

# Cervical Disc Arthroplasty: Rationale, Designs, and Results of Randomized Controlled Trials

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## ABSTRACT

**Background:** This review outlines clinical data and characteristics of current Food and Drug Administration (FDA)–approved implants in cervical disc replacement/cervical disc arthroplasty (CDR/CDA) to provide a centralized resource for spine surgeons.

**Methods:** Randomized controlled trials (RCTs) on CDR/CDA were identified using a search of the PubMed, Web of Science, and Google Scholar databases. The initial search identified 69 studies. Duplicates were removed, and the following inclusion criteria were applied when determining eligibility of RCTs for the current review: (1) discussing CDR/CDA prosthesis and (2) published within between 2010 and 2020. Studies without clinical data or that were not RCTs were excluded. All articles were reviewed independently by 2 authors, with the involvement of an arbitrator to facilitate consensus on any discrepancies.

**Results:** A total of 34 studies were included in the final review. Findings were synthesized into a comprehensive table describing key features and clinical results for each FDA-approved CDR/CDA implant and are overall suggestive of expanding indications and increasing utilization.

**Conclusions:** RCTs have provided substantial evidence to support CDR/CDA for treating single- and 2-level cervical degenerative disc disease in place of conventional anterior cervical discectomy and fusion.

**Clinical Relevance:** This review provides a resource that consolidates relevant clinical data for current FDA-approved implants to help spine surgeons make an informed decision during preoperative planning.

**Level of Evidence:** 5

Cervical Spine

Keywords: cervical, cervical disc arthroplasty, cervical disc replacement, anterior cervical discectomy and fusion, degenerative disc disease, myelopathy

## INTRODUCTION

Until recently, anterior cervical discectomy and fusion (ACDF) had been the customary surgical treatment option for patients with symptomatic cervical degenerative disc disease (DDD).<sup>1,2</sup> Although ACDF has been widely accepted as an efficacious treatment for radiculopathy or myelopathy secondary to cervical DDD, the incidence of adjacent segment disease (ASD) postoperatively remains a concern.<sup>3</sup> This significant limitation has since driven the search for treatment alternatives that can provide clinical outcomes similar to ACDF while preserving motion at the operative levels.

Over the past 2 decades, cervical disc replacement/cervical disc arthroplasty (CDR/CDA) has gained considerable traction as an alternative treatment option to ACDF. CDR shares many indications with ACDF but offers superior preservation of native spinal kinematics.<sup>4</sup> This characteristic feature is thought to be

protective against the development of ASD because it minimizes aberrant distribution of mechanical forces unto structures adjacent to the operative levels.<sup>5</sup> This theoretical advantage has driven substantial interest in the translation of these concepts into clinically relevant applications.

As such, many randomized controlled trials (RCTs) have been conducted to compare CDR to ACDF. Park et al assessed cervical spine kinematics following ACDF and CDR in a prospective RCT and found that CDR significantly improved the restoration of lordotic alignment and disc height while maintaining preoperative translational and angular motion at the operative level.<sup>6</sup> McAfee et al performed a meta-analysis of 4 prospective multicenter RCTs involving 1226 patients. Their analysis demonstrated superior long-term clinical outcomes and survivorship associated with CDA relative to ACDF.<sup>7</sup> Similarly, in a meta-analysis of 18 RCTs, Gao et al reported greater clinical efficacy with CDR over ACDF in treating single-level cervical DDD across a

number of outcome measures including visual analog scale neck and arm pain scores, neurological function, postoperative range of motion, and need for additional surgery.<sup>8</sup>

As increasing evidence surfaces to corroborate the clinical success of CDR, indications continue to expand as well.<sup>1</sup> CDR was initially used to treat single-level cervical DDD but has since extended its application to 2-level cervical pathologies in light of supporting literature.<sup>2,9–11</sup> As CDR continues to establish itself as a viable treatment option for cervical pathology, the authors of this study felt it was important to perform a thorough review of this procedure. The aim of this review study was 3-fold: (1) to discuss the background of CDR and its potential benefits compared with anterior discectomy and fusion, (2) to discuss the history of currently and previously available CDR prostheses and depict all Food and Drug Administration (FDA)–approved devices in a table format, and (3) to highlight all RCTs conducted comparing ACDF to CDR in a readily accessible, synthesized table. The main purpose of this article is to serve as a resource for spine surgeons to quickly refer, in table format, FDA-approved CDR implant characteristics and the available clinical data for each CDR implant.

## MATERIALS AND METHODS

### Search Strategy

In July 2020, a search using PubMed, Web of Science, and Google Scholar was conducted to identify RCTs on CDR/CDA. The following Boolean search terms were used to identify studies of interest: ([CDR OR CDA OR total disc replacement OR total disc arthroplasty] AND [RCT]). As such, studies published between 2010 and 2020 were eligible for inclusion. The same search terms were used for each database, and the syntax was adjusted accordingly. The reference lists of all included studies were also reviewed. Two authors (D.R. and S.S.) independently reviewed each article, and any discrepancies were discussed by an arbitrator (K.A.) until a consensus was reached. D.R. and S.S. performed data extraction once the list of included studies was finalized.

### Selection Criteria and Data Collection

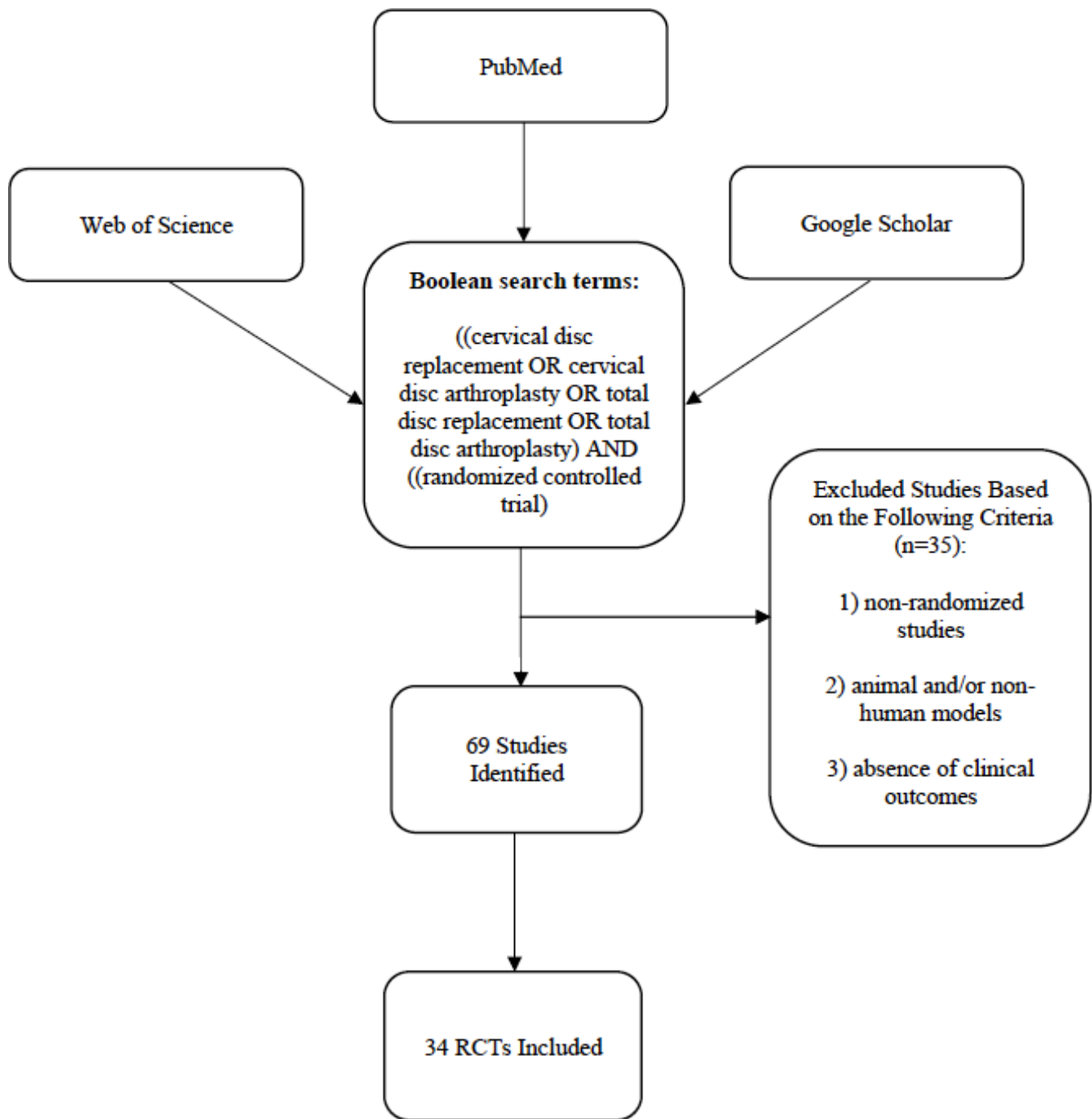
Overall, the initial search identified 69 studies. Duplicates were removed, after which the following search criteria were applied (1) studies discussing a CDR prosthesis, (2) published within the last 10 years, and (3) written in the English language. The full text

