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Cost Utility Analysis of the Cervical Artificial Disc vs Fusion for the Treatment of 2-Level Symptomatic Degenerative Disc Disease: 5-Year Follow-up

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WHAT IS THIS BOX?

A QR Code is a matrix barcode readable by QR scanners, mobile phones with cameras, and smartphones. The QR Code above links to Supplemental Digital Content from this article.

BACKGROUND: The cervical total disc replacement (cTDR) was developed to treat cervical degenerative disc disease while preserving motion.

OBJECTIVE: Cost-effectiveness of this intervention was established by looking at 2-year follow-up, and this update reevaluates our analysis over 5 years.

METHODS: Data were derived from a randomized trial of 330 patients. Data from the 12-Item Short Form Health Survey were transformed into utilities by using the SF-6D algorithm. Costs were calculated by extracting diagnosis-related group codes and then applying 2014 Medicare reimbursement rates. A Markov model evaluated quality-adjusted life years (QALYs) for both treatment groups. Univariate and multivariate sensitivity analyses were conducted to test the stability of the model. The model adopted both societal and health system perspectives and applied a 3% annual discount rate.

RESULTS: The cTDR costs \$1687 more than anterior cervical discectomy and fusion (ACDF) over 5 years. In contrast, cTDR had \$34 377 less productivity loss compared with ACDF. There was a significant difference in the return-to-work rate (81.6% compared with 65.4% for cTDR and ACDF, respectively; $P = .029$). From a societal perspective, the incremental cost-effective ratio (ICER) for cTDR was $-\$165\,103$ per QALY. From a health system perspective, the ICER for cTDR was \$8518 per QALY. In the sensitivity analysis, the ICER for cTDR remained below the US willingness-to-pay threshold of \$50 000 per QALY in all scenarios ($-\$225\,816$ per QALY to \$22 071 per QALY).

CONCLUSION: This study is the first to report the comparative cost-effectiveness of cTDR vs ACDF for 2-level degenerative disc disease at 5 years. The authors conclude that, because of the negative ICER, cTDR is the dominant modality.

KEY WORDS: Cervical artificial disc, Cervical spondylosis, Cost analysis, Cost-effectiveness, Decision analysis, Spine fusion, Total disc replacement

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ABBREVIATIONS: ACDF, anterior cervical discectomy and fusion; AWP, average wholesale price; CE, cost-effectiveness; CEA, cost-effectiveness analysis; CPT, Current Procedural Terminology; cTDR, cervical total disc replacement; CUA, cost-utility analysis; DDD, degenerative disc disease; DRG, diagnosis-related group; FDA, US Food and Drug Administration; ICER, incremental cost-effectiveness ratio; IDE, Investigational Device Exemption; NDI, neck disability index; QALY, quality-adjusted life years; RCT, randomized controlled trial; RTW, return-to-work; SF-12, 12-Item Short Form Health Survey; VAS, visual analog scale; WTP, willingness-to-pay

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.neurosurgery-online.com).

Cervical total disc replacement (cTDR) was developed to treat symptomatic cervical degenerative disc disease (DDD) while preserving motion. For single-level degenerative disc disease (DDD), noninferiority and cost-effectiveness (CE) of cTDR compared with anterior cervical discectomy and fusion (ACDF) have been demonstrated for several devices in numerous studies.^{1–8} For 2-level symptomatic DDD, ACDF had been the standard of care until a recent randomized controlled trial (RCT) exhibited superiority for cTDR, resulting in US Food and Drug Administration (FDA) approval.⁹ Similarly, the CE of 2-level cTDR was previously established looking at 2-year follow-up data from this trial.¹⁰ From the

societal perspective, 2-level cTDR dominated ACDF at 2 years in this analysis, meaning that it was more effective at less cost.¹⁰ Although the original model allowed for extrapolation, this is less than ideal for determining long-term sustainability. Therefore, the current article reevaluates our previous conclusion by analyzing the same cohort with updated 5-year trial data.

