	4	2	6
D	0	18	20	26	26	24
E	28	26	20	16	18	10
F	2	0	0	18	4	12
G	62	42	56	54	64	62
H	4	44	54	54	56	22

Return to Work Status

Return to work data are censored following intra-operative deviation or SSI. The historical ACDF control group work status is shown in **Table 136**. The Simplify® Cervical Artificial Disc group work status is shown in **Table 137**.

As shown in **Table 136**, 61% (103/170) of the historical ACDF control group were employed pre-operatively and 70% (101/145) were employed at final follow-up.

Table 136: Descriptive Work Status – Control Group (Primary Analysis Population)

	Pre-Op			Week 06			Month 03			Month 06			Month 12			Month 24		
	Control			Control			Control			Control			Control			Control		
	N	n	%	N	n	%	N	n	%	N	n	%	N	n	%	N	n	%
Currently working	170	103	61%	166	52	31%	162	98	60%	156	107	69%	150	103	69%	145	101	70%
Full time	103	88	85%															
Part time	103	15	15%															
Not currently working*	170	67	39%	166	114	69%	162	64	40%	156	49	31%	150	47	31%	145	44	30%
Long term disability																		
Short term disability																		
Not working due to Neck																		
Retired																		
Not employed																		

*Subjects can respond to more than 1, %'s will not add to 100%.
Source: Tables Work Status.sas; Analyzed: 16DEC2020

As shown in **Table 137**, 65% (112/173) of the Simplify® Cervical Artificial Disc group were employed pre-operatively and 74% (126/170) were employed at final follow-up.

Table 137: Descriptive Work Status – Simplify® Cervical Artificial Disc Group (Primary Analysis Population)

	Pre-Op			Week 06			Month 03			Month 06			Month 12			Month 24		
	Simplify Disc			Simplify Disc			Simplify Disc			Simplify Disc			Simplify Disc			Simplify Disc		
	N	n	%	N	n	%	N	n	%	N	n	%	N	n	%	N	n	%
Currently working	173	112	65%	181	89	49%	178	122	69%	178	132	74%	180	133	74%	170	126	74%
Full time	112	94	84%	89	78	88%	122	111	91%	132	121	92%	133	115	86%	126	110	87%
Part time	112	18	16%	89	11	12%	122	11	9%	132	11	8%	133	18	14%	126	16	13%
Not currently working*	173	61	35%	181	92	51%	178	56	31%	178	46	26%	180	47	26%	170	44	26%
Long term disability	61	10	16%	92	12	13%	56	12	21%	46	11	24%	47	12	26%	44	12	27%
Short term disability	61	11	18%	92	27	29%	56	7	13%	46	3	7%	47	2	4%	44	1	2%
Not working due to Neck	61	42	69%	92	42	46%	56	16	29%	46	7	15%	47	7	15%	44	5	11%
Retired	61	10	16%	92	11	12%	56	10	18%	46	11	24%	47	12	26%	44	13	30%
Not employed	61	18	30%	92	16	17%	56	21	38%	46	20	43%	47	20	43%	44	15	34%

*Subjects can respond to more than 1, %'s will not add to 100%.
Source: Tables Work Status.sas; Analyzed: 16DEC2020

Figure 5 is an Alluvial plot showing the Normal employment type at Pre-Op through Month 24 in all subjects who were Employed at baseline. The lines within each plot denote one subject's longitudinal Normal employment journey following their index procedure. In general, in the Simplify® Cervical Artificial Disc arm, it is observed that large proportions of subjects maintained their previous Normal employment type, with only five subjects reporting None as their Normal employment type at Month 6, and nine subjects by Month 24.

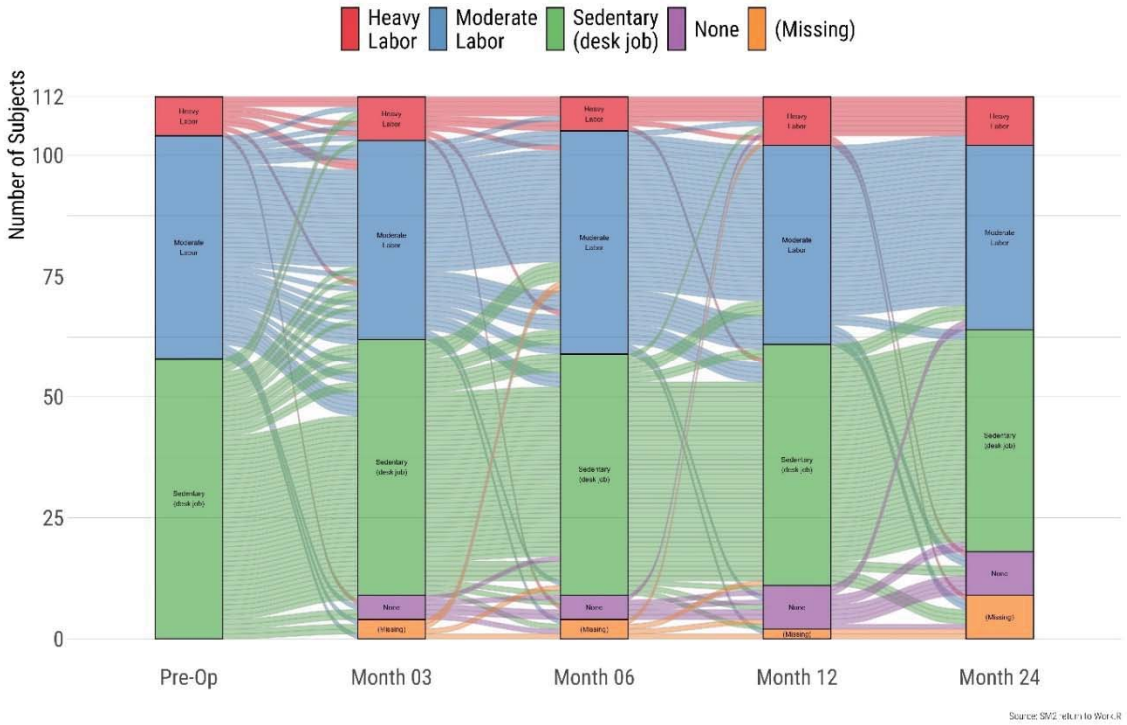


Figure 5: Work Status Alluvial Plot – Simplify® Cervical Artificial Disc Group

Time to Recovery

Time to recovery data are censored following intra-operative deviation or SSI. Time to recovery is defined as time to first 15-point improvement in NDI. At Week 6, 85.5% (153/179) of the investigational group and 62.3% (101/162) of the historical ACDF control group achieved recovery defined as an improvement of at least 15 points. By Month 3, 90.4% (160/177) of the Simplify group and 79.9% (123/154) of the historical ACDF control group achieved recovery.

Radiographic Assessments

<u>Average Disc Height – Superior Adjacent Level</u>

Table 138 describes the Average Disc Height at the superior adjacent level at pre-operative, surgery/discharge, 6-week, 3-month, 6-month, 12-month and 24-month timepoint.

Table 138: Average Disc Height (Superior Adjacent Level) [mm] (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Pre-Op	182	3.83	0.71	3.85	1.20	5.50
Surgery/Discharge	168	3.83	0.72	3.90	1.10	5.60
Week 06	178	3.80	0.72	3.80	1.20	5.50
Month 03	176	3.82	0.71	3.80	1.20	5.50
Month 06	175	3.83	0.73	3.90	1.20	5.50
Month 12	176	3.81	0.73	3.80	1.10	5.60
Month 24	164	3.83	0.71	3.90	1.10	5.60

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 138** the Average Disc Height of the superior adjacent level was maintained through Month 24. At pre-op and at Month 24, the mean Average Disc Height at the superior adjacent level for subjects in the Simplify® Cervical Artificial Disc group was 3.83 mm.

Table 139 describes the change in Average Disc Height at the superior adjacent level over time at surgery/discharge, 6-week, 3-month, 6-month, 12-month and 24-month follow-up visits as compared to baseline.

Table 139: Average Disc Height (Superior Adjacent Level) Change from Baseline (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Surgery/Discharge	168	0.02	0.19	0.00	-0.50	0.80
Week 06	178	-0.04	0.16	-0.10	-0.50	0.40
Month 03	176	-0.03	0.16	0.00	-0.40	0.50
Month 06	175	-0.02	0.16	0.00	-0.50	0.50
Month 12	176	-0.01	0.20	0.00	-0.60	0.50
Month 24	164	-0.03	0.21	0.00	-0.60	0.50

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 139**, the Average Disc Height at the superior adjacent level change compared to baseline was relatively unchanged through Month 24.

Table 140 describes the number and percentage of patients reporting relative maintenance of Average Disc Height of the superior adjacent level at follow-up visits as compared to week 6 (defined as decrease from week 6 of less than 2mm).

Table 140: Average Disc Height (Superior Adjacent Level) Responder (Primary Analysis Population)

	Simplify Disc		
	N	n	%
Month 03	173	173	100.0%
Month 06	173	173	100.0%
Month 12	174	174	100.0%
Month 24	164	164	100.0%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas;
Analyzed: 12DEC2020

As demonstrated in **Table 140**, all Simplify® Cervical Artificial Disc subjects exhibited relative maintenance of Average Disc Height at the superior adjacent level.

Average Disc Height – Index Levels

Table 141 describes the Average Disc Height at the superior index level at pre-operative, surgery/discharge, 6-week, 3-month, 6-month, 12-month and 24-month timepoints.

Table 141: Average Disc Height (Superior Index Level) [mm] (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Pre-Op	182	3.14	0.73	3.10	1.60	5.70
Surgery/Discharge	167	5.07	0.88	5.00	2.50	7.40
Week 06	178	4.59	0.85	4.60	2.00	7.20
Month 03	176	4.52	0.82	4.50	2.10	7.30
Month 06	175	4.47	0.83	4.50	1.80	7.30
Month 12	177	4.40	0.84	4.40	1.90	7.00
Month 24	164	4.33	0.82	4.35	2.40	7.00

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 141**, the Average Disc Height at the superior index level increased post-operatively and the increase was maintained through Month 24. At pre-op, the mean Average Disc Height at the superior index level for subjects in the Simplify® Cervical Artificial Disc group was 3.14 mm, which overall increased to 4.33 mm at Month 24.

Table 142 describes the change in Average Disc Height at the superior index level over time at surgery/discharge, 6-week, 3-month, 6-month, 12-month and 24-month at follow-up visits as compared to baseline.

Table 142: Average Disc Height (Superior Index Level) [mm] Change from Baseline (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Surgery/Discharge	167	1.92	0.75	2.00	-0.60	3.90
Week 06	178	1.45	0.78	1.45	-0.70	3.60
Month 03	176	1.37	0.77	1.30	-0.70	3.60
Month 06	175	1.31	0.80	1.30	-1.20	3.70
Month 12	177	1.26	0.81	1.30	-1.20	3.30
Month 24	164	1.19	0.81	1.20	-1.00	3.00

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 142**, the Average Disc Height at the superior index level increased post-operatively and the increase was maintained through Month 24. At surgery/discharge, the mean Average Disc Height at the superior index level for subjects in the Simplify® Cervical Artificial Disc group increased by 1.92 mm. At Month 24, the mean change in Average Disc Height at the superior index level for subjects in the Simplify® Cervical Artificial Disc group was 1.19 mm.

Table 143 describes the number and percentage of subjects reporting relative maintenance of Average Disc Height at the superior index level at follow-up visits as compared to week 6 (defined as decrease from week 6 of less than 2mm).

Table 143: Average Disc Height (Superior Index Level) Responder (Primary Analysis Population)

	Simplify Disc		
	N	n	%
Month 03	173	173	100.0%
Month 06	173	173	100.0%
Month 12	175	175	100.0%
Month 24	164	164	100.0%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas;
Analyzed: 12DEC2020

As demonstrated in **Table 143**, all subjects in the Simplify® Cervical Artificial Disc group were considered responders in Average Disc Height at the superior index level.

Table 144 describes the Average Disc Height at the inferior index level over time at pre-operative, surgery/discharge, 6-week, 3-month, 6-month, 12-month and 24-month timepoint.

Table 144: Average Disc Height (Inferior Index Level) [mm] (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Pre-Op	176	3.13	0.85	3.10	1.10	6.30
Surgery/Discharge	155	4.80	0.87	4.90	2.10	7.20
Week 06	172	4.29	0.92	4.40	1.00	6.60
Month 03	171	4.20	0.94	4.30	1.00	6.60
Month 06	167	4.15	0.92	4.20	0.90	6.40
Month 12	173	4.08	0.92	4.20	1.50	6.30
Month 24	159	3.98	0.97	4.10	1.40	6.30

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 144** , the Average Disc Height at the inferior index level increased post-operatively and the increase was maintained through Month 24. At pre-op, the mean Average Disc Height at the inferior index level for subjects in the Simplify® Cervical Artificial Disc group was 3.13 mm, which overall increased to 3.98 mm at Month 24.