was reviewed if any discrepancies arose while parsing through the studies. Studies were excluded if they were (1) case studies, (2) book chapters, (3) animal and/or nonhuman models, and (4) non-RCTs. RCTs that did not measure clinical outcomes were also excluded. For example, some studies only assessed radiographic outcomes and were therefore excluded. RCTs that were published from earlier results of the same initial trial were also excluded. A total of 34 studies met inclusion and exclusion criteria and were included in the review (Figure). Characteristics of CDR were prespecified and included the manufacturer, images and x-rays of the implant, articulating materials, center of rotation, internal fixation methodology, FDA approval characteristics, magnetic resonance imaging compatibility, and disc height availability. Finally, a comprehensive table highlighting the key features and results of each study was created.

## RESULTS

### CDR History

Although CDR has only gained substantial support in recent years, its history dates back to the 1960s. Disc replacement was first introduced in 1966 by Swedish surgeon, Ulf Fernstrom. His spherical stainless steel prosthesis aimed to preserve mobility and restore disc articulation and height.<sup>12</sup> This precursory model, however, was associated with hypermobility of adjacent segments, implant migration, subsidence, and vertebral body erosion.<sup>12</sup> In 1989, B.H. Cummins introduced a second generation of disc replacements through a stainless steel ball-and-socket design. This prosthesis, however, yielded standard preliminary results in a study of 18 patients, in which 100% of patients experienced lasting dysphagia, 22% fixation failure, and 6% instability.<sup>12,13</sup> Although presumed unsuccessful, this implant prompted the inception of the first successful cervical disc prosthesis. The Frenchay cervical disc, an iteration of Cummins's precedent model, demonstrated favorable results in a 2002 study and was subsequently developed into the Prestige ST Cervical Disc, one of the several cervical disc implants gaining FDA approval in the 2000s.<sup>14</sup> A current list of all FDA-approved CDR prostheses with accompanying clinical and radiographic images is listed in Table 1.




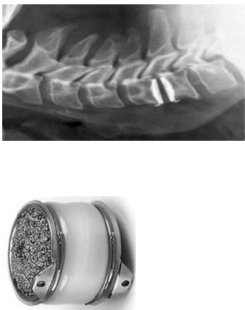


**Figure.** Flowchart of recorded articles related to randomized controlled trials comparing cervical disc arthroplasty to anterior discectomy and fusion.

### CDR Advantages

CDR offers several advantages over ACDF when treating single- and 2-level cervical DDD. The placement of artificial disc implants in lieu of rigid fusion constructs preserves motion at operative levels and facilitates normative load-sharing at index levels and their adjacent segments. Taken in conjunction, these features likely account for the notably lower incidence of ASD following CDR as compared with ACDF. In a

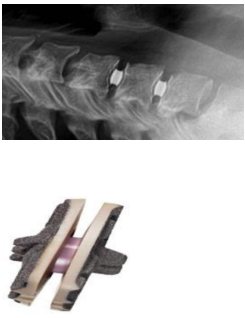

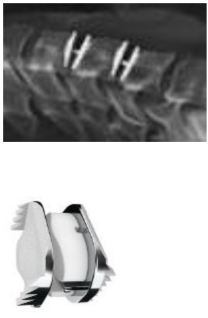
meta-analysis of 11 RCTs comparing CDR and ACDF outcomes in treating single- and 2-level cervical DDD, Xu et al found significantly reduced ASD incidence and reoperation requirement with CDR use.<sup>15</sup> With respect to long-term outcomes, Ghobrial et al similarly found significantly decreased development of symptomatic ASD requiring surgery in the cervical total disc replacement cohort compared with ACDF (6.9% vs 11.7% respectively) at 7 years.<sup>16</sup>

**Table 1.** Summary of current FDA-approved cervical disc arthroplasty devices with clinical and radiographic image examples.

Implant Name and Manufacturer	Picture and X-ray of Implant	Articulating Materials	Theoretical Center of Rotation	Internal Fixation	Year Approved by FDA	FDA Approved for: Single/2 Level	MRI Compatible <sup>a</sup>	Available Disc Heights (mm)	Commercially Available
Prestige LP—Medtronic		Titanium ceramic	Superior vertebra	Screws	2014	Yes	Yes	5, 6, 7, and 8	Yes
Bryan—Medtronic		Titanium-aluminum-vanadium alloy	Within implant	Milled bone	2009	Yes	No	8.5	Yes
Prodisc-C—Centinel Spine		Cobalt-chrome-molybdenum	Inferior vertebra	Keels	2007	Yes	No	5, 6, and 7	Yes
M6—Spinal Kinetics		Titanium-aluminum-vanadium alloy	Inferior vertebra	Serrated fins	2019	Yes	No	6 and 7	Yes

• Conditional  
 Maximum spatial  
 gradient magnetic  
 field of <4000  
 Gauss/cm (40  
 T/m)<sup>b</sup>

Table 1. Continued.

Implant Name and Manufacturer	Picture and X-ray of Implant	Articulating Materials	Theoretical Center of Rotation	Internal Fixation	Year Approved by FDA	FDA Approved for: Single/2 Level	MRI Compatible <sup>a</sup> :	Available Disc Heights (mm)	Commercially Available
Simplify— Simplify Medical		Polyetheretherketone and porous titanium plasma coating	Variable	Serrated fins and teeth	2020	Yes	Yes	4, 5, and 6	Yes
Secure-C— Globus Medical		Cobalt-chrome-molybdenum	“Natural”	Serrated keels	2012	Yes	No • Conditional <sup>b</sup> Maximum spatial gradient magnetic field of ≤4000 Gauss/cm (40 T/m)	7, 8, 9, 10, 11, and 12	Yes
Mobi-C— Zimmer Biomet		Cobalt-chrome-molybdenum, plasma sprayed titanium, and hydroxyapatite coating	Self-adjusting mobile core	Teeth	2013	Yes	Yes • Conditional <sup>b</sup> Maximum spatial gradient magnetic field of ≤970 Gauss/cm (9.7 T/m)	5, 6, and 7	Yes

Abbreviations: FDA, Food and Drug Administration; MRI, magnetic resonance imaging.

<sup>a</sup>MRI conditional are devices that are MRI safe under a very specific set of conditions/MRI settings provided in the labeling.<sup>b</sup>Patients can safely undergo magnetic resonance (MR) scanning based on the following MR specifications established through nonclinical testing: (1) static magnetic field of 1.5 and 3.0 Tesla only, (2) specified maximum spatial gradient magnetic field (implant specific), and (3) maximum MR system reported, whole body averaged specific absorption rate of 2 W/kg in normal operating mode.