To briefly review, 2 approaches are commonly used to conduct a cost-effectiveness analysis (CEA) for a clinical trial: simple incremental calculation vs decision analytical modeling. The simple calculation method is straightforward and uses quality-of-life data collected during the trial to calculate the aggregate for each arm to make comparisons between arms. Decision analytical modeling involves transforming the quality-of-life data into input parameters that are used to inform a decision model about the likelihood of clinical events occurring to trial subjects. The advantage of the latter is its flexibility. Decision analysis allows for time-frame extrapolation, subgroup analysis, and more robust sensitivity analyses to test generalizability. Obvious disadvantages include the time required to derive input parameters from the original trial data and the need for assumptions required to generate the model.¹¹

This study models a cost-utility analysis (CUA), a type of CEA, because it allows for the estimation of the ratio between the cost of a health-related intervention and the benefit experienced by the patient. Therefore, the purpose was to use the best estimates of cost and utility to assemble a model that compares the 5-year CE of cTDR with ACDF for the treatment of 2-level cervical DDD. A secondary goal was to identify the value of indirect cost to society (productivity loss) with a more comprehensive return-to-work (RTW) analysis than previously evaluated.

METHODS

Data Source

Data were derived from a published RCT⁹ comparing cTDR (US FDA Investigational Device Exemption [IDE] trial for Mobi-C) with ACDF for 2-level DDD. Patients included in the trial ($n = 330$) had to be diagnosed with radiculopathy or myeloradiculopathy at 2 contiguous levels from C3 to C7 that was unresponsive to conservative treatment for at least 6 weeks or demonstrated progressive symptoms. The specific methodology from the RCT is not included here for the sake of brevity. All statistical analysis was conducted by using SAS version 9.3 (SAS Institute, Inc, Cary, North Carolina). All modeling was performed using a common decision-analysis software package (TreeAge Pro 2013; TreeAge Software, Williamstown, Massachusetts).

Study Design

The study examined the cost and utility of cTDR vs ACDF during the 5 years after surgery. The analysis was conducted in accordance with the Panel on Cost-Effectiveness Health and Medicine convened by the US Public Health Service.¹² We assessed both societal and health system perspectives. The societal perspective accounts for both direct and indirect costs, whereas the health system perspective accounts for direct costs alone. Direct medical costs included operating room time, hospital stay, postoperative medications, follow-up visits (scheduled and unscheduled), and surgery-related complications (details in the “Direct

Medical Cost” section). Productivity loss was defined as lost workdays and/or the inability to continue working after having returned. Health-related utility outcome was expressed in quality-adjusted life years (QALYs). Both cost and QALY outcomes were discounted at a yearly rate of 3% to reflect their present value.¹² The cost-utility outcome was calculated as the incremental cost-effectiveness ratio (ICER) for cTDR. By definition, an ICER is the difference in cost divided by the difference in QALY for 2 interventions. A value under the commonly accepted United States-based willingness-to-pay (WTP) threshold of \$50 000 per QALY was considered to favor cTDR in comparison with ACDF in terms of comparative CE.

A Markov model (shown in Figure 1) was constructed to analyze postsurgical costs and health-related utility outcomes. The model initially assumed a target population of patients aged 44 years (based on the mean age from the RCT⁹). Each Markov state depicted both a patient's health and work status at any given time point evaluated. Overall quality of life was represented by 5 distinct health states, each having an assigned differential utility score (described further in the “Health States” section). According to the published RCT,⁹ preoperative demographics and health status (neck disability index [NDI], visual analog scale [VAS], and the 12-Item Short Form Health Survey [SF-12]) were not statistically different between the surgical cohorts. Return-to-work (RTW) status was dichotomized as either *yes* or *no*. In addition, if RTW was established, it was further stratified by persistence of work at each follow-up visit. Details pertaining to RTW status are described further in the “Productivity Loss” section. The model used varying time intervals per cycle to account for the *typical* clinical course: patients with DDD often experienced rapid initial symptomatic improvement that tapered over time. The model begins with 6-week cycles from the initial surgery up to 6 months, followed by 6-month cycles thereafter. All model input parameters included in the model are provided in Table 1.