Table 145 describes the change in Average Disc Height at the inferior index level over time at surgery/discharge, 6-week, 3-month, 6-month, 12-month and 24-month follow-up visits as compared to baseline.

Table 145: Average Disc Height (Inferior Index Level) [mm] Change from Baseline (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Surgery/Discharge	153	1.67	0.88	1.60	-1.50	4.00
Week 06	170	1.13	0.92	1.20	-1.70	3.60
Month 03	168	1.05	0.95	1.10	-1.70	3.50
Month 06	166	0.98	0.94	1.05	-1.80	3.40
Month 12	170	0.94	0.90	1.00	-1.50	3.60
Month 24	157	0.84	0.96	0.90	-2.40	3.30

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 145**, the Average Disc Height at the inferior index level increased post-operatively and the increase was maintained through Month 24. At surgery/discharge, the mean Average Disc Height at the inferior index level for subjects in the Simplify® Cervical Artificial Disc group increased by 1.67 mm. At Month 24, the mean change in Average Disc Height at the inferior index level for subjects in the Simplify® Cervical Artificial Disc group was 0.84 mm.

Table 146 describes the number and percentage of patients reporting relative maintenance of Average Disc Height of the inferior index level at follow-up visits as compared to week 6 (defined as decrease from week 6 of less than 2mm).

Table 146: Average Disc Height (Inferior Index Level) Responder (Primary Analysis Population)

	Simplify Disc		
	N	n	%
Month 03	167	167	100.0%
Month 06	165	165	100.0%
Month 12	169	169	100.0%
Month 24	159	156	98.1%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas;
Analyzed: 12DEC2020

As demonstrated in **Table** 146, all subjects in the Simplify® Cervical Artificial Disc group were considered responders in Average Disc Height at the inferior index level through Month 12. At Month 24, 156/159 subjects (98.1%) were considered responders in Average Disc Height at the inferior index level.

Average Disc Height – Inferior Adjacent Level

Table 147 describes the Average Disc Height at the inferior adjacent level at pre-operative, surgery/discharge, 6-week, 3-month, 6-month, 12-month and 24-month timepoint.

Table 147: Average Disc Height (Inferior Adjacent Level) [mm] (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Pre-Op	93	3.85	0.66	3.90	2.10	5.30
Surgery/Discharge	74	3.83	0.69	3.80	2.10	5.40
Week 06	91	3.74	0.67	3.80	1.80	5.50
Month 03	92	3.74	0.69	3.80	1.80	5.60
Month 06	90	3.74	0.67	3.80	1.80	5.60
Month 12	93	3.72	0.69	3.80	1.70	5.40
Month 24	89	3.68	0.69	3.70	1.80	5.20

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 147**, the Average Disc Height at the inferior adjacent level remained relatively unchanged as compared to pre-operative. At pre-op, the mean Average Disc Height at the inferior adjacent level for subjects in the Simplify® Cervical Artificial Disc group was 3.85 mm, which overall decreased to 3.68 mm at Month 24.

Table 148 describes the change in Average Disc Height of the inferior adjacent level at surgery/discharge, 6-week, 3-month, 6-month, 12-month and 24-month follow-up visits as compared to baseline.

Table 148: Average Disc Height (Inferior Adjacent Level) [mm] Change from Baseline (Primary Analysis Population)

	Simplify Disc					
	N	Mean	SD	Med	Min	Max
Surgery/Discharge	70	0.03	0.17	0.00	-0.30	0.50
Week 06	86	-0.05	0.15	-0.10	-0.40	0.50
Month 03	86	-0.06	0.18	-0.10	-0.60	0.40
Month 06	82	-0.07	0.18	-0.10	-0.50	0.40
Month 12	85	-0.08	0.21	-0.10	-0.90	0.40
Month 24	77	-0.09	0.23	-0.10	-1.20	0.40

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 148**, the Average Disc Height at the inferior adjacent level remained relatively unchanged with a mean Average Disc Height change of -0.09 at Month 24.

Table 149 describes the number and percentage of patients reporting relative maintenance of Average Disc Height of the inferior adjacent level at follow-up visits as compared to week 6 (defined as decrease from week 6 of less than 2mm).

Table 149: Average Disc Height (Inferior Adjacent Level) Responder (Primary Analysis Population)

	Simplify Disc		
	N	n	%
Month 03	85	85	100.0%
Month 06	82	82	100.0%
Month 12	85	85	100.0%
Month 24	80	80	100.0%

Subjects censored at Index level secondary surgical interventions.
Source: Tables Quantitative Radiography.sas;
Analyzed: 12DEC2020

As demonstrated in **Table 149**, all subjects in the Simplify® Cervical Artificial Disc group were considered responders in Average Disc Height at the inferior adjacent level through Month 24.

Intervertebral Angle (Flexion/Extension)
Measurements utilized for this assessment were made using line drawings for the historical control group and Quantitative Motion Analysis (QMA®) for the Simplify® Cervical Artificial Disc group.

Regression equations supplied by the independent core lab were used to correct for differences in the methodologies, reduce bias, and allow for direct comparison of the two methods.

Table 150 describes the Intervertebral Angle at the superior adjacent level at pre-operative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoint.

Table 150: Intervertebral Angle (Superior Adjacent Level) [degrees] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	181	10.32	4.56	10.50	0.10	21.70	162	13.02	5.30	12.86	1.37	24.98	<.001	-2.23	-3.42	-1.05
Week 06	160	9.14	3.95	8.90	0.00	23.20	150	10.45	4.60	10.35	1.61	25.28	0.100	-0.92	-2.01	0.18
Month 03	175	10.33	4.16	10.30	0.00	22.60	152	12.38	4.93	11.90	1.43	26.08	0.016	-1.41	-2.54	-0.27
Month 06	175	11.43	4.12	11.60	0.00	23.00	147	13.43	5.38	13.88	2.43	29.66	0.008	-1.64	-2.85	-0.43
Month 12	176	11.44	4.38	11.45	0.10	22.90	134	14.69	5.58	14.68	3.02	30.78	<.001	-2.68	-3.93	-1.43
Month 24	164	11.84	4.28	11.75	0.00	22.60	120	14.53	6.03	13.89	1.46	31.67	0.003	-2.07	-3.42	-0.72

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

The mean Intervertebral Angle at the superior adjacent level was significantly less for the Simplify® Cervical Artificial Disc group at pre-operative as compared to ACDF. As demonstrated, the Intervertebral Angle of the superior adjacent level was maintained through Month 24. At pre-op, the mean Intervertebral Angle at the superior adjacent level for subjects in the Simplify® Cervical Artificial Disc group was 10.32°, which overall increased to 11.84° at Month 24. Similarly, the mean Intervertebral Angle at the superior adjacent level for the historical ACDF control group was 13.02°, which overall increased to a mean of 14.53° at Month 24.

Table 151 describes the change in Intervertebral Angle at the superior adjacent level at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to pre-operative.

Table 151: Intervertebral Angle (Superior Adjacent Level) [degrees] Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	159	-1.29	3.68	-1.30	-12.80	13.40	142	-2.84	5.09	-3.04	-16.36	9.74	0.009	1.52	0.38	2.66
Month 03	174	-0.11	3.87	-0.20	-14.50	13.60	144	-0.80	5.50	-0.63	-15.70	12.40	0.143	0.89	-0.30	2.08
Month 06	174	1.10	3.72	0.90	-7.50	15.80	140	0.18	5.62	0.35	-15.79	17.35	0.179	0.83	-0.38	2.03
Month 12	175	1.13	3.98	0.80	-9.40	17.10	127	1.67	6.07	1.31	-11.88	21.78	0.688	-0.26	-1.55	1.02
Month 24	163	1.61	3.98	0.80	-10.10	17.60	114	1.72	6.80	1.71	-16.25	16.12	0.707	0.27	-1.16	1.71

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 151**, relatively similar change scores were exhibited across the Simplify® Cervical Artificial Disc and historical ACDF control group. The mean Intervertebral Angle change from baseline at the superior adjacent level at Month 24 was 1.61° for the Simplify® Cervical Artificial Disc group and 1.72° for the historical ACDF control group.

Table 152 describes the Intervertebral Angle at the superior index level at pre-operative, post-operative, Month 3, Month 6, Month 12, and Month 24 timepoint.

Table 152: Intervertebral Angle (Superior Index Level) [degrees] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	178	7.96	4.60	7.60	0.20	23.80	162	9.51	5.09	8.94	1.53	24.66	0.176	-0.80	-1.97	0.36
Week 06	160	6.99	3.75	6.40	0.10	18.60	149	4.38	2.36	3.80	1.29	13.00	<.001	2.75	1.94	3.55
Month 03	175	8.23	4.30	7.60	0.60	21.10	151	3.97	2.56	3.29	1.16	13.58	<.001	4.56	3.66	5.46
Month 06	174	9.04	4.57	8.60	0.40	20.60	148	3.12	1.44	2.82	1.04	7.16	<.001	6.45	5.57	7.33
Month 12	176	8.85	5.27	8.10	0.10	21.40	134	2.67	1.26	2.46	1.08	7.85	<.001	6.61	5.58	7.65
Month 24	163	9.53	5.39	8.80	0.10	21.70	123	3.10	1.60	2.87	1.11	10.01	<.001	6.93	5.82	8.03

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated, Intervertebral Angle at the superior index level increased at 3 Months and the increase was maintained through the latest follow-up for the investigational group. In contrast the historical control group exhibited a decrease in Intervertebral Angle as expected with a fusion procedure. Statistically significant differences were seen between the two groups at all follow-up timepoints. At pre-op, the mean Intervertebral Angle at the superior index level for subjects in the Simplify® Cervical Artificial Disc group was 7.96°, which overall increased to 9.53° at Month 24. Similarly, the mean Intervertebral Angle at the superior index level for the historical ACDF control group was 9.51°, which overall decreased to a mean of 3.10° at Month 24.

Table 153 describes the change in Intervertebral Angle at the superior index level over time at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to pre-operative.

Table 153: Intervertebral Angle (Superior Index Level) [degrees] Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	156	-1.07	4.34	-0.70	-13.10	13.60	141	-5.16	5.67	-4.92	-20.15	8.09	<.001	3.48	2.18	4.77
Month 03	171	0.18	4.70	0.50	-13.30	14.80	143	-5.55	5.69	-4.75	-21.41	6.14	<.001	5.38	4.05	6.70
Month 06	171	1.06	5.10	1.00	-11.00	16.50	141	-6.60	5.29	-5.75	-19.28	2.81	<.001	7.46	6.12	8.79
Month 12	172	0.90	5.47	0.55	-13.60	15.40	127	-6.94	5.43	-6.41	-22.09	3.73	<.001	7.62	6.20	9.04
Month 24	161	1.62	5.81	1.50	-12.30	18.50	117	-6.44	4.92	-6.08	-19.79	1.30	<.001	7.93	6.47	9.38

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 153**, statistically significant differences were seen between the two groups at all timepoints, with the Simplify® Cervical Artificial Disc group reporting a mean increase from baseline in Intervertebral Angle at the Superior Index Level of 1.62° at Month 24, compared to the historical ACDF control group, which reported a mean decrease from baseline in Intervertebral Angle at the Superior Index Level of -6.44° ($p<0.001$).

Table 154 describes the Intervertebral Angle at the inferior index level at pre-operative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 154: Intervertebral Angle (Inferior Index Level) [degrees] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	165	6.56	4.02	6.20	0.20	21.30	148	7.44	3.90	6.60	1.44	23.21	0.159	-0.72	-1.72	0.28
Week 06	147	7.27	3.75	7.10	0.00	18.00	141	4.76	2.45	4.25	1.05	14.15	<.001	2.47	1.64	3.31
Month 03	157	8.47	4.50	8.10	0.30	24.30	142	4.04	2.22	3.90	1.01	11.23	<.001	4.72	3.78	5.65
Month 06	160	8.90	4.96	8.25	0.20	22.30	139	3.11	1.76	2.58	1.10	13.93	<.001	6.22	5.22	7.21
Month 12	162	8.48	5.45	8.60	0.10	23.00	125	2.93	1.71	2.49	1.07	10.95	<.001	5.83	4.71	6.95
Month 24	150	8.86	5.62	8.45	0.00	23.20	120	3.91	2.93	3.01	1.09	23.01	<.001	5.38	4.13	6.63

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 154**, the Intervertebral Angle at the inferior index level increased post-operatively and the increase was maintained through the latest follow-up for the investigational group. Statistically significant differences were seen at all timepoints between the two groups. At pre-op, the mean Intervertebral Angle at the inferior index level for subjects in the Simplify® Cervical Artificial Disc group was 6.56°, which overall increased to 8.86° at Month 24. The mean Intervertebral Angle at the inferior index level for the historical ACDF control group at pre-op was 7.44°, which overall decreased to a mean of 3.91° at Month 24.