**Table 2.** Overview of randomized controlled trials on cervical disc arthroplasty.

Author (y)	Study Treatment	Follow-Up (mo)	Number of Levels
Radcliff et al (2017) <sup>9</sup>	Mobi-C	84	1
Vaccaro et al (2018) <sup>18</sup>	Secure-C	84	1
Garrido et al (2010) <sup>19</sup>	Bryan	48	1
Burkus et al (2014) <sup>20</sup>	Prestige ST	48	1
Rožanković et al (2014) <sup>21</sup>	Discover	24	1
Hisey et al (2016) <sup>22</sup>	Mobi-C	60	1
Janssen et al (2015) <sup>24</sup>	ProDisc-C	84	1
Phillips et al (2015) <sup>23</sup>	Porous Coated Motion (PCM)	60 and 84	1
Sasso et al (2017) <sup>26</sup>	Bryan	84 and 120	1
Sasso et al (2007) <sup>25</sup>	Bryan	24	1
Skeppholm et al (2015) <sup>10</sup>	Discover	24	1
Lavelle et al (2019) <sup>27</sup>	Bryan artificial disc	120	1
Vleggeert-Lankamp et al (2019) <sup>28</sup>	ActivC	24	1
Zhang et al (2012) <sup>29</sup>	Bryan	24	1
Zhang et al (2014) <sup>30</sup>	Mobi-C	48	1
Coric et al (2018) <sup>31</sup>	Kineflex C	60	1
Coric et al (2006) <sup>32</sup>	Bryan	24	1
Donk et al (2017) <sup>33</sup>	Bryan	60	1
Cheng et al (2011) <sup>34</sup>	Bryan	36	1, 2, and 3
Porchet et al (2004) <sup>35</sup>	Prestige II	24	1
Miller et al (2008) <sup>36</sup>	Bryan	84	1
McAfee et al (2010) <sup>37</sup>	PCM	24	1
Nabhan et al (2007) <sup>39</sup>	ProDisc-C	36	1
Nabhan et al. (2007) <sup>39</sup>	ProDisc-C	6	1
Hou et al (2016) <sup>40</sup>	Mobi-C	60	1
Riina et al (2008) <sup>41</sup>	Prestige ST	24	1
Sundseth et al (2017) <sup>42</sup>	Discover	24	1
Hacker (2005) <sup>43</sup>	Bryan	12	1
Skeppholm et al (2013) <sup>44</sup>	Discover	24	1
MacDowall et al (2019) <sup>45</sup>	Discover	60	1
Radcliff et al (2017) <sup>9</sup>	Mobi-C	84	2
Skeppholm (2015) <sup>10</sup>	Discover	24	2
Cheng et al (2009) <sup>48</sup>	Bryan	24	2
Yang et al (2018) <sup>47</sup>	Mobi-C	81	2

Biomechanical advantages seen with CDA also translate into improved clinical outcomes. Findlay et al affirmed this notion through a meta-analysis of 14 studies showing superior clinical outcomes—from 2 to 7 years—with respect to Neck Disability Index (NDI) and 36-Short-Form Health Survey (SF-36) physical component scores, as well as overall patient satisfaction.<sup>6</sup> Another meta-analysis conducted by Zhu et al further attributed superior NDI scores in addition to a safer risk profile. ACDF, however, was associated with shorter operative times and noninferiority across blood loss, hospital length of stay (LOS), and requirement for additional procedures.<sup>17</sup> Tables 2 and 3 provide a concise overview of design features and published outcomes from RCTs associated with various cervical disc implants.<sup>9,10,18–47</sup>

Longitudinal evidence further indicates CDR as a more cost-effective treatment relative to conventional ACDF. Radcliff et al performed a 7-year health

economics analysis demonstrating superior cost efficiency with CDR for the treatment of single-level cervical DDD, whereby CDR was associated with a mean cost savings of \$12,789 per patient compared with ACDF.<sup>49</sup> These findings lend support to a surgical decision model proposed by Qureshi et al, which established 14 years as the minimal time period in which CDR function needs to be preserved to maintain greater cost-effectiveness over ACDF.<sup>31</sup>

### CDR and Heterotrophic Ossification

Heterotrophic ossification (HO) frequently occurs after CDR and is thought to be a sequelae of either extensive vertebrae endplate preparation or colli muscle debridement. Arthrodesis resulting from HO induces aberrant loading across the index and adjacent segments, leading to decreased range of motion and increased prosthesis failure. Despite these alterations to spinal kinematics, the overall prevalence of ASD after CDR remains relatively low compared with ACDF.<sup>50</sup> Similarly, in line with other arthroplasty procedures, HO progresses slowly in CDR, displaying an incremental increase in prevalence over time. In a meta-analysis of 8 articles examining the prevalence of HO at 1 and 2 years after CDR, Chen et al reported the pooled prevalence of HO to be 44.6% and 58.2% at 1 and 2 years, respectively.<sup>48</sup> Over a more extensive follow-up period, Sheng reported pooled prevalences of 50%, 60%, and 70% at 1 or 2, 5 or 6, and 10 years postoperatively.<sup>50</sup>

The association between CDR and the development of HO has yet to be fully elucidated, but evidence suggests that the incidence of HO may be contingent on the biomechanic properties of individual prostheses. In a retrospective analysis, Yi et al compared the HO incidence of ProDisc-C, Mobi-C, and Bryan prosthesis in 170 patients with a minimum of 12-month follow-up, revealing that Bryan had the lowest occurrence of HO, while ProDisc-C had the highest.<sup>51</sup> A prior study by Zeng et al that compared HO incidence between the same 3 prostheses in patients 4 years postoperatively also found HO to occur most with the ProDisc-C and least with the Bryan prosthesis.<sup>52</sup> The Bryan and Mobi-C allow more degrees of freedom of motion compared with the ProDisc-C, which is a fixed-core prosthesis. This distinction may contribute to increased stress at the prosthesis-endplate interface, potentially contributing to the development of HO in more constrained implant designs.