Health States

The development of health states was described in detail in the 2-year article.¹⁰ In brief, they include mild, moderate, severe, crippled, and bedbound; they were created by stratifying the NDI and VAS for neck and arm pain, which are 2 principle quantitative measurements used in the RCT.⁹ The model then assessed transition probability between health states (see **Tables, Supplemental Digital Content 1 and 2**, <http://links.lww.com/NEU/A841>, <http://links.lww.com/NEU/A842>).

Each health state was assigned a health-related utility score measured in QALYs. The QALYs were evaluated by using SF-12 data collected preoperatively and at 6 weeks, and at 3, 6, 12, 24, 36, 48, and 60 months. As in the previous 2-year CEA,¹⁰ we opted to use SF-6D for converting SF-12 data into utilities.¹⁵ This SAS-based mapping algorithm was obtained from the University of Sheffield. Mean utility and standard deviations were computed for each of the 5 health states and were found to directly correlate.¹⁶ Preoperative and postoperative health states with associated utility values were then determined for each of the surgical cohorts.

Productivity Loss

Per the original RCT, data for productivity loss were limited to 3 years of follow-up for both surgical cohorts because no additional change in RTW was observed between the 2- and 3-year postoperative time points. Preoperatively, 204 (61.6%) patients worked; 74 (22.4%) were unable to work secondary to their disease; and 53 (16.0%) did not work for reasons other than the disease (ie, retired). We only included patients from the former 2 groups ($n = 278$) in our analysis. The proportion of patients working