Table 155 describes the change in Intervertebral Angle at the inferior index level over time at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to pre-operative.

Table 155: Intervertebral Angle (Inferior Index Level) [degrees] Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	139	0.83	3.87	1.00	-9.70	11.30	128	-3.14	4.72	-2.84	-16.30	6.54	<.001	3.87	2.70	5.04
Month 03	149	1.81	4.11	1.70	-12.90	14.70	129	-3.69	4.68	-3.17	-17.20	6.49	<.001	5.76	4.57	6.95
Month 06	154	2.43	4.65	2.45	-12.50	16.00	127	-4.68	3.97	-3.61	-19.25	4.63	<.001	7.40	6.23	8.57
Month 12	155	2.07	5.04	1.70	-11.00	16.80	112	-4.59	4.11	-4.13	-19.86	9.20	<.001	6.89	5.61	8.16
Month 24	145	2.47	5.23	2.20	-12.70	16.20	106	-3.71	4.97	-3.47	-21.27	17.45	<.001	6.60	5.17	8.03

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

Statistically significant differences were seen between the two groups at all timepoints in favor of the Simplify® Cervical Artificial Disc group, indicating a maintenance of motion in the Simplify® Cervical Artificial Disc group and a loss of motion in the historical ACDF control group. At Month 24, the change in mean Intervertebral Angle at the inferior index level as compared to baseline was 2.47° for the Simplify® Cervical Artificial Disc group. For the historical ACDF control group, the change in mean Intervertebral Angle at the inferior index level at Month 24 as compared to baseline was -3.71°.

Table 156 describes the Intervertebral Angle of the inferior adjacent level at pre-operative, Week 6, Month 3, Month 6, Month 12, and Month 24 timepoint.

Table 156: Intervertebral Angle (Inferior Adjacent Level) [degrees] (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Pre-Op	81	5.16	4.00	4.80	0.00	17.00	103	6.87	3.95	5.60	1.25	19.34	0.016	-1.71	-3.10	-0.32
Week 06	67	4.72	3.85	3.80	0.20	17.50	93	7.20	3.51	6.68	1.44	18.34	<.001	-2.38	-3.77	-0.99
Month 03	81	5.57	4.21	4.70	0.20	19.70	87	7.71	3.90	6.99	1.26	18.90	0.004	-2.19	-3.69	-0.70
Month 06	85	5.84	4.22	5.30	0.00	21.20	87	8.68	4.66	8.05	1.83	22.60	<.001	-3.04	-4.62	-1.47
Month 12	82	5.96	4.56	4.65	0.00	21.00	83	7.89	4.39	6.80	1.49	20.68	0.122	-1.26	-2.86	0.34
Month 24	81	6.64	4.68	6.00	0.10	21.60	96	8.61	4.63	7.59	1.51	20.81	0.065	-1.53	-3.15	0.10

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated, the Intervertebral Angle of the inferior adjacent level was maintained through latest follow-up. At pre-op, the mean Intervertebral Angle at the inferior adjacent level for subjects in the Simplify® Cervical Artificial Disc group was 5.16°, which overall increased to 6.64° at Month 24. Similarly, the mean Intervertebral Angle at the inferior adjacent level for the historical ACDF control group at pre-op was 6.87°, which overall increased to a mean of 8.61° at Month 24.

Table 157 describes the change in Intervertebral Angle of the inferior adjacent level at Week 6, Month 3, Month 6, Month 12, and Month 24 timepoints as compared to pre-operative.

Table 157: Intervertebral Angle (Inferior Adjacent Level) [degrees] Change from Baseline (Primary Analysis Population)

	Simplify Disc						ACDF						Group Difference*			
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p	Δ	LB	UB
Week 06	55	-0.40	3.45	-0.50	-9.70	6.80	77	0.28	4.86	0.52	-12.67	11.86	0.609	-0.48	-2.32	1.36
Month 03	70	0.25	3.07	-0.05	-8.90	8.80	73	0.98	3.67	0.58	-7.81	10.74	0.474	-0.48	-1.82	0.85
Month 06	70	0.82	3.44	0.40	-6.20	10.20	73	1.66	4.49	1.33	-8.80	12.36	0.201	-1.03	-2.61	0.56
Month 12	64	0.89	3.10	1.00	-7.10	8.40	66	1.53	4.77	0.90	-12.89	12.74	0.897	0.11	-1.53	1.75
Month 24	62	1.76	3.31	1.30	-5.40	9.00	67	2.53	4.64	2.89	-7.04	12.84	0.579	0.45	-1.14	2.03

Subjects censored at Index level secondary surgical interventions.
*Device group mean differences and 95% CI adjusting for propensity score (PS) subclass using two-way analysis of variance.
Source: Tables Quantitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated in **Table 157**, relatively similar changes in Intervertebral Angle at the inferior adjacent level were exhibited in the Simplify® Cervical Artificial Disc group and historical ACDF control group through Month 24.

Device Failure

Device Condition was assessed in the Simplify® Cervical Artificial Disc group as follows:

Simplify® Cervical Artificial Disc Device

0. Intact: No evidence of dislocation or fracture of the device components.
1. Failed Superior Component: Fracture or deformation of the superior endplate.
2. Failed Core: Fracture or other failure of the core.
3. Failed Inferior Component: Fracture or deformation of the inferior endplate.
4. Disassembled: Dislocation or permanent subluxation of the articulating components of the implant. (Permanent subluxation is defined as severe (i.e., >50%) misalignment of the device components that does not reduce in flexion-extension or lateral bending.)

There is little or no motion across the implant in the plane of the subluxation or dislocation.

Device Migration was evaluated in the Simplify® Cervical Artificial Disc group to assess significant movement of the implant and is graded as None or Present. A threshold of >3 mm of implant motion was used to define significance.

In the historical ACDF control group all postoperative radiographs of the spine were evaluated for signs of bending or fracture and separation of the components. Additionally, AP and lateral neutral radiographs were evaluated for signs of migration >3mm in the anterior, posterior, or lateral direction compared to the baseline (surgery/ discharge) films.

There were no observations of failure of device condition or device migration in either group according to the device specific definitions.

Kellgren-Lawrence Adjacent Level Disc Degeneration (ALDD)

Kellgren-Lawrence ALDD at adjacent levels is graded as None, Doubtful, Minimal, Moderate or Severe and adapted from Kellgren and Lawrence.[14]

0. None: No degenerative changes.
1. Doubtful: Minimal osteophytosis only.
2. Minimal: Definite osteophytosis with some sclerosis of anterior part of vertebral plates.
3. Moderate: Marked osteophytosis and sclerosis of vertebral plates with slight narrowing of disk space.
4. Severe: Large osteophytes, marked sclerosis of vertebral plates, and marked narrowing of disk space.

The assessment of Kellgren-Lawrence ALDD is graded by the reviewers based on an assessment from x-ray of three component factors: disc space narrowing (assessed relative to a nearby normal disc), osteophyte formation and endplate sclerosis. This measurement was performed in the investigational group only.

Table 158 reports the number and percentage of patients with radiographic confirmation of disc space narrowing, osteophyte formation, and endplate sclerosis at the superior adjacent level at pre-operative, Month 3, Month 6, Month 12, and Month 24 timepoints.

[14] Kellgren J, Lawrence J. Osteo-arthrosis and disk degeneration in an urban population. *British Medical Journal* 1958;17:388

Table 158: KL Grade (Superior Adjacent Level) (Primary Analysis Population)

	Pre-Op		Month 03		Month 06		Month 12		Month 24	
	Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc	
	n	%	n	%	n	%	n	%	n	%
None	122	67%	118	67%	115	65%	114	64%	100	60%
Doubtful	43	24%	44	25%	44	25%	46	26%	45	27%
Minimal	12	7%	10	6%	12	7%	12	7%	16	10%
Moderate	3	2%	3	2%	2	1%	4	2%	2	1%
Severe	2	1%	1	1%	2	1%	1	1%	1	1%
Indeterminate	0	0%	0	0%	0	0%	0	0%	0	0%
Unable to assess	0	0%	0	0%	1	1%	0	0%	2	1%
Not Applicable	0	0%	0	0%	0	0%	0	0%	0	0%
Not Required	0	0%	0	0%	0	0%	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Qualitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated, the majority of patients were given a Kellgren-Lawrence grade of 'None' at all timepoints. A total of 60% (100/166) of Simplify® Cervical Artificial Disc subjects were given a Kellgren-Lawrence grade of 'None' at Month 24.

Table 159 reports the number and percentage of patients with radiographic confirmation of disc space narrowing, osteophyte formation, and endplate sclerosis at the inferior adjacent level at pre-operative, Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 159: KL Grade (Inferior Adjacent Level) (Primary Analysis Population)

	Pre-Op		Month 03		Month 06		Month 12		Month 24	
	Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc	
	n	%	n	%	n	%	n	%	n	%
None	140	77%	130	74%	124	70%	124	70%	110	66%
Doubtful	19	10%	17	10%	17	10%	19	11%	20	12%
Minimal	6	3%	5	3%	6	3%	9	5%	9	5%
Moderate	3	2%	3	2%	2	1%	2	1%	2	1%
Severe	0	0%	1	1%	1	1%	1	1%	1	1%
Indeterminate	14	8%	20	11%	24	14%	21	12%	21	13%
Unable to assess	0	0%	0	0%	2	1%	1	1%	3	2%
Not Applicable	0	0%	0	0%	0	0%	0	0%	0	0%
Not Required	0	0%	0	0%	0	0%	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Qualitative Radiography.sas; Analyzed: 12DEC2020

As demonstrated, the majority of patients were given a Kellgren-Lawrence grade of None at all timepoints. A total of 66% (110/166) of Simplify® Cervical Artificial Disc subjects were given a Kellgren-Lawrence grade of 'None' at Month 24.

Facet Degeneration

Facet degeneration was assessed using MRI and graded in accordance with the following definitions:[15,16]

0. None: Normal facet joint space.
1. Mild: Narrowing of the facet joint space and/or small osteophytes and/or mild hypertrophy of the articular process.
2. Moderate: Narrowing of the facet joint space and/or moderate osteophytes and/or moderate hypertrophy of the articular process and/or mild subarticular bone erosions.
3. Severe: Narrowing of the facet joint space and/or large osteophytes and/or sever hypertrophy of the articular process and/or severe subarticular bone erosions and/or subchondral cysts.

This measurement was performed in the Simplify® Cervical Artificial Disc group only.

Table 160 presents the number and percentage of subjects with evidence of facet degeneration at the superior adjacent level at the pre-operative and 24-month timepoints. Similar rates of facet degeneration were seen in the Simplify® Cervical Artificial Disc group at pre-operative and Month 24 at the superior adjacent level. At pre-op, 25% (46/182) of Simplify® Cervical Artificial Disc subjects were identified to have some degree of facet degeneration at the superior adjacent level, while similarly 26% (43/166) were found to have some degree of facet degeneration at Month 24.

Table 160: Facet Degeneration (Superior Adjacent Level) (Primary Analysis Population)

	Pre-Op		Month 24	
	Simplify Disc		Simplify Disc	
	n	%	n	%
None	134	74%	121	73%
Mild	34	19%	33	20%
Moderate	10	5%	8	5%
Severe	2	1%	2	1%
Indeterminate	0	0%	0	0%
Unable to assess	2	1%	2	1%
Not Applicable	0	0%	0	0%
Not Required	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Qualitative Radiography.sas; Analyzed: 12DEC2020

Table 161 presents the number and percentage of subjects with evidence of facet degeneration at the superior index level observed at the pre-operative and 24-month timepoints. Pre-operatively,

[15] Weishaupt D, Zanetti M, Boos N, Hodler J. MR imaging and CT in osteoarthritis of the lumbar facet joints. Skeletal Radiology 28:215-219. (1999) 28:215-219. 1999.
[16] Fujiwara A, Tamai K, Yamato M, An HS, Yoshida H, Saotome K, Kurihashi A. The relationship between facet joint osteoarthritis and disc degeneration of the lumbar spine: an MRI study. Eur Spine J 8:396-401. 1999.