**Table 3.** Summary of cervical disc arthroplasty randomized controlled trials.

Author (y)	Sample Size	Patient-Reported Outcomes	Secondary Surgery	ASD at Follow-Up	Conclusions
Radcliff et al (2017) <sup>9</sup> Intervention	N = 245 n = 164	<u>NDI recovery ratio:</u> 67% <u>VAS neck pain recovery ratio:</u> 71% <u>VAS arm pain recovery ratio:</u> 73% <u>SF-12 PCS recovery ratio:</u> 22% <u>SF-12 MCS recovery ratio:</u> 11% <u>NDI status at follow-up:</u> 84.6% improved, 14.2% not improved, and 1.2% worse <u>Patient satisfaction:</u> 90.9% <sup>a</sup> <u>VAS neck pain status at follow-up:</u> 87.5% improved, 8.8% not improved, and 3.8% worse	3%	40.4% (superior level) and 43.8% (inferior level) <sup>a</sup>	The intervention provided a similar reduction in patient-reported outcomes of pain and function while providing a lower risk for reoperation at both treated and adjacent levels.
Control	n = 81	<u>NDI recovery ratio:</u> 64% <u>VAS neck pain recovery ratio:</u> 71% <u>VAS arm pain recovery ratio:</u> 63% <u>SF-12 PCS recovery ratio:</u> 17% <u>SF-12 MCS recovery ratio:</u> 13% <u>NDI status at follow-up:</u> 84.8% improved, 12.7% not improved, and 2.5% worse <u>Patient satisfaction:</u> 77.8% <u>VAS neck pain status at follow-up:</u> 83.3% improved, 8.8% not improved, and 1.3% worse	12.3%	65.1% (superior level) and 63% (inferior level)	
Vaccaro et al (2018) <sup>18</sup> Intervention	N = 225 n = 124	<u>NDI improvement &gt;25%:</u> 90.4% <u>NDI improvement &gt;15%:</u> 88.8% <u>VAS neck pain success:</u> 85.7% <u>VAS arm pain success, left:</u> 85.7% <u>VAS arm pain success, right:</u> 84.9% <u>SF-36 PCS success:</u> 72% <u>SF-36 MCS success:</u> 47.2% <u>Neurological status stable/improved:</u> 94.2% <u>Patient satisfaction:</u> 96% <sup>a</sup>	4.2%	17% (symptoms attributable to adjacent level disease)	1. Intervention was noninferior to control in terms of providing long-term pain relief and functional improvement in patients diagnosed with single-level cervical degenerative disc refractory to nonoperative treatment.
Control	n = 101	<u>NDI improvement &gt;25%:</u> 86% <u>NDI improvement &gt;15%:</u> 84.1% <u>VAS neck pain success:</u> 78.3% <u>VAS arm pain success, left:</u> 75.5% <u>VAS arm pain success, right:</u> 72.6% <u>SF-36 PCS success:</u> 74.5% <u>SF-36 MCS success:</u> 43.4% <u>Neurological status stable/improved:</u> 87.1% <u>Patient satisfaction:</u> 88.8%	15.3%	37.5% (symptoms attributable to adjacent level disease)	2. Intervention statistically superior to control in terms of composite overall success and patient satisfaction. 3. Intervention had lower rates of secondary surgery (index and adjacent levels).
Garrido et al (2010) <sup>19</sup> Intervention	N = 47 n = 21	<u>NDI Success:</u> 93.3% <u>Neck pain score % improvement:</u> 80% <u>Arm pain score % improvement:</u> 86% <u>SF-36 PCS score % improvement:</u> 50% <u>SF-36 MCS score % improvement:</u> 24%	4.7%	5% (secondary surgery due to adjacent level disease)	Although not statistically significant, there appear to be clinically favorable outcomes regarding functional outcomes and adjacent segment disease for the arthroplasty cohort.
Control	n = 26	<u>NDI success:</u> 82.4% <u>Neck pain score % improvement:</u> 67% <u>Arm pain score % improvement:</u> 73% <u>SF-36 PCS score % improvement:</u> 50% <u>SF-36 MCS score % improvement:</u> 13%	23%	12% (secondary surgery due to adjacent level disease)	
Burkus et al (2014) <sup>20</sup> Intervention	N = 395 n = 212	<u>NDI Success:</u> 83.4% <u>Arm pain improvement:</u> 46.4 points <u>Neck pain improvement:</u> 55.1 points <u>SF-36 PCS scores:</u> 45.1 points at final follow-up	4.8%	4.6% (secondary surgery at adjacent levels)	Intervention has the potential for preserving motion at the operated level while providing mechanical stability and global neck mobility and pay result in a reduction in adjacent segment degeneration.
Control	n = 183	<u>Neurological success:</u> 88.2% <sup>a</sup> <u>NDI Success:</u> 80.1% <u>Arm pain improvement:</u> 47.4 points <u>Neck pain improvement:</u> 49.9 points <u>SF-36 PCS scores:</u> 43.2 points at final follow-up <u>Neurological success:</u> 79.7%	13.7%	11.9% (secondary surgery at adjacent levels)	

**Table 3.** Continued.

Author (y)	Sample Size	Patient-Reported Outcomes	Secondary Surgery	ASD at Follow-Up	Conclusions
Rožanković et al (2014) <sup>21</sup>	<i>N</i> = 101				
Intervention	<i>n</i> = 51	<u>NDI score</u> : 11.60 final (preop 50.90) <sup>a</sup> <u>VAS arm score</u> : 1.70 final (preop 7.70) <u>VAS neck pain</u> : 2.36 final (preop 7.56) <sup>a</sup>	-	-	The intervention provided better results after a 2-y follow-up compared with control.
Control	<i>n</i> = 50	<u>NDI score</u> : 19.68 final (preop 51.20) <u>VAS arm score</u> : 2.42 final (preop 7.66) <u>VAS neck pain</u> : 3.46 final (preop 7.50)	-	-	
Hisey et al (2016) <sup>22</sup>	<i>N</i> = 245				
Intervention	<i>n</i> = 164	<u>NDI, VAS (neck and arm), and SF-12 scores</u> : statistically similar between intervention and control	4.9% and 3%	37.1% (superior level) <sup>a</sup>	The intervention has the potential advantage of lower rates of reoperation and adjacent segment degeneration through 60 mo in treatment of single-level symptomatic cervical degenerative disc disease.
Control	<i>n</i> = 81		17.3% and 11.1%	54.7% (superior level)	
Janssen et al (2015) <sup>24</sup>	<i>N</i> = 152				
Intervention	<i>n</i> = 79	Score/Point Improvements <u>NDI</u> : 31.87 <u>SF-36 PF</u> : 10.99 <u>SF-36 role limitation due to physical health</u> : 16.03 <u>SF-36 role limitation due to emotional problems</u> : 9.67 <u>SF-36 energy/fatigue</u> : 12.43 <u>SF-36 emotional well-being</u> : 7.59 <u>SF-36 social functioning</u> : 15.64 <u>SF-36 bodily pain</u> : 16.05 <u>SF-36 general health</u> : 0.21 <u>SF-36 PCS</u> : 12.24 <u>SF-36 MCS</u> : 8.93 <u>VAS neck pain</u> : 45.67 <u>VAS arm pain</u> : 40.72 <u>VAS satisfaction with surgery</u> : 85.81/100	7% <sup>a</sup>	5.8% <sup>a</sup> (secondary surgery at adjacent level)	At 7 y postoperatively, all outcomes were similar between the 2 cohorts. However, intervention was associated with a lower risk of secondary surgery at both index and adjacent vertebral levels.
Control	<i>n</i> = 73	<u>Neurological success</u> : 88% Score/Point Improvements <u>NDI</u> : 30.3 <u>SF-36 PF</u> : 9.89 <u>SF-36 role limitation due to physical health</u> : 15.24 <u>SF-36 role limitation due to emotional problems</u> : 8.01 <u>SF-36 energy/fatigue</u> : 10.21 <u>SF-36 emotional well-being</u> : 5.94 <u>SF-36 social functioning</u> : 15.02 <u>SF-36 bodily pain</u> : 15.94 <u>SF-36 general health</u> : 0.64 <u>SF-36 PCS</u> : 12.09 <u>SF-36 MCS</u> : 6.93 <u>VAS neck pain</u> : 42.88 <u>VAS arm pain</u> : 38.83 <u>VAS satisfaction with surgery</u> : 81.81/100 <u>Neurological success</u> : 89%	18%	12.2% (secondary surgery at adjacent level)	
Phillips et al (2015) <sup>23</sup>	<i>N</i> = 293				



Table 3. Continued.