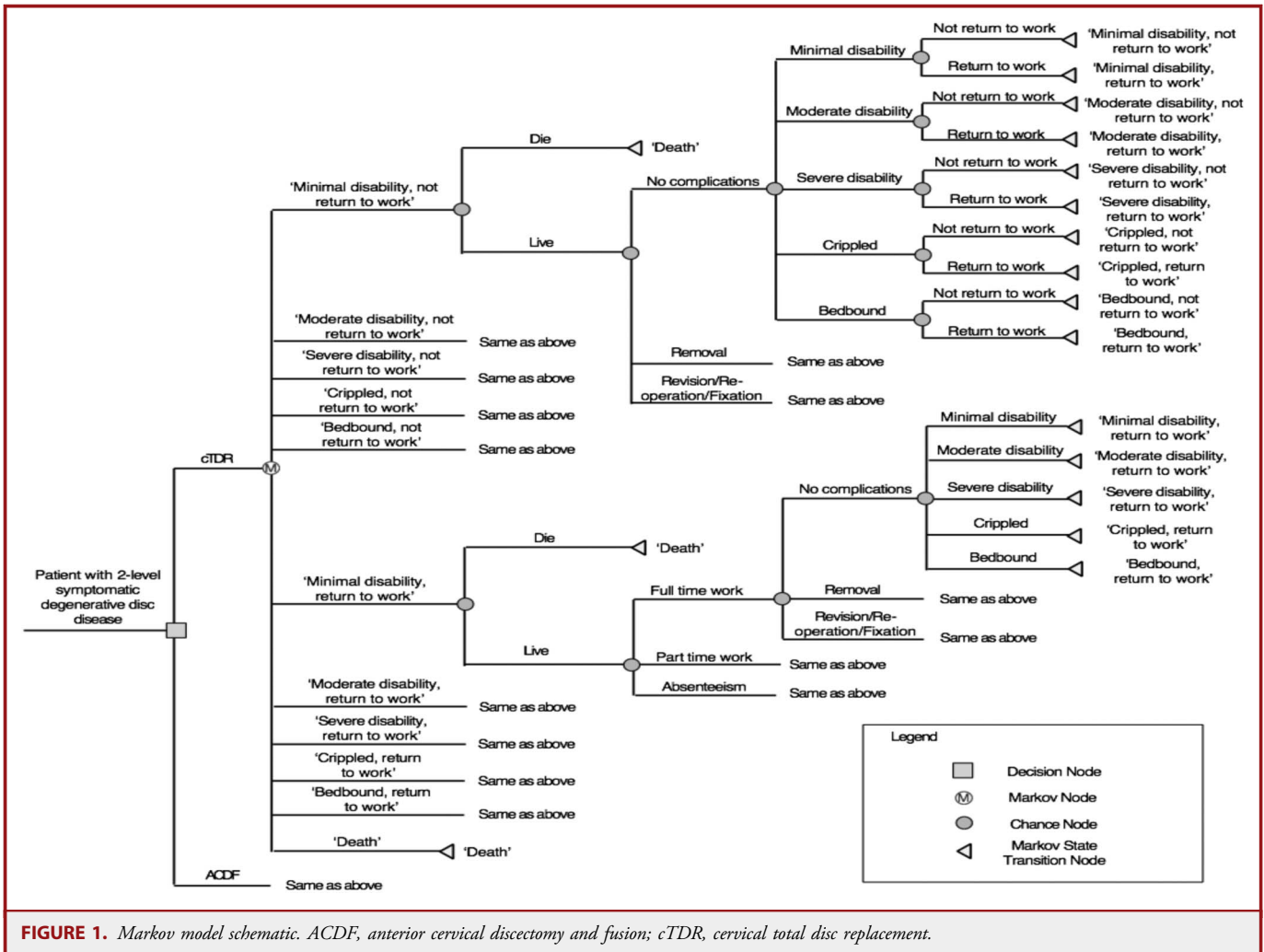


FIGURE 1. Markov model schematic. ACDF, anterior cervical discectomy and fusion; cTDR, cervical total disc replacement.

preoperatively did not significantly differ between surgical cohorts (58.4% in the ACDF group compared with 61.4% in the cTDR group; $P = .313$, 2-tailed z test). We considered 2 aspects when defining productivity loss: workdays missed (ie, RTW) and work persistence once returned.

For RTW, we calculated both the associated health state-specific and time-specific probabilities to inform the model (shown in Tables 2 and 3). With respect to work status persistence, we derived the health state-specific probabilities for continuing to work full-time, part-time, and complete cessation. We assumed part-time work to be 50% of full-time work hours. A monetary value for productivity loss was calculated by multiplying the 2013 national average wage¹⁴ (2014 average wage is not available as of this analysis) with the corresponding proportion of time away from work postoperatively.

Direct Medical Cost

The cost-related trial data contain the following elements: operative time, hospital stay, medication use, adverse event rates, and follow-up office visits. Operating room time and hospital stay could not be directly translated into dollar amounts because the unit cost (eg, operating room

per hour cost) was unknown. Instead, we used 2014 national average Medicare reimbursement rates for the associated diagnosis-related group (DRG) and Current Procedural Terminology (CPT) codes, assuming that operational differences were reflected by the difference in the Medicare reimbursement rates (Table 1). The model also considered costs associated with adverse events, but only those requiring subsequent surgeries, such as *revision*, *fixation*, or *reoperation* and *removal*. The analysis of medication use and unscheduled office visits were believed to capture other adverse events, such as pain, dysphagia (not requiring surgery), and adjacent segment disease (not requiring surgery). Revisions occurring within 30 days of the initial surgery were excluded because they are bundled with the initial DRG.

With respect to medication costs, we hypothesized that the type and number of medications taken immediately postoperatively should differ from later follow-up periods. In addition, this difference (particularly with analgesics, antispasmodics, and neuroleptics) was associated with the patient's health status. For medications missing a start date, the middle of the month (ie, the 15th) was imputed. The number of medications prescribed by postoperative follow-up period and health status is illustrated in **Supplemental Digital Content 3** (see Table, <http://links.lww.com/NEU/A843>).