37% (68/182) of Simplify® Cervical Artificial Disc subjects were identified to have some degree of facet degeneration at the superior index level, while 46% (77/166) were found to have some degree of facet degeneration at Month 24.

Table 161: Facet Degeneration (Superior Index Level) (Primary Analysis Population)

	Pre-Op		Month 24	
	Simplify Disc		Simplify Disc	
	n	%	n	%
None	112	62%	87	52%
Mild	54	30%	64	39%
Moderate	14	8%	13	8%
Severe	0	0%	0	0%
Indeterminate	0	0%	0	0%
Unable to assess	2	1%	2	1%
Not Applicable	0	0%	0	0%
Not Required	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Qualitative Radiography.sas; Analyzed: 12DEC2020

Table 162 presents the number and percentage of subjects with evidence of facet degeneration at the inferior index level at the pre-operative and 24-month timepoints. Similar rates of facet degeneration were seen in the Simplify® Cervical Artificial Disc group pre-operatively and at Month 24 at the inferior index level. Pre-operatively, 34% (62/182) of Simplify® Cervical Artificial Disc subjects were identified to have some degree of facet degeneration at the inferior index level, while 41% (68/166) were found to have some degree of facet degeneration at Month 24.

Table 162: Facet Degeneration (Inferior Index Level) (Primary Analysis Population)

	Pre-Op		Month 24	
	Simplify Disc		Simplify Disc	
	n	%	n	%
None	118	65%	96	58%
Mild	53	29%	60	36%
Moderate	9	5%	8	5%
Severe	0	0%	0	0%
Indeterminate	0	0%	0	0%
Unable to assess	2	1%	2	1%
Not Applicable	0	0%	0	0%
Not Required	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Qualitative Radiography.sas; Analyzed: 12DEC2020

Table 163 presents the number and percentage of subjects with evidence of facet degeneration at the inferior adjacent level at the pre-operative and 24-month timepoints. Similar rates of facet degeneration were seen in the Simplify® Cervical Artificial Disc group pre-operatively and at Month 24 at the inferior adjacent level. Pre-operatively, 8% (14/182) of Simplify® Cervical Artificial Disc subjects were identified to have some degree of facet degeneration at the inferior

adjacent level, while 10% (16/166) were found to have some degree of facet degeneration at Month 24.

Table 163: Facet Degeneration (Inferior Adjacent Level) (Primary Analysis Population)

	Pre-Op		Month 24	
	Simplify Disc		Simplify Disc	
	n	%	n	%
None	165	91%	148	89%
Mild	11	6%	13	8%
Moderate	3	2%	3	2%
Severe	0	0%	0	0%
Indeterminate	1	1%	0	0%
Unable to assess	2	1%	2	1%
Not Applicable	0	0%	0	0%
Not Required	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Qualitative Radiography.sas; Analyzed: 12DEC2020

Heterotopic Ossification

Heterotopic ossification was measured in the investigational group using the following definitions:

0. None (Grade 0): No evidence of osteophyte formation or heterotopic ossification.

1. Mild (Grade 1): HO is detectable in the front or sides or the vertebral body, or as islands of bone in the adjacent soft tissue, but is not in the intervertebral disc space. Bone is not present between the planes formed by the two vertebral endplates.

2. Moderate (Grade 2): HO is growing into the disc space. Bone is present between the planes formed by the two adjacent endplates but is not significantly blocking or articulating between adjacent vertebral endplates or osteophytes.

3. Severe (Grade 3): The range of motion of the vertebral endplates is likely blocked by the formation of HO and/ or postoperative osteophytes on the radiographs, but some movement of the prosthesis may remain.

4. Bridging (Grade 4): HO is causing bony ankylosis. An apparent continuous connection of bridging bone exists between the adjacent vertebral endplates with little or no motion occurring across the treated segment.

Table 164 presents heterotopic ossification grades of the superior index level for all treated subjects at Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 164: Heterotopic Ossification (Superior Index Level) (Primary Analysis Population)

	Month 03		Month 06		Month 12		Month 24	
	Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc	
	n	%	n	%	n	%	n	%
None (Grade 0)	119	68%	92	52%	46	26%	21	13%
Mild (Grade 1)	41	23%	40	23%	29	16%	21	13%
Moderate (Grade 2)	15	9%	40	23%	92	52%	106	64%
Severe (Grade 3)	1	1%	3	2%	5	3%	8	5%
Bridging (Grade 4)	0	0%	0	0%	5	3%	8	5%
Indeterminate	0	0%	0	0%	0	0%	0	0%
Unable to assess	0	0%	1	1%	0	0%	2	1%
Not Applicable	0	0%	0	0%	0	0%	0	0%
Not Required	0	0%	0	0%	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Qualitative Radiography.sas; Analyzed: 12DEC2020

As shown above, moderate or lower heterotopic ossification was observed in the majority of subjects (89% - 148/166) at Month 24. Few Simplify® Cervical Artificial Disc subjects experienced Grade 3 (5% - 8/166) or Grade 4 (5% - 8/166) heterotopic ossification at Month 24.

Table 165 presents heterotopic ossification grades of the inferior index level for all treated subjects at Month 3, Month 6, Month 12, and Month 24 timepoints.

Table 165: Heterotopic Ossification (Inferior Index Level) (Primary Analysis Population)

	Month 03		Month 06		Month 12		Month 24	
	Simplify Disc		Simplify Disc		Simplify Disc		Simplify Disc	
	n	%	n	%	n	%	n	%
None (Grade 0)	116	66%	74	42%	36	20%	19	11%
Mild (Grade 1)	40	23%	47	27%	29	16%	18	11%
Moderate (Grade 2)	18	10%	52	30%	101	57%	104	63%
Severe (Grade 3)	0	0%	1	1%	9	5%	17	10%
Bridging (Grade 4)	0	0%	0	0%	2	1%	5	3%
Indeterminate	2	1%	1	1%	0	0%	1	1%
Unable to assess	0	0%	1	1%	0	0%	2	1%
Not Applicable	0	0%	0	0%	0	0%	0	0%
Not Required	0	0%	0	0%	0	0%	0	0%

Subjects censored at Index level secondary surgical interventions.
Source: Table Qualitative Radiography.sas; Analyzed: 12DEC2020

As shown above, moderate or lower heterotopic ossification was observed in the majority of subjects (85% - 141/166) at Month 24. Additionally, 10% (17/166) Simplify® Cervical Artificial Disc subjects experienced Grade 3 heterotopic ossification at Month 24. Few Simplify® Cervical Artificial Disc subjects experienced a Grade 4 (3% - 5/166) heterotopic ossification at Month 24.

Bridging Bone

Bridging bone was assessed in the control subjects. Relative to the original position of the allograft ring, the independent radiographic core lab evaluated if there was evidence of a

continuous bony connection (“bridging”) from the superior vertebral body to the inferior vertebral body in one or more of the following areas:

- Lateral
- Anterior
- Posterior
- Through the graft

This evaluation was performed independently for superior and inferior levels.

Bridging bone was observed in 100% (126/126) of superior levels and 97% (121/123) of inferior levels in the historical ACDF control subjects through 24 months.

5. Conclusions Drawn from the Clinical Study

The valid scientific evidence presented in the preceding sections in conjunction with scientific evidence provides reasonable assurance that the Simplify® Cervical Artificial Disc is a safe and effective disc replacement in skeletally mature patients for reconstruction of the disc at one or two contiguous levels from C3-C7 following discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to abnormality localized to the disc space and manifested by at least one of the following conditions confirmed by radiographic imaging (e.g., X-rays, computed tomography (CT), magnetic resonance imaging (MRI)): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels. Patients receiving Simplify® Cervical Artificial Disc should have failed at least six weeks of non-operative treatment or demonstrated progressive signs or symptoms despite non-operative treatment prior to implantation. Simplify® Cervical Artificial Disc is implanted via an open anterior approach.

How Supplied

Simplify® Cervical Artificial Disc is supplied pre-packaged and sterile. Each implant is packaged in a double sterile packaging system, which includes an inner and outer tray enclosed in a pressboard shelf carton. A liner and sheet surround the implant inside the inner tray. The integrity of the packaging should be checked to ensure that the sterility of the contents is not compromised. Remove Simplify® Cervical Artificial Disc from packaging using aseptic technique, only after the correct size has been determined.

Instrument Cleaning

Refer to Simplify® Cervical Artificial Disc Instrument Set Instructions for Use.

Sterilization

Implants are supplied sterile from Simplify Medical and should be used directly from the sterile package. Refer to Simplify® Cervical Artificial Disc Instrument Set Instructions for Use for description of sterilization of instruments.

Non-clinical testing has demonstrated that Simplify® Cervical Artificial Disc is MR Conditional. A patient can be safely scanned under the following conditions:

- Static magnetic field of 1.5 Tesla (1.5T) or 3.0 Tesla (3.0T).
- Maximum spatial gradient field less than or equal to 5990 Gauss/cm (59.9 T/m).
- Maximum whole-body specific absorption rate (SAR) of 2.0 W/kg for 15 minutes of scanning in Normal Operating Mode.
- Transmit/receive body coil.

Under the scan conditions defined above, Simplify® Cervical Artificial Disc is expected to produce a maximum temperature rise of less than 3.0ºC after 15 minutes of continuous scanning.

In non-clinical testing per ASTM F2119, the image artifact caused by the device extends approximately 5mm at 1.5T and 8 mm at 3.0T from Simplify® Cervical Artificial Disc when imaged with a gradient echo pulse sequence.

Device Retrieval

Should it be necessary to explant Simplify® Cervical Artificial Disc, please contact Simplify Medical to receive instructions regarding data collection, including histopathological, mechanical, patient, and AE information. Please refer to Simplify® Cervical Artificial Disc Surgical Technique Guide for instructions on the required surgical technique for device retrieval. Please note the explanted Simplify® Cervical Artificial Disc should be removed as carefully as possible in order to keep the disc and surrounding tissue intact. To facilitate the analysis, please note descriptive information about the gross appearance of the device in situ as well as the removal method. In addition, Simplify Medical will ask for information regarding the reason for removal, patient information, and clinical outcomes.

Limited warranty and disclaimer: Simplify Medical, Inc. products are provided with a limited written warranty to the original purchaser against defects in workmanship and materials. Any other express or implied warranties, including warranties of merchantability or fitness for a particular purpose, are hereby disclaimed.

Product Complaints

Any health care professional (e.g., customer or user of this system), who has complaints or who has experienced any dissatisfaction in the product quality, identity, durability, reliability, safety, effectiveness and/ or performance should notify Simplify Medical. Further, if the Simplify® Cervical Artificial Disc or Simplify® Cervical Artificial Disc Instruments ever "malfunction," (i.e. does not meet any of the performance specifications or otherwise does not perform as intended) or may have caused or contributed to the death or serious injury of a patient, Simplify Medical should be notified immediately by telephone or written correspondence. When filing a complaint, please provide the device name, lot number, your name and address, and the nature of the complaint. Complaints may also be reported directly to Medwatch at http://www.fda.gov/medwatch.