Author (y)	Sample Size	Patient-Reported Outcomes	Secondary Surgery	ASD at Follow-Up	Conclusions
Intervention	<i>n</i> = 163	<u>NDI success: 85%<sup>a</sup></u> <u>VAS neck pain success: 71.9%</u> <u>VAS arm pain success: 80.6%</u> <u>SF-36 PCS score improvement: 73.7%<sup>a</sup></u> <u>SF-36 MCS score improvement: 46.2%</u> <u>Neurological success: 92.4%</u> <u>Patient satisfaction: 86.9/100<sup>a</sup></u>	8.5%	Degeneration at Adjacent Levels 33.1% (superior) <sup>a</sup> and 49.2% (inferior)	1. Compared with the control, the intervention group demonstrated equivalent or better clinical outcomes while preserving cervical motion.
Control	<i>n</i> = 130	<u>NDI success: 74.2%</u> <u>VAS neck pain success: 75.8%</u> <u>VAS arm pain success: 71.1%</u> <u>SF-36 PCS score improvement: 56.7%</u> <u>SF-36 MCS score improvement: 54.3%</u> <u>Neurological success: 87.5%</u> <u>Patient satisfaction: 78.3/100</u>	13%	Degeneration at Adjacent Levels 50.9% (superior) and 51.7% (inferior)	2. Intervention had improved function, lower rates of prolonged dysphagia, greater patient satisfaction, lower incidence of adjacent level degeneration, and lower rate of secondary surgery.
Sasso et al (2017) <sup>26</sup>	<i>N</i> = 42				
Intervention	<i>n</i> = 19	Mean Scores at Final Follow-up <u>NDI: 8.05<sup>a</sup></u> <u>VAS neck pain: 1.3</u> <u>VAS arm pain: 0.84</u>	9%	-	At the final 120 mo follow-up, both groups demonstrated sustained improvement compared with the baseline. The intervention group demonstrated greater improvement in NDI compared with the control group. The reoperation rate was lower in the intervention group, but this was not statistically significant.
Control	<i>n</i> = 23	Mean Scores at Final Follow-up <u>NDI: 15.48</u> <u>VAS neck pain: 1.5</u> <u>VAS arm pain: 0.74</u>	32%	-	
Sasso et al (2007) <sup>25</sup>	<i>N</i> = 115				
Intervention	<i>n</i> = 56	Scores at Final Follow-up <u>NDI: 11<sup>a</sup></u> <u>Neck pain VAS: 16<sup>a</sup></u> <u>Arm pain VAS: 14<sup>a</sup></u> <u>SF-36 PCS: 51<sup>a</sup></u> <u>SF-36 MCS: 54</u>	3.57%	3.57% (secondary procedure for adjacent level disease)	At a 2 y follow-up, the intervention group demonstrated statistically significant improvements in NDI, neck pain, and SF-36 PCS.
Control	<i>n</i> = 59	Scores at Final Follow-up <u>Final NDI: 20</u> <u>Neck pain VAS: 32</u> <u>Arm pain VAS: 28</u> <u>SF-36 PCS: 46</u> <u>SF-36 MCS: 52</u>	6.7%	3.39% (secondary procedure for adjacent level disease)	
Skeppholm et al (2015) <sup>10</sup>	<i>N</i> = 125				
Intervention	<i>n</i> = 67	Mean Score at Final Follow-up <u>NDI: 39.1</u> <u>EQ-5D: 0.72</u> <u>VAS neck pain: 25.6</u> <u>VAS arm pain: 19.2</u>	11%	-	1. No significant superiority in NDI or secondary outcome variables in the intervention group compared with the ACDF group.
Control	<i>n</i> = 58	Mean Score at Final Follow-up <u>NDI: 40.1</u> <u>EQ-5D: 0.71</u> <u>VAS neck pain: 28.7</u> <u>VAS arm pain: 20.1</u>	4%	-	2. Reoperations were higher in the intervention group, but not significantly so. 3. No differences in secondary surgery for adjacent segment disease were seen after 2 y. 4. Artificial disc replacement did not result in better outcomes compared with fusion measured with NDI 2 y after surgery.
Lavelle et al (2019) <sup>27</sup>	<i>N</i> = 232				

Table 3. Continued.

Author (y)	Sample Size	Patient-Reported Outcomes	Secondary Surgery	ASD at Follow-Up	Conclusions
Intervention	<i>n</i> = 128	Mean NDI improvement: $\Delta 38.3^a$ NDI success rate: 90.5% <sup>a</sup> Mean VAS neck pain improvement: $\Delta 54.3$ Mean VAS arm pain score: $\Delta 58.1$ SF-36 PCS score improvement: $\Delta 14.9^a$	9.7%	9.7% (secondary surgery at adjacent levels)	While there may be some convergence of clinical benefit over time, there is maintenance of advantage in preserved motion and rates of reoperation for cervical disc arthroplasty.
Control	<i>n</i> = 104	Mean NDI improvement: $\Delta 31.1$ NDI success rate: 75.7% Mean VAS neck pain improvement: $\Delta 49.2$ Mean VAS arm pain score: $\Delta 51.6$ SF-36 PCS score improvement: $\Delta 12.6$	15.8%	15.8% (secondary surgery at adjacent levels)	
Vleggeert-Lankamp et al (2019) <sup>28</sup>	<i>N</i> = 98				
Intervention	<i>n</i> = 32	Score at Final Follow-up NDI: $20 \pm 22$ (preop $47 \pm 17$ ) VAS arm pain: $17 \pm 30$ (preop $60 \pm 24$ ) VAS neck pain: $23 \pm 32$ (preop $50 \pm 27$ ) EQ-5D: $0.82 \pm 0.23$ (preop $0.59 \pm 0.20$ ) VAS health: $74 \pm 25$ (preop $45 \pm 22$ ) Likert global health recovery (% satisfied): 65.6% Likert arm pain (% satisfied): 65.6% SF-36 PCS: $72.2 \pm 27$ (preop $41.3 \pm 14$ ) SF-36 MCS: $74.3 \pm 25$ (preop $54.9 \pm 25$ )	6.2%	-	It seems that there is no strong evidence in favor of 1 of the 3 treatment strategies based on the 2 y evaluation of results. They all give comparable clinical results, and all 3 options are acceptable.
Control 1 (ACDF)	<i>n</i> = 34	Score at Final Follow-up NDI: $19 \pm 18$ (preop $41 \pm 13$ ) VAS arm pain: $15 \pm 23$ (preop $57 \pm 20$ ) VAS neck pain: $23 \pm 27$ (preop $53 \pm 26$ ) EQ-5D: $0.83 \pm 0.18$ (preop $0.70 \pm 0.18$ ) VAS health: $74 \pm 24$ (preop $53 \pm 23$ ) Likert global health recovery (% satisfied): 67.6% Likert arm pain (% satisfied): 73.5% SF-36 PCS: $75.9 \pm 23$ (preop $44.7 \pm 15$ ) SF-36 MCS: $81.6 \pm 19$ (preop $61.7 \pm 22$ )	11.8%	-	
Control 2 (ACD)	<i>n</i> = 32	NDI: $19 \pm 15$ (preop $45 \pm 16$ ) VAS arm pain: $18 \pm 25$ (preop $64 \pm 22$ ) VAS neck pain: $21 \pm 23$ (preop $56 \pm 31$ ) EQ-5D: $0.83 \pm 0.17$ (preop $0.54 \pm 0.20$ ) VAS health: $69 \pm 24$ (preop $48 \pm 26$ ) Likert global health recovery (% satisfied): 62.5% Likert arm pain (% satisfied): 68.8% SF-36 PCS score: $68.3 \pm 24$ (preop $41.2 \pm 14$ ) SF-36 MCS score: $71.2 \pm 23$ (preop $57.9 \pm 21$ )	6.2%	-	
Zhang et al (2012) <sup>29</sup>	<i>N</i> = 109				Baseline changes in NDI and neck and arm pain were similar in patients in the intervention and control groups.
Intervention	<i>n</i> = 56	NDI improvement: $\Delta 36.89$ VAS neck pain improvement: $\Delta 49.27$ VAS arm pain improvement: $\Delta 54.96$	1.8%	-	
Control	<i>n</i> = 53	NDI improvement: $\Delta 38.98$ VAS neck pain improvement: $\Delta 47.38$ VAS arm pain improvement: $\Delta 55.45$	7.5%	-	
Zhang et al (2014) <sup>30</sup>	<i>N</i> = 111				
Intervention	<i>n</i> = 55	JOA, VAS, and NDI scores at final follow-up:	-	-	
Control	<i>n</i> = 56	Not statistically different between groups	-	-	
Coric et al (2018) <sup>31</sup>	<i>N</i> = 269				There were statistically significant differences between the groups, favoring the intervention group when evaluating ASD and some clinical outcome measures. At no point was there a significant difference favoring the control.
Intervention	<i>n</i> = 136	NDI score: 18.5 (preop 62.8) VAS pain score: 20.8 (preop 77.1)	8.8% (rate of reoperation or revision)	ASD scores at final follow-up: 65.7% (superior level, preop 51.1%) <sup>a</sup> and 84.9% (inferior level, preop 47.4%)	
Control	<i>n</i> = 133	NDI score: 23 (preop 61.8) VAS pain scores: 24.2 (preop 75.7)	8.3% (rate of reoperation or revision)	ASD scores at final follow-up: 93.2% (superior level, preop 53.1%) and 86.8% (inferior level, preop 53.3%)	
Coric et al (2006) <sup>32</sup>	<i>N</i> = 33				

Table 3. Continued.