TABLE 1. Model Input Parameters^a

Parameters	Value, % (±SD)	Source
1. Distribution of health state prior to initial surgery		
Mild	0.0 (0.0)	RCT
Moderate	6.0 (1.3)	
Severe	22.8 (2.3)	
Crippled	52.8 (2.7)	
Bedbound	18.4 (2.1)	
2. Time-specific transition probabilities between health states		
After ACDF surgery	See Table, Supplemental Digital Content 2	RCT
After cTDR surgery	See Table, Supplemental Digital Content 3	
3. Probability of unscheduled office visit, per 6 wk		
Mild	0.9 (0.4)	RCT
Moderate	0.8 (0.4)	
Severe	1.6 (0.5)	
Crippled	4.5 (0.9)	
Bedbound	3.6 (0.8)	

Parameters	Value, % (±SD)		Source
	ACDF	cTDR	
4. Risk of complication per Markov transition^a			
Revision, fixation, or reoperation			RCT
0-6 mo	0.0 (0.0)	0.1 (0.3)	
6-12 mo	1.9 (1.0)	0.4 (0.6)	
1-2 y	1.4 (0.9)	0.2 (0.4)	
After 2 y	0.0 (0.0)	0.0 (0.0)	
Removal			
0-6 mo	0.0 (0.0)	0.4 (0.6)	NVSR ¹³
6-12 mo	3.8 (1.4)	0.1 (0.3)	
1-2 y	3.8 (1.4)	0.4 (0.6)	
After 2 y	0.1 (0.1)	0.6 (0.7)	
5. Age-specific mortality	2013 national statistics		

Parameters	Value, % (±SD)		Source
	DRG/CPT	Cost (\$)	
6. Medical cost, 2014 dollars			
cTDR			2014 Medicare reimbursement rate
2015 DRG	518	17 965	
Discectomy with end plate preparation (single)	22856	1676	
Discectomy with endplate preparation (additional)	22858	672	
Autograft	20937	175	
ACDF			
DRG	473	13 025	
Device (2 levels)	22851	842	
Discectomy & decompression (single)	63075	1404	
Discectomy & decompression (additional)	63076	256	
Arthrodesis	22554	1302	
Structural allografts	20931	116	
Revision, fixation, or reoperation of cTDR			
DRG	518	17 965	
Removal of disc (single)	22864	2035	
Removal of disc (additional)	00951 ^b	472	
Revision of disc	22861	2262	

(Continues)

TABLE 1. Continued			
Parameters	Value, % (±SD)		Source
	DRG/CPT	Cost (\$)	
Revision, fixation, or reoperation of ACDF			
DRG	473	13 025	
Removal of pseudarthrosis	22855	1147	
Discectomy & decompression (single)	63075	1404	
Discectomy & decompression (additional)	63076	256	
Arthrodesis	22554	1302	
Structural allografts	20931	116	
Office visit	99213	72	
Office visit (severe condition)	99214	106	
7. Productivity Loss			
Average full-time wage index, 2013		\$44 888	SSA ¹⁴
Return-to-work, time-specific	See Table 2		RCT
Work Persistence, after return-to-work	See Table 2		

Parameters	Value, % (±SD)		Source
	≤6 wk, \$ (±SD)	>6 wk, \$ (±SD)	
8. Medication cost, per 6 wk			
Mild	63.6 (47.2)	37.1 (30.4)	RCT
Moderate	100.7 (54.3)	58.3 (47.2)	
Severe	116.6 (87.9)	74.2 (49.3)	
Crippled	148.4 (93.4)	68.3 (42.4)	
Bedbound	174.9 (89.4)	84.8 (59.6)	

Parameters	Value, % (±SD)	Source
9. Quality-of-life values		
Mild	0.849 (0.117)	RCT
Moderate	0.689 (0.117)	
Severe	0.609 (0.111)	
Crippled	0.548 (0.099)	
Bedbound	0.478 (0.100)	

^aACDF, anterior discectomy and fusion; CPT, Current Procedural Terminology; cTDR, cervical total disc replacement; DRG, diagnosis-related group; NVSR, National Vital Statistics Report; RCT, randomized controlled trial; SD, standard deviation; SSA, Social Security Administration.