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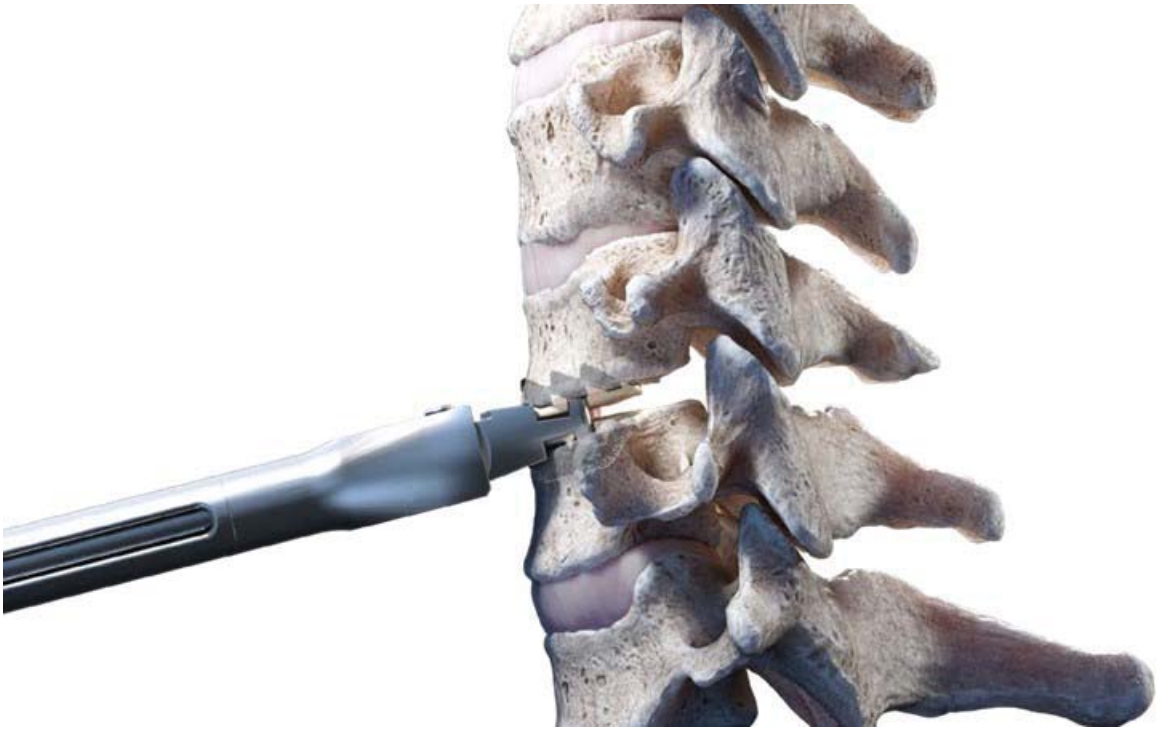
Please see *ifu.simplifymedical.com* for complete instructions for use for Simplify® Cervical Artificial Disc and Simplify® Cervical Artificial Disc Instruments.

Simplify® Cervical Artificial Disc

Surgical Technique Guide



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INDICATIONS

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

CONTRAINDICATIONS

Simplify® Cervical Artificial Disc should not be implanted in patients with the following conditions:

- An active systemic infection or an infection at the operative site.
- Osteoporosis or osteopenia defined as DEXA bone mineral density T-score less than -1.5.
- Known allergy to the implant materials (PEEK, ceramic, titanium).
- Severe facet disease or facet degeneration.
- Bridging osteophytes.
- Marked cervical instability on neutral lateral or flexion/extension radiographs (e.g., radiographic signs of subluxation > 3.0mm or angulation of the disc space more than 11° greater than adjacent segments).
- Significant cervical anatomical deformity at the index level or clinically compromised cervical vertebral bodies at the index level due to current or past trauma (e.g., by radiographic appearance of fracture callus, malunion, or nonunion) or disease (e.g., ankylosing spondylitis, rheumatoid arthritis).

WARNINGS

- Simplify® Cervical Artificial Disc should only be used by surgeons who are experienced with anterior cervical spinal procedures and have undergone hands-on training in the use of this device. Only surgeons who are familiar with Simplify® Cervical Artificial Disc components, instruments, procedure, clinical applications, biomechanics, adverse events, and risks associated with Simplify® Cervical Artificial Disc should use this device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events, including neurological complications.
- Correct selection of the appropriate implant size and correct placement of Simplify® Cervical Artificial Disc are essential to ensure proper performance and functioning of the device. Information regarding implant size selection and correct implant placement is provided in this Surgical Technique Guide.
- Removal of the disc may be required during device re-positioning or for other surgical

considerations. This process could cause damage that is not visually apparent—if a disc is removed during the implantation procedure, a new device should be implanted in its place

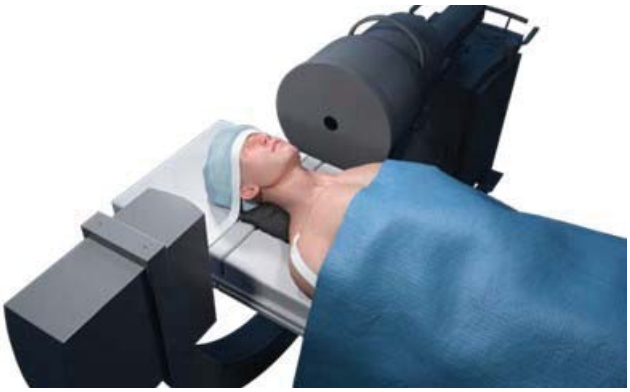
- Due to the proximity of vascular structures, neurological structures, and major organ systems to the implantation site, there are risks of serious or fatal hemorrhage and risks of neurological damage and/or injury to adjacent organs with the use of Simplify® Cervical Artificial Disc. Care must be taken to identify and protect these structures.
- There is a risk of heterotopic ossification associated with artificial cervical discs which could lead to reduced cervical motion or fusion at either the treated level(s) or adjacent levels.

SIMPLIFY® CERVICAL ARTIFICIAL DISC PROCEDURE SUMMARY

The Simplify® Cervical Artificial Disc surgical procedure is comprised of three main steps following a complete discectomy:

1. Disc space sizing,
2. Slot cutting,
3. Simplify® Cervical Artificial Disc placement.

PATIENT PREOPERATIVE SETUP



Patient positioning is critical to Simplify® Cervical Artificial Disc Surgical Technique to ensure proper placement of Simplify® Cervical Artificial Disc.

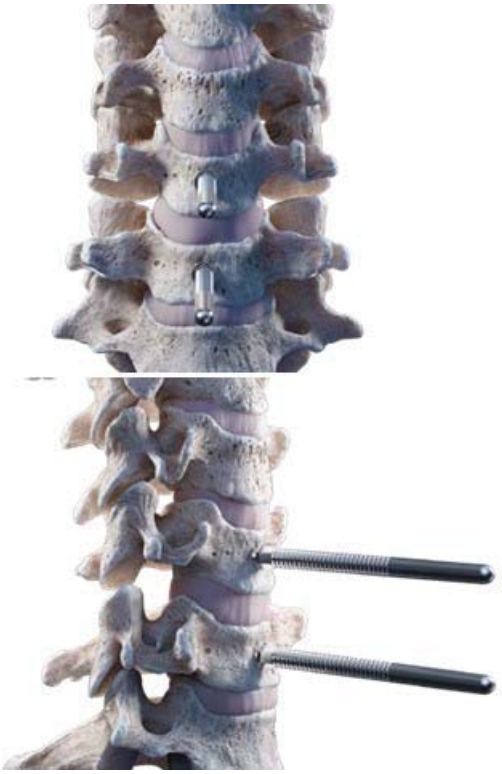
The patient's cervical spine should be placed in a supine, neutral position (as confirmed by X-ray) on a radiolucent operating table, with the patient's neck firmly positioned. Maintain anatomic lordosis and avoid hyperextension. Proper patient positioning should be maintained throughout the procedure to ensure correct instrument orientation and device placement.

NOTE: The operating table should allow for fluoroscopic imaging in both the anterior-posterior (A/P) and lateral positions. It is important to ensure that the shoulders do not limit visibility during X-ray monitoring.

APPROACH

Using a standard right or left anterior cervical approach after confirming the target disc level with fluoroscopy, preserve the longus colli muscles and identify the midline of the vertebral bodies.

CASPAR PIN PLACEMENT



Caspar distractor pins should be placed centrally in the vertebral body with pins parallel to the vertebral endplates to ensure parallel distraction. Choose the correct length Caspar pin to acquire good bone purchase and confirm placement with fluoroscopy.

NOTE: Midline placement of the Caspar distractor pins is important, as they will provide a reference for midline placement of the implant. Accurate midline placement is critical for optimizing the biomechanical success of Simplify® Cervical Artificial Disc.

Typically, the most diseased level is completed first, but the order of implanting is at the discretion of the surgeon.

Complete the implant steps at the first level prior to advancing to the second level

DISCECTOMY

A complete discectomy should be performed out to the lateral annulus, removing all disc material from the intervertebral space. Carefully clear the endplates of cartilaginous material while preserving cortical bone. Remove anterior and posterior osteophytes as necessary to accomplish a complete decompression. The extent of decompression is determined by the surgeon based upon patient pathology.

To achieve ligamentous balance and facilitate parallel endplate distraction, the posterior longitudinal ligament (PLL) may need to be released completely and bilaterally. Releasing the PLL may facilitate parallel vertebral body distraction for proper restoration of disc height.

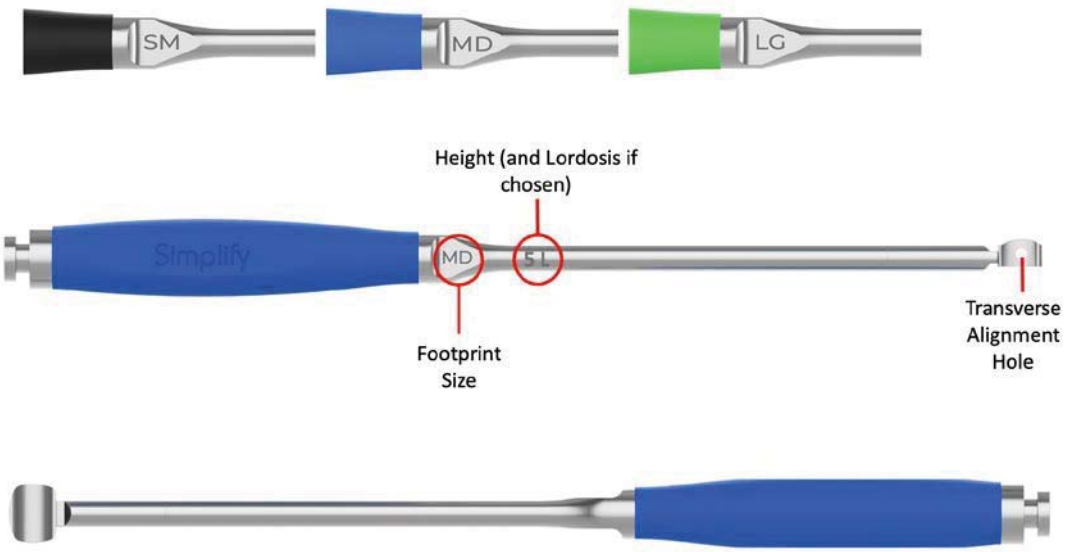
Utilizing an intervertebral parallel distractor may be beneficial to aid in complete posterior release and restoration of desired disc space height.

Under fluoroscopic control and with Caspar distraction released, align the Intervertebral Distractor to the endplates taking care not to exceed the posterior endplate margins. Distract the disc space carefully to obtain parallelism.

STEP 1: SIMPLIFY® CERVICAL ARTIFICIAL DISC SIZING

Determine the footprint and height of the disc space to ensure the proper Simplify® Cervical Artificial Disc is selected. Note that Simplify® Cervical Artificial Disc sizing options include three endplate sizes (SM, MD, LG) and three disc heights at zero degrees lordosis (4mm, 5mm, 6mm). In addition, there are four sizes with 5 degrees of lordosis. Additionally, the assembled disc features two different core sizes

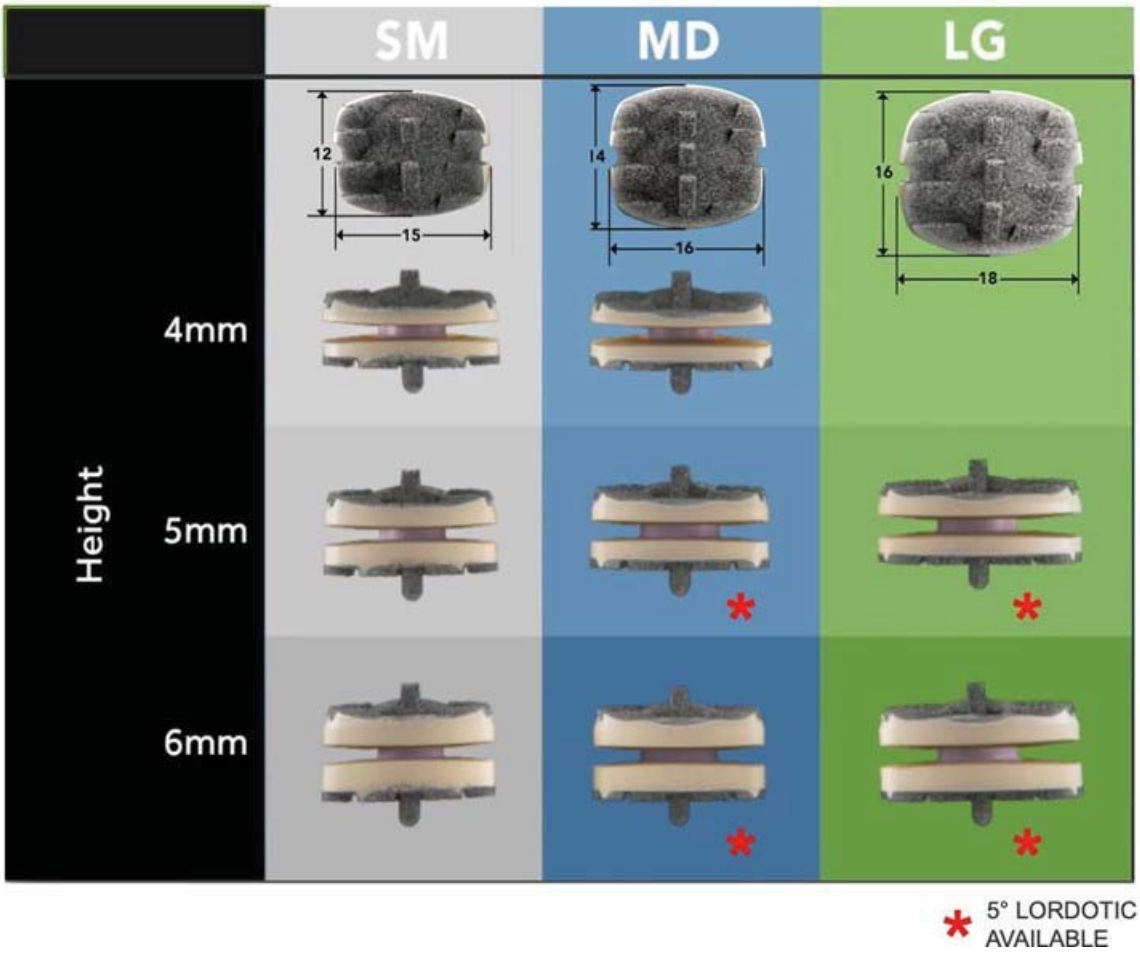
(small and large). Core size is not determined by the surgeon as it is preassembled according to footprint size and height. A Trial is provided that corresponds to each Simplify® Cervical Artificial Disc size.