Author (y)	Sample Size	Patient-Reported Outcomes	Secondary Surgery	ASD at Follow-Up	Conclusions
Intervention	<i>n</i> = 17	Score at Final Follow-up NDI: 9 (preop 41) SF-36 PCS: 50 (preop 34) SF-36 MCS: 56 (preop 48) VAS arm pain: 10 (preop 60) VAS neck pain: 18 (preop 79)	-	-	Similar improvements in the clinical parameters were observed in both groups, but in the intervention group, there was radiographic evidence of motion at the treated level.
Control	<i>n</i> = 16	Score at Final Follow-up NDI: 23 (preop 48) SF-36 PCS: 46 (preop 32) SF-36 MCS: 49 (preop 51) VAS arm pain: 30 (preop 61) VAS neck pain: 38 (preop 68)	-	-	
Donk et al (2017) <sup>33</sup>	<i>N</i> = 140	All Groups at Final Follow-up NRS arm pain: 1.8 ± 2.5 NRS neck pain: 1.9 ± 2.6			
Intervention	<i>n</i> = 49	Mean Improvement at Final Follow-up NDI: 7.5 ± 8.5 (preop 18.8 ± 7.5) SF-36 PCS: 32.1 ± 2.5 (preop 44.1 ± 13.9) SF-36 MCS: 22.8 ± 2.1 (preop 58.3 ± 22.2)	2% <sup>a</sup>	0% (surgery for ASD)	This trial did not detect a difference between 3 surgical modalities for treating a single-level degenerative disc disease. There was also no statistically significant difference between groups regarding surgery for adjacent segment disease.
Control 1 (ACDF)	<i>n</i> = 46	Mean Improvement at Final Follow-up NDI: 7.5 ± 8.5 (preop 18.8 ± 7.4) SF-36 PCS: 32.1 ± 2.5 (preop 44.0 ± 11.0) SF-36 MCS: 22.8 ± 2.1 (preop 55.7 ± 21.1)	13% <sup>a</sup>	10.6% (surgery for ASD)	
Control 2 (ACD)	<i>n</i> = 45	Mean Improvement at Final Follow-up NDI: 7.5 ± 8.5 (preop 17.1 ± 6.4) SF-36 PCS: 32.1 ± 43.6 SF-36 MCS: 22.8 ± 2.1 (preop 62.1 ± 18.8)	8.9% <sup>a</sup>	6.7% (surgery for ASD)	
Cheng et al (2011) <sup>34</sup>	<i>N</i> = 83	Both Groups at Final Follow-up NDI, SF-36, and JOA scores: Patients in intervention group had significantly better Modified Odom's Criteria score at final follow-up: 58.5% excellent, 34.1% good, and 7.3% fair			
Intervention	<i>n</i> = 41	Modified Odom's Criteria score at final follow-up: 58.5% excellent, 34.1% good, and 7.3% fair	-	-	Intervention is safe for the treatment of patients with cervical myelopathy and comparable to control in improving functional outcomes at 1 and up to 3 y after surgery.
Control	<i>n</i> = 42	Modified Odom's Criteria score at final follow-up: 58.5% excellent, 25% good, 15% fair, and 5% poor	-	-	
Porchet et al (2004) <sup>35</sup>	<i>N</i> = 55				
Intervention	<i>n</i> = 27	NDI and arm pain frequency and intensity at final follow-up: Improvement seen was statistically equivalent between both groups	0%	0%	Most outcomes measured seemed to favor the intervention group, but the differences were not statistically superior. Radiographic analyses showed that the intervention maintained motion at the treated level without actual adjacent segment compromise.
Control	<i>n</i> = 28	Neck pain frequency and intensity: Statistical equivalence could not be shown between the 2 groups SF-36 at final follow-up: Differences in scores between treatment groups were not statistically significant	7.47% (adjacent level secondary surgery due to secondary myelopathy)		
Miller et al (2018) <sup>36</sup>	<i>N</i> = 70				
Intervention	<i>n</i> = 34	-	-	Adjacent level degeneration: 0.318 (preop 0.313) at 84 mo; 0.295 (preop 0.313) at 60 mo	Adjacent level degeneration occurred in a similar manner in both the intervention and control groups.
Control	<i>n</i> = 36	-	-	Adjacent level degeneration: 0.299 (preop 0.310) at 84 mo; 0.310 (preop 0.310) at 60 mo	
McAfee et al (2010) <sup>37</sup>	<i>N</i> = 251				

Table 3. Continued.

Author (y)	Sample Size	Patient-Reported Outcomes	Secondary Surgery	ASD at Follow-Up	Conclusions
Intervention	<i>n</i> = 151	Incidence at Final Follow-up <u>Dysphagia</u> : 85% none, 11.9% mild, 2.9% moderate, and 0% severe <sup>a</sup> <u>Dysphonia</u> : 9.0 ± 15.4	-	-	In this study, the incidence of postoperative dysphagia and the long-term resolution of dysphagia were greatly improved in the intervention group compared with the control group.
Control	<i>n</i> = 100	Incidence at Final Follow-up <u>Dysphagia</u> : 72.4% none, 13.8% mild, 13.8% moderate, and 0% severe <u>Dysphonia</u> : 13.1 ± 18.8	-	-	
Nabhan et al (2007) <sup>38</sup>	<i>N</i> = 41				
Intervention	<i>n</i> = 20	<u>VAS neck pain</u> : 1.7 (preop 6.0) <u>VAS arm pain</u> : 1.2 (preop 7.3)	-	-	After both procedures, a significant pain reduction in neck and arm was observed, with no significant differences between both groups.
Control	<i>n</i> = 21	<u>VAS neck pain</u> : 2.5 (preop 6.2) <u>VAS arm pain</u> : 1.7 (preop 7.2)	-	-	
Nabhan et al., 2007 <sup>39</sup>	<i>N</i> = 33				
Intervention	<i>n</i> = 16	<u>VAS neck pain</u> : 2.8 (preop 6.2) <u>VAS arm pain</u> : 1.4 (preop 7.6)	-	-	Both treatments resulted in significant reduction of neck and arm pain without statistical difference between groups
Control	<i>n</i> = 17	<u>VAS neck pain</u> : 2.0 (preop 6.4) <u>VAS arm pain</u> : 1.7 (preop 7.2)	-	-	
Hou et al (2016) <sup>40</sup>	<i>N</i> = 99				
Intervention	<i>n</i> = 51	<u>JOA score</u> : 14.7 <u>VAS for pain scores</u> : 0.4 <u>NDI scores</u> : 19.7	1.97%	-	Both intervention and control treatments are effective in improving clinical status at up to 5 y follow-up. Intervention is a safe and encouraging alternative to the control treatment, particularly in patients with single-level cervical disc degeneration who require surgery.
Control	<i>n</i> = 48	<u>JOA score</u> : 14.5 <u>VAS for pain scores</u> : 0.4 <u>NDI scores at final follow-up</u> : 18.5	14.6%	-	
Riina et al (2008) <sup>41</sup>	<i>N</i> = 16				
Intervention	<i>n</i> = 9	Improvement at Final Follow-up <u>VAS neck pain</u> : 17.9 (preop 74.8) <u>VAS arm pain</u> : 17.2 (preop 69.1) <u>NDI</u> : 18.9 (preop 65.5) <u>Neurological status</u> : 100% motor function and reflexes, 77.8% sensory function, and overall <u>SF-36 PCS success rate</u> : 77.8% <u>SF-36 MCS success rate</u> : 66.7%	-	-	Neurological function and neck pain were better addressed in the intervention group, but arm pain was better addressed in the control group. The intervention performed as least as well as the control.
Control	<i>n</i> = 7	Improvement at Final Follow-up <u>VAS neck pain</u> : 17.4 (preop 71.6) <u>VAS arm pain</u> : 8.6 (preop 72.7) <u>NDI</u> : 22.3 (preop 60.2) <u>Neurological status</u> : 100% motor, 85.7% sensory and reflexes, and 71.4% overall <u>SF-36 PCS success rate</u> : 100% <u>SF-36 MCS success rate</u> : 57.1%			
Sundseth et al (2017) <sup>42</sup>	<i>N</i> = 120				
Intervention	<i>n</i> = 60	Improvement at Final Follow-up <u>NDI</u> : 25 (preop 45.7) <u>EQ-5D-3L</u> : 0.72 (preop 0.37) <u>SF-36 PCS</u> : 46.4 (preop 32.9) <u>SF-36 MCS</u> : 52.3 (preop 47.4) <u>NRS 11th arm pain</u> : 2.0 (preop 6.0) <u>NRS 11th neck pain</u> : 3.0 (preop 7.0)	13.3% (reoperations at index level)	-	Intervention treatment was not superior to control treatment regarding clinical outcomes. The rate of index level reoperations was significantly higher, and the duration of the surgical procedure was longer with the intervention treatment.
Control	<i>n</i> = 60	Improvement at Final Follow-up <u>NDI</u> : 21.2 (preop 51.2) <u>EQ-5D-3L</u> : 0.72 (preop 0.28) <u>SF-36 PCS</u> : 46.9 (34.9) <u>SF-36 MCS</u> : 50.3 (preop 44.2) <u>NRS 11th arm pain</u> : 1.5 (preop 6.5) <u>NRS 11th neck pain</u> : 3.0 (preop 7.0)	1.67% <sup>a</sup> (reoperations at index level)	-	
Hacker (2005) <sup>43</sup>	<i>N</i> = 28		-	-	