^bProbabilities are in “per transition” term. The time-specific cumulative probability in a period approximately equals the probabilities per transition × number of transitions in the period. For example, the probability of having a revision per transition during “0 to 6 month” equals 0.11 and there are 4 transitions during “0 to 6 months” (6-week cycle per transition), which means that during “0 to 6 months” the cumulative probability of having a revision is about 0.11 × 4 = 0.44.

Supplemental Digital Content 1, 2, and 3 can be accessed here: <http://links.lww.com/NEU/A841>, <http://links.lww.com/NEU/A842>, and <http://links.lww.com/NEU/A843>.

We cross-referenced our data with the 2011 Redbook MarketScan¹⁷ to calculate medication costs. The Redbook file contains the average wholesale price (AWP) for all drugs assigned a national drug code. Cost was estimated using AWP times 85% (seen in Table 4). This multiplier was based on Medicare’s 2010 reimbursement rate for medications. After 2010, Medicare changed to an average sales price reimbursement method that is not publicly available. The estimated AWP was inflated to dollars in 2014 by using the medical Consumer Price Index.¹⁸

Finally, costs associated with follow-up office visits (both scheduled and unscheduled) were included in the model. Scheduled office visits were those occurring at 6 weeks, and at 3, 6, 12, 24, 36, 48, and 60 months postoperatively. An analysis of the trial data revealed that the likelihood of having an unscheduled office visit is associated with worsening health state ($P = .002$). Therefore, we looked at health state-specific likelihood of

office visits per 6 weeks (Markov cycle). As a result, for each scheduled or unscheduled office visit, the model assigned a CPT code based on the health state. For example, a normal office visit (CPT 99213) was used for mild and moderate disability states, whereas a higher-level visit (CPT 99214) was used for the severe and crippled health states.

Sensitivity Analysis

To examine the uncertainty in our CUA, we conducted scenario, probabilistic, and threshold sensitivity analyses. First, we modified model inputs (such as age and time horizon) to examine costs and utilities under alternative scenarios (see Table 5). The target population was varied to include 30-, 55-, and 70-year age groups to assess how lifespan (and productivity) affect the model. Age-specific mortality rates were based on

TABLE 2. Probability of Return to Work by Time and Disability Status, and Work Persistence After Return to Work by Disability Status

	Mild	Moderate	Severe	Crippled	Bedbound
Return to work (RTW)					
<6 wk					
Total	94	90	62	30	2
RTW	72	50	17	7	0
%	76.6	55.6	27.4	23.3	0.0
6 wk-3 mo					
Total	52	34	23	15	6
RTW	38	17	7	4	1
%	73.1	50.0	30.4	26.7	16.7
3-6 mo					
Total	20	15	15	10	2
RTW	11	4	3	3	0
%	55.0	26.7	20.0	30.0	0.0
6-12 mo					
Total	6	10	16	7	2
RTW	3	2	3	2	0
%	50.0	20.0	18.8	28.6	0.0
1-1.5 y					
Total	2	8	12	6	3
RTW	1	2	2	0	0
%	50.0	25.0	16.7	0.0	0.0
1.5-2 y					
Total	1	4	2	1	1
RTW	0	1	0	0	0
%	0.0	25.0	0.0	0.0	0.0
>2 y					
Total	1	3	1	1	1
RTW	0	0	0	0	0
%	0.0	0.0	0.0	0.0	0.0
Work persistence					
Full time (%)	69.6	69.6	72.3	63.5	40.4
Part time (%)	18.2	18.2	20.3	22.6	32.2
None (%)	12.2	12.2	7.4	13.9	27.4