All Trials are color coded for size and laser marked for size, height and lordosis. An additional "L" to the height indicates a 5-degree lordosis. The distal end of each Trial corresponds to the shape and dimensions of Simplify® Cervical Artificial Disc (with the endplates oriented parallel to each other). A transverse hole is provided to help align the Trial under fluoroscopy.

SIMPLIFY® CERVICAL ARTIFICIAL DISC SIZES

SIZING GOALS



Moderate to low distraction: Begin with the 4mm Trial and increase height as needed. Observe the index level facets to prevent over-distraction of the disc space.

Maximum endplate coverage: Select the largest size footprint that will cover the endplate anterior to posterior without exceeding endplate margins. If necessary, slight resection of the medial aspect of the uncinates may be required to accommodate the correct footprint size. Observing the length of the Caspar pins may aid in initial selection of the footprint in A/P dimension.

Anatomic fit: The dome of the Simplify® Cervical Artificial Disc superior endplate is designed to match the normal anatomy of the disc space. The domed portion of the Trial should be situated within the concavity of the superior endplate during Trial sizing.

PLACEMENT OF THE TRIAL

Confirm the midline and that any distraction has been released.

Begin with the 4mm Size SM Trial if there is uncertainty of the correct height or footprint size.

Align the Trial to the midline of the disc space. A midline marker is etched onto the Trial handle. If the Caspar pins were correctly placed, they will reference the vertebral body midline.

The Trial handle should be held parallel to the disc space and not tilted to the right or left of midline. Tilting the handle caudal may be necessary to accommodate the lordosis of the spine.

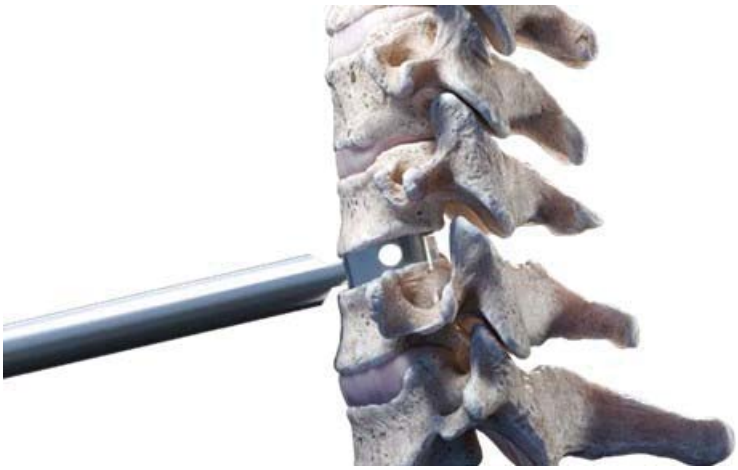
If the C-arm is aligned perpendicular to the spine, the transverse alignment hole will appear as a complete circle on imaging if the handle is correctly positioned.

Under direct fluoroscopic control, carefully advance the Trial with a mallet. Observe the transverse alignment hole to confirm correct positioning is maintained.

WARNING: Do not allow the Trial to advance beyond the posterior disc space border.

With the dome of the Trial within the concavity of the superior disc space, confirm the endplate coverage and disc space height.
Observing the index facets may be helpful in determining any over- distraction.

For disc spaces that have a significant lordotic angle, 4 sizes of Trials with 5° of lordosis are available.



If the endplate coverage is acceptable, note the location of the posterior edge of the Trial relative to the posterior vertebral body. This will reference the desired location of the Slot Cutter in the next step.

The Trial may be removed manually or with the Slide Hammer.

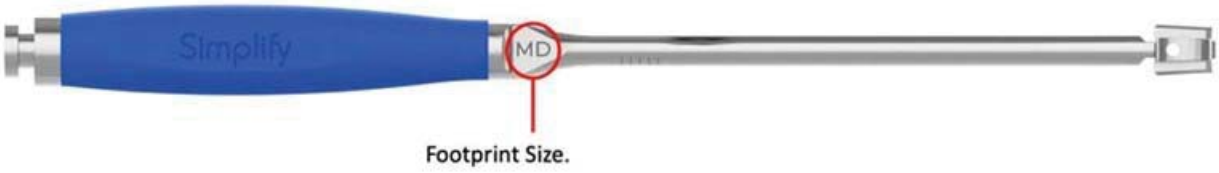
Repeat the steps with the next size footprint and / or height Trial if the coverage is too small in the A/P dimension or if the height is insufficient.

STEP 2: SIMPLIFY® CERVICAL ARTIFICIAL DISC SLOT CUTTING

STEP 2: SLOT CUTTING

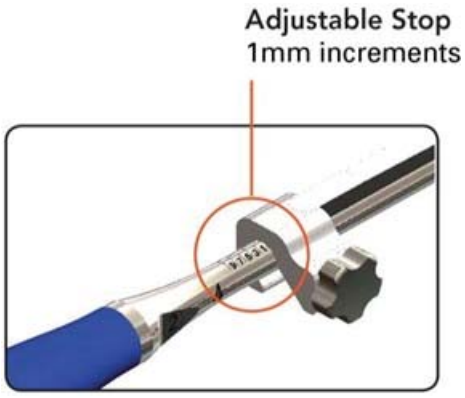
Slot Cutters are color coded to match the Trial footprint sizes, Size SM, MD and LG, and are used for heights 5, 5L, 6 and 6L. If a 4mm height Trial was selected, a special Slot Cutter for the appropriate footprint should be used and is identified by a “4” mark along with SM or MD on the handle.

Indicates Special
Height 4 Slot Cutter



Footprint Size.

Always use the Adjustable Stop. The Adjustable Stop can be adjusted to accommodate the patient's anatomy. One mm increments are provided. Mount the Stop
onto the shaft of the Slot Cutter, using the etched markings as adjusting guides.

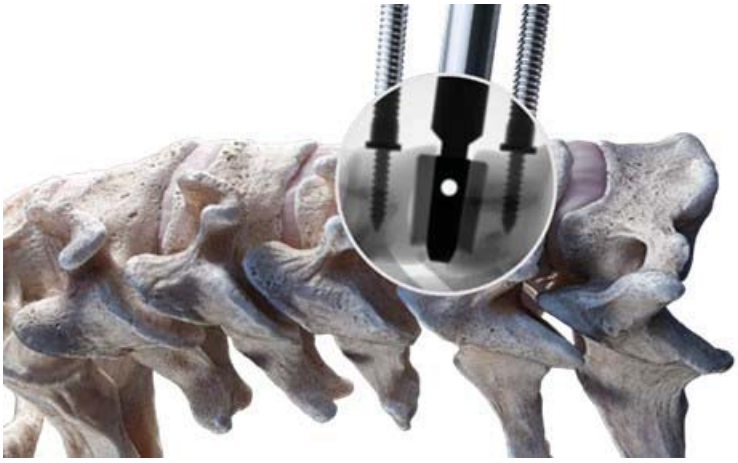


Choose the same Slot Cutter size as the Trial (Size SM, MD, or LG) for 5mm or 6mm Trials (or the Size SM 4 or Size MD 4 for 4mm Trials).

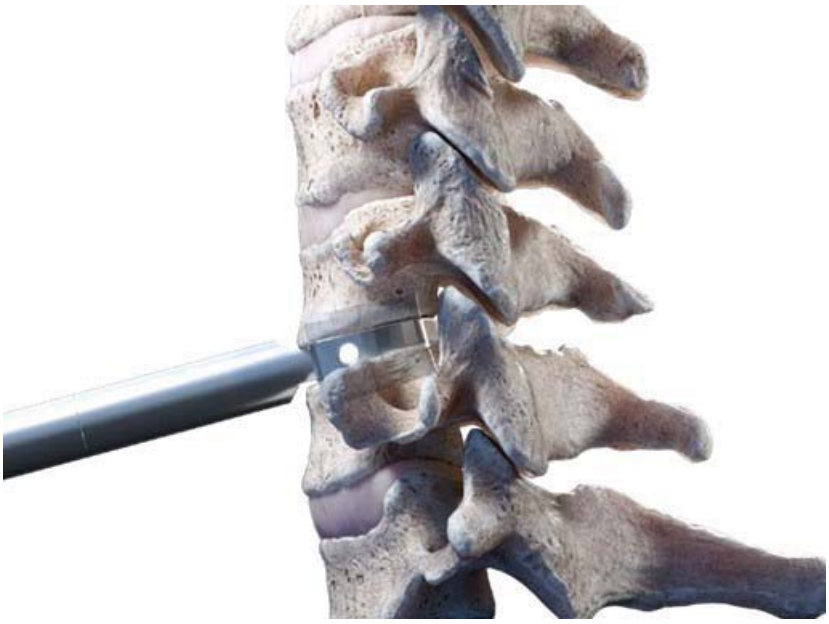
Align the Slot Cutter to the midline and adjust the handle parallel to the endplates without tilting right or left. The Transverse Alignment Hole will appear as a perfect circle on fluoroscopy if the C-arm is perpendicular to the spine and the Slot Cutter is correctly positioned.

Under fluoroscopic visualization, carefully advance the Slot Cutter with a mallet, maintaining correct orientation of the handle.

Observe that the blades of the Slot Cutter are engaging into the cortical bone and are not "pushing off" creating shallow cuts. Locking the Caspar distractor may prevent any distraction caused by the cutting blades.



Re-adjust the Stop as needed to obtain the desired advancement of the Slot Cutter.



Continue advancing the Slot Cutter under serial fluoroscopy until the posterior edge has reached the reference point from the posterior endplate as determined in the Trial positioning step.

Confirm the Slot Cutter is in the desired posterior location.

WARNING: Allowing the Slot Cutter to advance beyond the posterior vertebral border may result in patient injury.

Remove the Slot Cutter using the Slide Hammer.

IMPORTANT: Copiously irrigate the wound after removing the Slot Cutter and visually inspect the cuts for any loose bone fragments.

STEP 3: SIMPLIFY® CERVICAL ARTIFICIAL DISC PLACEMENT

Select the disc size to match the Trial size chosen in Step 1.

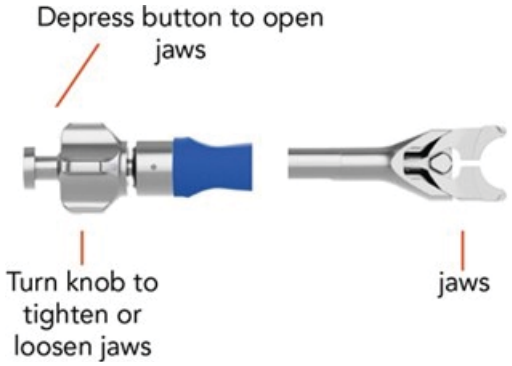
The implant is provided sterile in an inner and outer package. Open the inner package onto the sterile field using standard practices.