Table 3. Continued.

Author (y)	Sample Size	Patient-Reported Outcomes	Secondary Surgery	ASD at Follow-Up	Conclusions
Intervention	<i>n</i> = 13	<u>NDL, neck pain, arm pain, SF-36 PCS, and</u>	-	-	Preoperative symptoms improved more in intervention group than in control group, but the difference was not statistically significant.
Control	<i>n</i> = 15	<u>SF-36 MCS: No significant difference between groups</u>	-	-	
Skeppholm et al (2013) <sup>44</sup>	<i>N</i> = 136				
Intervention	<i>n</i> = 76	<u>Median dysphagia symptom questionnaire (DSQ) level at final follow-up: 0<sup>a</sup></u>	-	-	Prolonged postoperative dysphagia could be explained by factors such as the bulk of implants and decreased motion of the cervical spine.
Control	<i>n</i> = 60	<u>Median DSQ level at final follow-up: 1</u>	-	-	
MacDowall et al (2019) <sup>45</sup>	<i>N</i> = 137				
Intervention	<i>n</i> = 67	Improvement at Final Follow-up NDI: 36 (preop 64) EQ-5D: 0.62 (preop 0.37) EQ-5D health: 67.3 (preop 47.2) VAS neck pain: 29.1 (preop 47.2) VAS arm pain: 24 (preop 57) DSQ level: 1.6 (preop 1.4)	25.4%	7.46% (secondary surgery due to clinical adjacent segment pathology at final follow-up) 24% (incidence of mild clinical adjacent segment pathology at final follow-up)	At 5 y, patients in the intervention group did not have better clinical or radiographic outcomes compared with the control group. However, the intervention group had a significantly lower mean DSQ score than the control group at the final follow-up.
Control	<i>n</i> = 70	Improvement at Final Follow-up NDI: 32.2 (preop 61) EQ-5D: 0.72 (preop 0.46) EQ-5D health: 70.1 (preop 44) VAS neck pain: 31.8 (preop 58.6) VAS arm pain: 23.8 (preop 56.7) DSQ level: 2.3 (preop 1.4)	10%	7.41% (secondary surgery due to clinical adjacent segment pathology at final follow-up) 20% (incidence of mild clinical adjacent segment pathology at final follow-up)	
Phillips et al (2021) <sup>23</sup>	<i>N</i> = 316				
Intervention	<i>n</i> = 152	-	1.9%	Did not assess	-
Control	<i>n</i> = 164	-	4.8%	Did not assess	-
Radcliff et al (2017) <sup>9</sup>	<i>N</i> = 330				
Intervention	<i>n</i> = 225	Improvement at Final Follow-up NDI: 18.0 ± 19.1 (preop 53.8 ± 15.4) <sup>a</sup> VAS neck pain: 19.0 ± 27.1 (preop 71.2 ± 20.5) VAS arm pain: 15.9 ± 25.7 (preop 68.8 ± 25.0) SF-12 PCS: 46.3 ± 11.1 (preop 33.4 ± 6.7) SF-12 MCS: 52.0 ± 10.1 (preop 41.9 ± 11.3) NDI and pain status: 80.8% improved, 16.5% not improved, and 2.7% worse	4.4% (index level) <sup>a</sup> and 4.4% (adjacent level) <sup>a</sup>	Adjacent Level Degeneration 37.5% (superior level) and 30.3% (inferior level)	The intervention provided a similar reduction in patient-reported outcomes of pain and function while providing a lower risk for reoperation at both treated and adjacent levels. The difference in clinical effectiveness of intervention vs control becomes more apparent as treatment increases from 1 to 2 levels, indicating a significant benefit for intervention treatment over control treatment for 2-level procedures.
Control	<i>n</i> = 105	Improvement at Final Follow-up NDI: 26.2 ± 22.4 (preop 55.7 ± 15.2) VAS neck pain: 28.7 ± 30.4 (preop 75.1 ± 18.9) VAS arm pain: 18.4 ± 27.0 (preop 73.1 ± 21.9) SF-12 PCS: 43.7 ± 11.9 (preop 32.5 ± 7.7) SF-12 MCS: 49.1 ± 12.7 (preop 42.0 ± 12.0) NDI and pain status: 70.2% improved, 25.9% not improved, and 3.8% worse	10.5% (index level) and 11.4% (adjacent level)	Adjacent Level Degeneration 80.8% (superior level) and 66.7% (inferior level)	
Skeppholm (2015) <sup>10</sup>	<i>N</i> = 125				
Intervention	<i>n</i> = 67	-	11%	-	-
Control	<i>n</i> = 58	-	4%	-	-
Cheng et al (2009) <sup>46</sup>	<i>N</i> = 62				

Table 3. Continued.

Author (y)	Sample Size	Patient-Reported Outcomes	Secondary Surgery	ASD at Follow-Up	Conclusions
Intervention	<i>n</i> = 30	Improvement at Final Follow-up <u>VAS neck pain</u> : 1.5 (preop 7.3) <sup>a</sup> <u>VAS arm pain</u> : 1.4 (preop 7.1) <sup>a</sup> <u>NDI</u> : 11 (preop 50) <sup>a</sup> <u>SF-36 PCS</u> : 50 (preop 35) <sup>a</sup>	-	-	Intervention treatment was shown to be reliable and safe for the treatment of patients with 2-level cervical disc disease.
Control	<i>n</i> = 32	Improvement at Final Follow-up <u>VAS neck pain</u> : 2.6 (preop 7.1) <u>VAS arm pain</u> : 2.7 (preop 7.2) <u>NDI</u> : 19 (preop 51) <u>SF-36 PCS</u> : 45 (preop 34)	-	-	
Yang et al (2018) <sup>47</sup>	<i>N</i> = 80				
Intervention	<i>n</i> = 38	Improvement at Final Follow-up <u>NDI</u> : Scores at final follow-up were significantly higher in the control group than intervention group <u>JOA</u> : Scores at final follow-up were statistically similar between groups	0%	Adjacent Segment Degeneration 15.7% (superior level) <sup>a</sup> and 7.8% (inferior level) <sup>a</sup>	Intervention treatment was safe and effective and a statistically superior alternative to ACDF for degenerative disc disease at 2 contiguous levels.
Control	<i>n</i> = 42	<u>VAS</u> : Scores were significantly lower in the intervention group than in the control group	0%	Adjacent Segment Degeneration 45.7% (superior level) and 33.35% (inferior level)	Intervention treatment could reduce the occurrence of ASD at the superior and inferior adjacent segments by reducing the ROM.