the 2013 National Vital Statistics Report,¹³ with a maximum age set at 100 years. Standard retirement age was assumed to be ≥ 65 , after which no postoperative productivity loss occurred. The model time horizon was also varied from the base case of 5 years to include both 2- and 8-year scenarios. Second, a probabilistic analysis was used to address parameter uncertainty. The uncertainty regarding the model input parameters were characterized by probability distributions.¹⁹ β distributions (best fit for binomial data) were assigned to all probability parameters based on their point estimates and 95% confidence intervals derived from the trial data. γ distributions were used for cost items with the standard deviation, by convention, assumed to be 25% of the national reimbursement rate.¹⁹ γ distributions were also assigned to decrements in QALYs, with lower and upper bounds of 0 and 1, respectively. With distributions assigned, we ran a Monte Carlo simulation with 3000 iterations, and the parameter values were simultaneously sampled based on their specified distributions. Simulation findings are presented in a CE acceptability curve (Figure 2). Finally, a threshold analysis was used to determine the values of key clinical parameters required to cause an absolute change in CE

TABLE 3. Return to Work, by Surgery Type^a

	Fusion, n (%)	cTDR, n (%)	P Value ^b
<6 wk	38 (36.5)	108 (47.6)	.059
6-3 mo	20 (19.2)	47 (20.7)	.749
3-6 mo	6 (5.8)	15 (6.6)	.779
6-12 mo	1 (1.0)	9 (4.0)	.145
1-1.5 y	2 (1.9)	3 (1.3)	.675
1.5-2 y	1 (1.0)	1 (0.4)	.509
2-3 y	0 (0.0)	0 (0.0)	N/A
No return to work	36 (34.6)	44 (19.4)	.003
Total	104 (100.0)	227 (100.0)	

^acTDR, cervical total disc replacement; N/A, not available.

^bBased on 2-tailed t test.

between the 2 surgical arms (Table 6). Absolute change was defined as the amount of parameter manipulation required for the ICER to fall below or exceed the WTP threshold of \$50 000 per QALY.

TABLE 4. Cost and Utility of a Patient With 2-level Symptomatic DDD Undergoing cTDR vs ACDF in 5 Years After Surgery^a

	ACDF	cTDR	Δ
Cost			
Direct medical cost, \$ (%)			
Initial surgery	16 945 (78)	20 488 (87)	3543
Adverse events	2292 (11)	689 (3)	-1603
Medication	1944 (9)	1736 (7)	-209
Office visit	591 (3)	546 (2)	-45
Total medical cost	21 772 (100)	23 459 (100)	1687
Productivity loss, \$	91 824	54 447	-34 777
Medical cost + productivity loss, \$	113 596	80 906	-32 690
Health state and utility			
Months in a health state, n (%)			
Minimal disability	25.1 (42)	35.5 (59)	10.4
Moderate disability	13.0 (22)	11.9 (20)	-1.1
Severe disability	11.6 (19)	6.9 (12)	-4.7
Crippled	6.6 (11)	4.8 (8)	-1.8
Bedbound	3.7 (6)	0.9 (2)	-2.8
Total	60.0 (100)	60.0 (100)	0
Health-related utility, QALYs	3.376	3.574	0.198
Cost-utility			
ICER, societal perspective ^b			-\$165 103
ICER, health system perspective ^c			\$8518

^aACDF, anterior cervical discectomy and fusion; cTDR, cervical total disc replacement; ICER, incremental cost-effectiveness ratios; QALY, quality-adjusted life year.

^bCost from a societal perspective includes direct medical cost and productivity loss.

^cCost from a health system perspective includes direct medical cost, but no productivity loss.