The implant is held together in one piece within a loading clip. Do not remove the implant from the clip manually. Follow the Inserter loading steps below.

LOADING THE INSERTER

The Inserter sizes are color coded to match the Trial and Slot Cutter footprint sizes without regard to the height. Choose the same size, (Size SM, MD, or LG) as in the previous step.

Turn the knob to loosen the jaws completely.

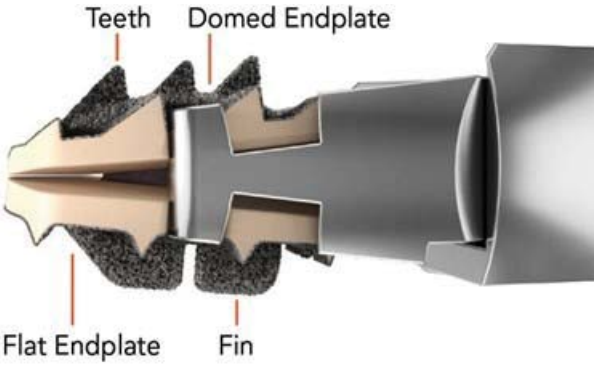


Load the disc implant onto the jaws of the Inserter taking care that the “T” arms of the Inserter are seating into the slots on the sides of the implant.

Once the arms are seated into the slots, turn the knob to close and tighten the jaws.

IMPORTANT: Confirm that the arms are correct within the slots of the implant prior to releasing the clip.

Release the implant from the clip by squeezing the back end of the clip and pulling the clip away.


Teeth
Domed Endplate
Flat Endplate
Fin

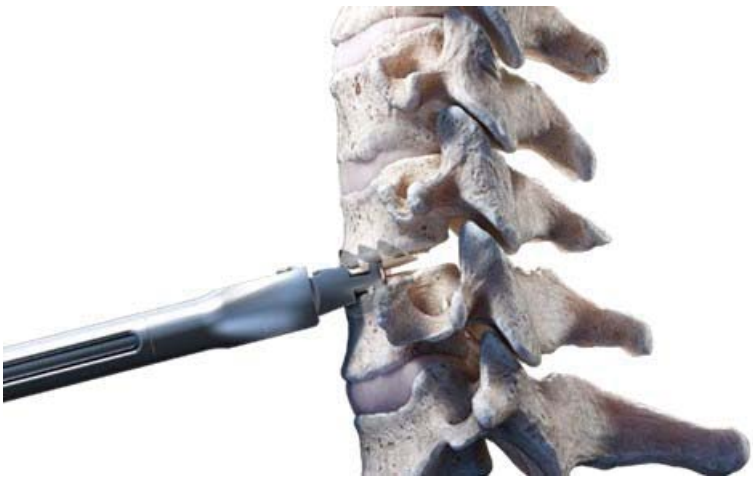
IMPLANTING THE FIRST SIMPLIFY® CERVICAL ARTIFICIAL DISC

The Inserter should be positioned so the disc implant is oriented as shown, with the domed endplate with teeth cephalad and the flat endplate with the fin caudal.

With the disc implant correctly oriented, align the superior teeth and inferior fin(s) to the slots cut in the previous step.

Orient the Inserter parallel to the vertebral disc space, and under fluoroscopic guidance, advance the implant carefully into the disc space.

Once the implant has reached just past 50% of the anterior-posterior depth as seen on lateral fluoroscopy, stop advancement and release the implant from the Inserter.

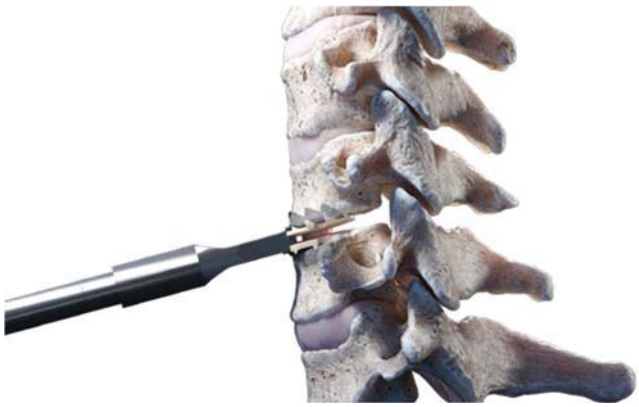


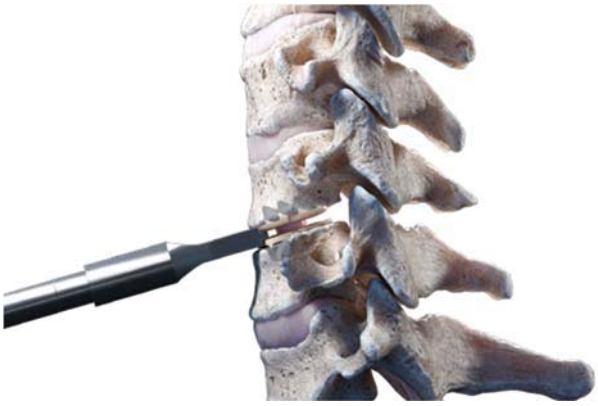
To release the Implant, loosen the knob and depress the button to open the jaws.

Carefully remove the Inserter from the disc implant and disc space.

FINAL PLACEMENT OF THE SIMPLIFY® CERVICAL ARTIFICIAL DISC

The final positioning of the Simplify® Cervical Artificial Disc is accomplished by use of the Tamp.



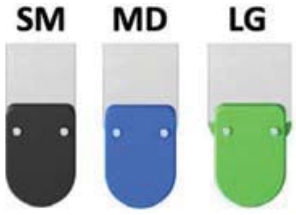


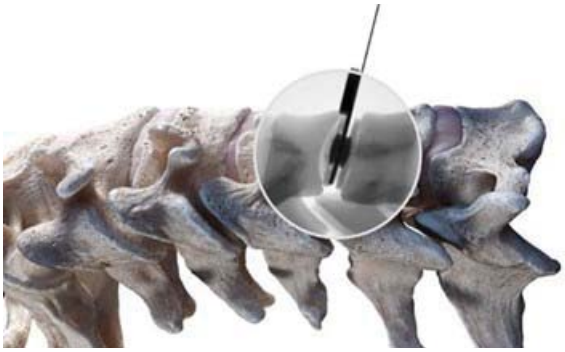
Align the Tamp to the upper and lower endplates of the Simplify® Cervical Artificial Disc and under fluoroscopic control, gently advance the implant to the desired position as obtained by the Slot Cutter in the previous step.

USE OF THE DEPTH GAUGE

Occasionally patient anatomy may make it difficult to easily visualize the Simplify® Cervical Artificial Disc endplates under fluoroscopy to verify desired placement. Use of the Depth Gauge will facilitate visualization.

Choose the correct size Depth Gauge corresponding to the implanted Simplify® Cervical Artificial Disc footprint, Size SM, MD or LG.





The Depth Gauge slides in between the endplates of the implanted disc and rests against the anterior edge of the endplate. The Depth Gauge will enhance the visualization of the A/P location of the Simplify® Cervical Artificial Disc on fluoroscopy.

Insert the correct size Depth Gauge until the stop is in firm contact with either the upper or lower endplate. Confirm positioning with fluoroscopy.

WARNING: Never use a larger Depth Gauge than indicated.

Note: The Depth Gauge may appear up to 1mm anterior of the implanted disc's posterior edge due to the curvature of the implant endplate.

FINAL PLACEMENT ASSESSMENT

Evaluate the final placement of the Simplify® Cervical Artificial Disc with both lateral and A/P imaging.

Copiously irrigate the wound prior to closure.

IMPLANTING THE SECOND SIMPLIFY® CERVICAL ARTIFICIAL DISC

Following the satisfactory evaluation of the first implant, remove the most caudal or cephalad Caspar pin and replace it in the appropriate vertebral body above or below the current implanted disc space for access to the second level.

Follow the steps above regarding:

- Correct pin placement
- Discectomy and decompression endplate preparation and intervertebral distraction
- Disc Sizing and placement of the Trial
- Slot cutting
- Placement of the Simplify® Cervical Artificial Disc
- Final Placement Assessment

Evaluate the final placement of the Simplify® Cervical Artificial Discs with both lateral and A/P imaging.

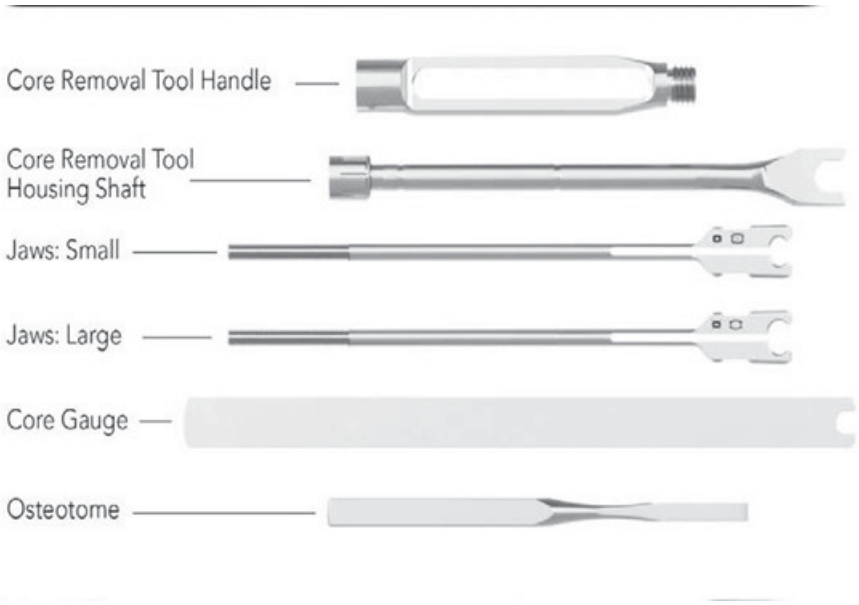
Copiously irrigate the wound prior to closure.

SIMPLIFY® CERVICAL ARTIFICIAL DISC REMOVAL

Removal of the Simplify® Cervical Artificial Disc, either in an acute or chronic situation, can be accomplished using the Core Removal Instruments within the Simplify® Cervical Artificial Disc Instrument Set.

REMOVAL INSTRUMENTS

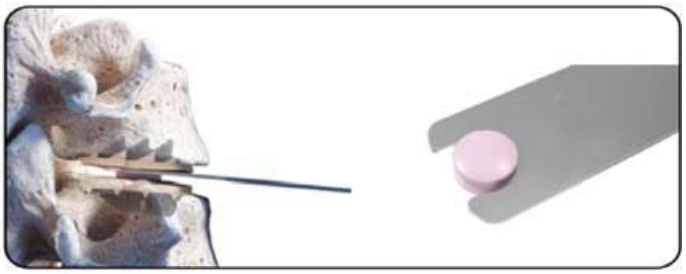
Core Removal Instruments



Identify the Core Removal Instruments as shown.

DETERMINE THE CORE SIZE

With the disc space exposed to the anterior aspect of the implanted Simplify® Cervical Artificial Disc, determine the core size by taking the Core Gauge and slipping it between the upper and lower Disc endplates, advancing until it reaches the core.



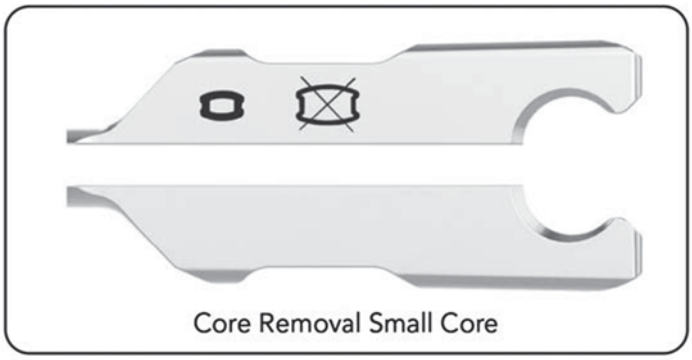
Core Gauge fits completely around small size core

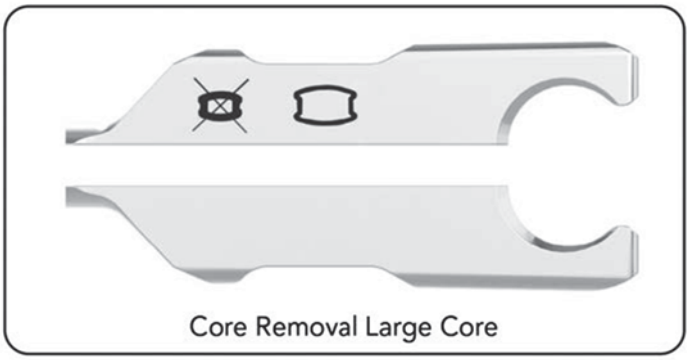
Core Gauge does not fit completely around large size core

The Core Gauge will fit completely around the small core size as shown, but will not fit completely around the large core size.