Abbreviations: ACDF, anterior cervical discectomy and fusion; ASD, adjacent segment disease; JOA, Japanese Orthopaedic Association ; NDI, Neck Disability Index; preop, preoperative; ROM, range of motion; SF-36, short form-36; SF-12 MCS, short form-12 mental component score; SF-36 MCS, short form 36-mental component score; SF-12 PCS, short form-12 physical component score; SF-36 PCS, short form-36 physical component score; VAS, visual analog scale.

<sup>a</sup>Findings were based on sample sizes that varied from the original cohort due to loss of follow-up (attrition rates <5%).

## DISCUSSION

When appropriately indicated, CDR may provide a beneficial alternative to conventional ACDF for the treatment of degenerative cervical spine pathology on account of its motion-preserving features. This notion has been widely and consistently reported across prior studies and bypasses the major limitations imposed by ACDF.<sup>7,53</sup> While indications remain relatively confined for CDR, increasing adoption of this technique will lend to expanding indications for its use in multilevel pathologies.

### Future Directions—Expanding Indications

Investigational device exemptions (IDEs) with strict inclusion and exclusion criteria are required for FDA approval. These criteria are utilized by the FDA to establish appropriate indications and contraindications in the clinical setting.<sup>54</sup> Common indications and contraindications for current CDA implants are listed in Table 4.<sup>55–57</sup> Despite strict criteria set by device companies and the FDA, surgeons have been expanding their indications for CDA in recent years.

Promising outcomes seen consistently across studies have contributed to increasing off-label uses of CDR.<sup>58</sup> Routine utilization of CDR for extensive multilevel cervical disc pathology may potentially be on the horizon with forthcoming data to assess its clinical efficacy

in these settings. In a recent study published in 2020, Gornet et al reported on 7-year outcomes for 3- (contiguous and noncontiguous) and 4-level (contiguous) CDA. The authors reported favorable results across all patient-reported outcome measures in tandem with low reoperation rates (3.6%) in a cohort of 139 patients.<sup>59</sup> It is important to note, however, that this study did not include an ACDF cohort for comparison and was therefore not listed among the RCTs tabulated within the present study. Chang et al conducted a comparative analysis of patients undergoing either 3-level CDR or ACDF, where both groups achieved similar outcomes and complication rates; CDR nonetheless preserved a greater postoperative range of motion relative to the ACDF group.<sup>60</sup> In a bibliometric analysis of 957 articles concerning CDA, Tu et al noted an exponential rise in publications pertaining to multilevel CDA (>2 levels) over the past decade, although the majority of these were composed of 2-level procedures.<sup>61</sup> Nonetheless, studies on 3-level applications have seen a recent and sustained increase from 2017 to the present. This trend is believed to signify the growing acceptance of CDA as a viable surgical alternative for multilevel disease among spine surgeons, particularly in geographic regions with less stringent indications for CDA. Interestingly, research and application of multilevel CDA beyond currently established indications continues to expand in Asia and



**Table 4.** Most common indications and contraindications for cervical disc arthroplasty.

Indications
<ol style="list-style-type: none"> <li>1. Skeletally mature patients</li> <li>2. Reconstruction of the disc from C3 to C7 following discectomy</li> <li>3. Single or 2 contiguous levels</li> <li>4. Intractable radiculopathy (with or without neck pain) or myelopathy (due to abnormality at the level of the disc space)</li> <li>5. At least 1 of the following confirmed by imaging (computed tomography, magnetic resonance imaging, or x-rays): <ul style="list-style-type: none"> <li>• Herniated nucleus pulposus</li> <li>• Spondylosis (defined by the presence of osteophytes)</li> <li>• Visible loss of disc height compare to with adjacent levels</li> </ul> </li> <li>6. Failed 6 wk of conservative management or progressive signs or symptoms despite nonoperative treatment</li> </ol>
Contraindications
<ol style="list-style-type: none"> <li>1. Acute or chronic infection (systemic or at the operative site)</li> <li>2. Osteoporosis or osteopenia (defined as DEXA bone density measured T-score <math>\leq -2.5</math> or <math>\leq 1.5</math>, respectively)</li> <li>3. Known allergy or sensitivity to implant materials (cobalt, chromium, molybdenum, titanium, hydroxyapatite, or polyethylene)</li> <li>4. Compromised vertebral bodies at the index level(s) due to previous trauma to the cervical spine or significant cervical anatomical deformity or disease (eg, ankylosing spondylitis and rheumatoid arthritis)</li> <li>5. Marked cervical instability on resting lateral or flexion/extension radiographs (demonstrated by translation <math>&lt;3.5</math> mm and/or <math>&gt;11^\circ</math> angular difference to that of either level adjacent to the treated level(s))</li> <li>6. Severe facet joint disease or degeneration</li> <li>7. Severe spondylosis (defined as bridging osteophytes, loss of disc height <math>&gt;50\%</math>, or <math>&lt;2^\circ</math> of motion), as this may lead to limited range of motion and may encourage bone formation (eg, heterotopic ossification and fusion)</li> </ol>

Abbreviation: DEXA, dual-energy x-ray absorptiometry.

<sup>a</sup>Derived from Summary of Safety and Effectiveness Data for the ProDisc Total Disc Replacement and Mobi-C Cervical Disc Prosthesis.

Europe, yielding precursory evidence to support its use as a safe and effective alternative in select patients. Although preliminary data on multilevel CDR appears promising, additional high-quality RCTs with longer follow-up intervals are required for a comprehensive, longitudinal assessment of its clinical efficacy.

Hybrid surgery is an emerging concept that combines features of ACDF and CDR. Existing literature on this novel strategy has been in part limited by the exclusion of patients with preexisting fusions in prior RCTs.<sup>8,11,31</sup> Support surrounding this technique is driven by the idea that patients with multilevel cervical pathologies have varying degrees of degeneration at each level.<sup>62</sup> As such, a hybridized approach incorporating both fusion and arthroplasty elements may be applied independently across affected levels to provide tailored treatments suited to patients' unique pathologies.<sup>58</sup> A recent retrospective database analysis comparing CDA, ACDF, and hybrid surgeries found no significant differences in 30-day postoperative complications or unplanned readmissions, although patients who underwent hybrid surgeries had shorter LOS on average. Conclusions from this study, however, should

take into consideration that patients in the hybrid surgery cohort were younger and had fewer comorbidities.<sup>63</sup> Wang et al compared 3-level variations across 64 patients with cervical DDD in the context of hybrid procedures using 2 cohorts: single-level ACDF with adjacent CDR or single-level CDR with contiguous 2-level ACDF of caudal segments. Both hybrid techniques produced outcomes to adequately support their safety and efficacy in clinical practice but also revealed distinctive features relative to one another. Single-level CDR with contiguous 2-level fusion achieved greater accuracy with correction of cervical lordosis but was associated with higher incidence of heterotopic ossification, while single-level fusion with 2-level CDR maintained superior range of motion.<sup>53</sup> With only preliminary evidence to corroborate the use of cervical hybrid constructs, further longitudinal studies such as ZimVie's Mobi-C Hybrid Surgery Trial—following recent FDA approval of its IDE status in September 2023—are warranted to assess the long-term impact of hybrid techniques in the clinical setting.<sup>64 60</sup>

## CONCLUSIONS

CDA was developed to provide a motion-preserving alternative to ACDF. Numerous RCTs have demonstrated the procedure to be as safe and effective as ACDF for the treatment of radiculopathy and myelopathy refractory to conservative management of cervical DDD. As further evidence arises to corroborate its utility in various clinical settings, CDA indications and utilization will increase correspondingly. Establishing a centralized resource that consolidates relevant details and clinical data of current FDA-approved implants would help spine surgeons make better-informed decisions during preoperative planning.

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