ASSEMBLE CORE REMOVAL TOOL

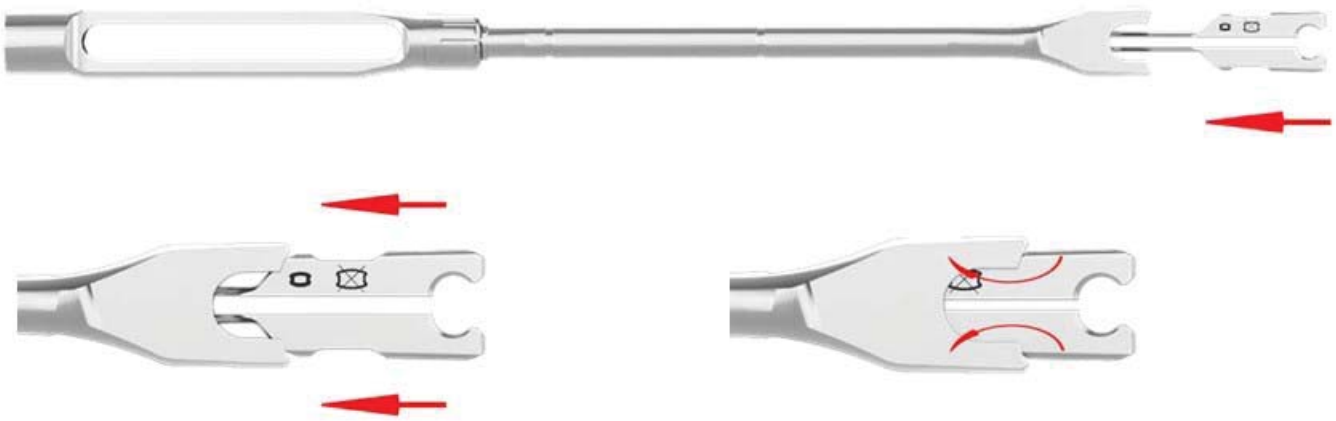
Choose the correct size Jaw (Small or Large) based on the core size as determined in the previous step. The Jaw size is noted by the pictograms on each instrument as shown.



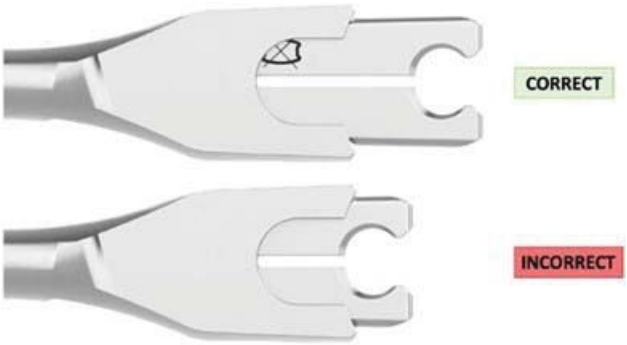


Assemble the Core Removal Tool Handle and Core Removal Housing Shaft by connecting the threaded portion of the Shaft onto the knob of the Handle and tighten the knob.

Slide the correct size Jaws into the open end of the Assembly and advance. Gently squeeze the Jaws together to snap into the final position within the Assembly.



Take care not to advance the Jaws too deeply into the Assembly.



WITHDRAW THE CORE

Carefully advance the Core Removal Instrument into the disc space so that the Jaws are aligned between the Simplify® Cervical Artificial Disc endplates. Under fluoroscopic control, gently advance until the edge of the Assembly contacts the anterior Disc endplates and the Jaws encircle the core completely.

NOTE: Use slight distraction of the vertebral endplates with a Caspar distractor as needed.

Remove the core by turning the Core Removal Tool Handle while maintaining slight pressure on the Simplify® Cervical Artificial Disc endplates with the Assembly. This will close the Jaws around the core and retrieve it back into the Housing Shaft.

Once the core is captured within the Housing Shaft, carefully remove the complete instrument from the wound.

REMOVING THE SIMPLIFY® CERVICAL ARTIFICIAL DISC ENDPLATES

With the core removed, the Simplify® Cervical Artificial Disc endplates can be gently disconnected from the vertebral endplates. A small Osteotome is provided with the instruments as needed to aid in removal.

Device Retrieval

Should it be necessary to explant a Simplify® Cervical Artificial Disc, please contact Simplify Medical to receive instructions regarding data collection, including histopathological, mechanical, patient, and adverse event information. Please note the explanted Simplify® Cervical Artificial Disc should be removed as carefully as possible in order to keep the disc and surrounding tissue intact. To facilitate the analysis, please note descriptive information about the gross appearance of the device in situ as well as the removal method. In addition, Simplify Medical will ask for information regarding the reason for removal, patient information, and clinical outcomes.

SIMPLIFY® CERVICAL ARTIFICIAL DISC PRODUCT DESCRIPTION

Simplify® Cervical Artificial Disc is a weight-bearing implant consisting of PEEK (polyetheretherketone) endplates and one semi-constrained, fully articulating, mobile ceramic (ZTA) core. Simplify® Cervical Artificial Disc is provided packaged and preassembled in one of twelve configurations: three footprint sizes, three heights, and two lordosis angles.

In addition to serrated surfaces, the inferior endplate has an in-line fin and the superior endplate has two to three teeth to facilitate endplate fixation. Both endplates have concave articulating surfaces. The superior endplate's concave articulating surface features a retention ring which mates with the corresponding core retention feature.
The PEEK endplates are coated with a titanium plasma spray (TPS) coating on the bone contacting surfaces.

Simplify® Cervical Artificial Disc, instruments, and surgical technique are designed such that Simplify® Cervical Artificial Disc can be packaged, handled, and implanted as a single unit.

Features

Modular design minimizes surgical steps.

-Entire implantation in three steps with simple, precise instrumentation.
-Simplify® Cervical Artificial Disc inserted as one unit rather than in pieces.
-Twelve implant sizes with three endplate footprints, two lordosis options, three disc heights, and two cores, which are preselected based on footprint size and height.

Caution
Handle devices with care to prevent cutting surgical gloves with sharp-edged surgical instruments.

Special Instructions
Simplify® Cervical Artificial Disc Instrument Set life span is normally determined by wear and damage due to use. Instruments should not be expected to last indefinitely. These items are often subjected to high loads and/or impact forces. Before each use carefully inspect all instruments. Do not use an instrument that is severely corroded, marred or worn or cutting instruments with dull edges.

NOTE: At some point in time, instruments wear out and should be replaced. It is the responsibility of the user to ensure each instrument is visually inspected according to the instructions provided in the following sections.

IMPORTANT:
- Do not use these instruments for any action for which it was not intended, such as prying or lifting.
- To avoid injury, the instruments should be carefully examined prior to use for functionality or damage. A damaged instrument should not be used.

IMPORTANT: Simplify® Cervical Artificial Disc is provided sterile. The instruments are provided non-sterile and must be sterilized using the validated instructions.

MRI SAFETY INFORMATION

Non-clinical testing has demonstrated that Simplify® Cervical Artificial Disc is MR Conditional. A patient can be safely scanned under the following conditions:

- Static magnetic field of 1.5 Tesla (1.5T) or 3.0 Tesla (3.0T).
- Maximum spatial gradient field less than or equal to 5990 Gauss/cm (59.9 T/m).
- Maximum whole-body specific absorption rate (SAR) of 2.0 W/kg for 15 minutes of scanning in Normal Operating Mode
- Transmit/receive body coil.

Under the scan conditions defined above, Simplify® Cervical Artificial Disc is expected to produce a maximum temperature rise of less than 3.0°C after 15 minutes of continuous scanning.

In non-clinical testing per ASTM F2119, the image artifact caused by the device extends approximately 5mm at 1.5T and 8mm at 3.0T from Simplify® Cervical Artificial Disc when imaged with a gradient echo pulse sequence.

Limited warranty and disclaimer:

Simplify Medical, Inc. products are provided with a limited written warranty to the original purchaser against defects in workmanship and materials. Any other express or implied warranties, including warranties of merchantability or fitness for a particular purpose, are hereby disclaimed.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician who has appropriate training or experience.

Product Complaints

Any health care professional (e.g., customer or user of this system), who has complaints or who has experienced any dissatisfaction in the product quality, identity, durability, reliability, safety, effectiveness and/ or performance

should notify Simplify Medical. Further, if the Simplify® Cervical Artificial Disc or Simplify® Cervical Artificial Disc Instruments ever "malfunction," (i.e. does not met any of the performance specifications or otherwise does not perform as intended) or may have caused or contributed to the death or serious injury of a patient, Simplify Medical should be notified immediately by telephone or written correspondence. When filing a complaint, please provide the device name, lot number, your name and address, and the nature of the complaint. Complaints may also be reported directly to Medwatch at http://www.fda.gov/medwatch.

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Please see ***ifu.simplifymedical.com*** for complete instructions for use for Simplify® Cervical Artificial Disc and Simplify® Cervical Artificial Disc Instrument Set.

Simplify® Cervical Artificial Disc Sizes

Catalog #	Description
SM-4	Simplify® Cervical Artificial Disc Size SM, Height 4
SM-5	Simplify® Cervical Artificial Disc Size SM, Height 5
SM-6	Simplify® Cervical Artificial Disc Size SM, Height 6
MD-4	Simplify® Cervical Artificial Disc Size MD, Height 4
MD-5	Simplify® Cervical Artificial Disc Size MD, Height 5
MD-5L	Simplify® Cervical Artificial Disc Size MD, Height 5, 5° Lordosis
MD-6	Simplify® Cervical Artificial Disc Size MD, Height 6
MD-6L	Simplify® Cervical Artificial Disc Size MD, Height 6, 5° Lordosis
LG-5	Simplify® Cervical Artificial Disc Size LG, Height 5
LG-5L	Simplify® Cervical Artificial Disc Size LG, Height 5, 5° Lordosis
LG-6	Simplify® Cervical Artificial Disc Size LG, Height 6
LG-6L	Simplify® Cervical Artificial Disc Size LG, Height 6, 5° Lordosis

Simplify® Disc Instrument Set

Catalog #	Description
T-SM-4	Simplify® Trial, Size SM, Height 4
T-SM-5	Simplify® Trial, Size SM, Height 5
T-SM-6	Simplify® Trial, Size SM, Height 6
T-MD-4	Simplify® Trial, Size MD, Height 4
T-MD-5	Simplify® Trial, Size MD, Height 5
T-MD-6	Simplify® Trial, Size MD, Height 6
T-MD-5L	Simplify® Trial, Size MD, Height 5, 5° Lordosis
T-MD-6L	Simplify® Trial, Size MD, Height 6, 5° Lordosis
T-LG-5	Simplify® Trial, Size LG, Height 5
T-LG-6	Simplify® Trial, Size LG, Height 6
T-LG-5L	Simplify® Trial, Size LG, Height 5, 5° Lordosis
T-LG-6L	Simplify® Trial, Size LG, Height 6, 5° Lordosis
SC-SM-4	Simplify® Slot Cutter, Size SM, 4mm
SC-MD-4	Simplify® Slot Cutter, Size MD, 4mm
SC-SM-5/6	Simplify® Slot Cutter, Size SM, 5/6mm
SC-MD-5/6	Simplify® Slot Cutter, Size MD, 5/6mm
SC-LG-5/6	Simplify® Slot Cutter, Size LG, 5/6mm
I-SM	Simplify® Inserter, Size SM
I-MD	Simplify® Inserter, Size MD
I-LG	Simplify® Inserter, Size LG
SH	Simplify® Slide Hammer
TMP	Simplify® Tamp
AS	Simplify® Adjustable Stop
DG-SM	Simplify® Depth Gauge, Size SM
DG-MD	Simplify® Depth Gauge, Size MD
DG-LG	Simplify® Depth Gauge, Size LG
ID	Simplify® Intervertebral Distractor
CR-JL	Simplify® Jaws, Large
CR-JS	Simplify® Jaws, Small
CR-H	Simplify® Handle Core
CR-A	Simplify® Housing Assembly
CR-CG	Simplify® Core Gauge
OST	Simplify® Osteotome
TRAY	Simplify® Tray 3 Level