TABLE 5. Scenario Sensitivity Analysis^a

	Direct Medical Cost + Productivity Loss	Direct Medical Cost	Utility, in QALY	ICER, Societal Perspective ^b	ICER, Health System Perspective ^c
Base case scenario					
5-y horizon, mean age 44					
cTDR	\$80 906	\$23 459	3.574	−165 103	8518
ACDF	\$113 596	\$21 772	3.376		
Alternative scenarios					
5-y horizon, mean age 30					
cTDR	81 166	23 986	3.619	−167 029	9816
ACDF	114 739	22 013	3.418		
5-y horizon, mean age 55					
cTDR	72 352	23 011	3.574	−165 148	8724
ACDF	104 722	21 301	3.378		
5-y horizon, mean age 70					
cTDR	22 870	22 870	3.406	9551	9551
ACDF	21 093	21 093	3.220		
2-y horizon, all age groups					
cTDR	47 473	21 938	1.576	−70 340	22 071
ACDF	53 381	20 084	1.492		
8-y horizon, all age groups					
cTDR	109 488	25 313	5.353	−225 816	6148
ACDF	176 781	23 481	5.055		

^aACDF, anterior cervical discectomy and fusion; cTDR, cervical total disc replacement; ICER, incremental cost-effectiveness ratios; QALY, quality-adjusted life year.

^bCost from a societal perspective includes direct medical cost and productivity loss.

^cCost from a health system perspective includes direct medical cost, but no productivity loss.

RESULTS

The baseline analysis examined the cost and utility (in QALYs) of cTDR vs ACDF for a patient with 2-level symptomatic cervical DDD during a 5-year postoperative time horizon. The results are summarized in Table 4.

With respect to direct medical cost, cTDR was projected to have a higher initial surgical cost (\$20 488) than ACDF (\$16 945), but lower costs associated with adverse events (\$689), medications (\$1736), and office visits (\$546) compared with ACDF (\$2292, \$1944, and \$591, respectively). Taken together, cTDR costs \$1687 more than ACDF over 5 years. In contrast, cTDR had substantially less productivity loss than ACDF, \$57 447 vs \$91 824 over 3 years, respectively. This is likely secondary to significant differences in RTW rates between the 2 surgical cohorts (Table 3), a total of 80.6% compared with 65.4% for cTDR and ACDF, respectively. Looking specifically at the 6-week postoperative period, cTDR also demonstrated a statistical trend toward higher RTW rates compared with ACDF, 47.6% vs 36.5%, respectively ($P = .059$).

In terms of quality of life, on average, the model projected that a patient undergoing cTDR enjoyed 35.5 of 60 months in the

health state of *mild disability*, a total of 10.4 months greater than the ACDF cohort. The ACDF cohort spent longer, on average, in all health states worse than *mild disability*. Consequently, cTDR patients had 3.574 QALYs compared with the ACDF patient with 3.376 QALYs at 5 years.

Therefore, from a societal perspective, thereby incorporating productivity loss, the ICER for cTDR was −\$165 103 per QALY at 5 years, indicating that cTDR dominated ACDF. From a health system perspective, and only considering direct medical cost, the ICER for cTDR was \$8518 per QALY at 5 years.

When target age and time horizon were varied (Table 5), the ICER for cTDR compared with ACDF remained below the US WTP threshold of \$50 000 per QALY in all scenarios (−\$225 816 per QALY to \$22 071 per QALY). Results were similar with multivariate probabilistic sensitivity analysis (Figure 2): cTDR was cost-effective in more than 95% of simulation iterations when the WTP threshold was >\$20 000 per QALY, regardless of perspective. In the final test of generalizability, extreme thresholds were required for ACDF to be cost-effective compared with cTDR (Table 6). Similarly, only when the cTDR DRG was reimbursed at \$26 217 or \$62 637 for the health system and societal perspectives, respectively, the ICER exceeded the WTP threshold.

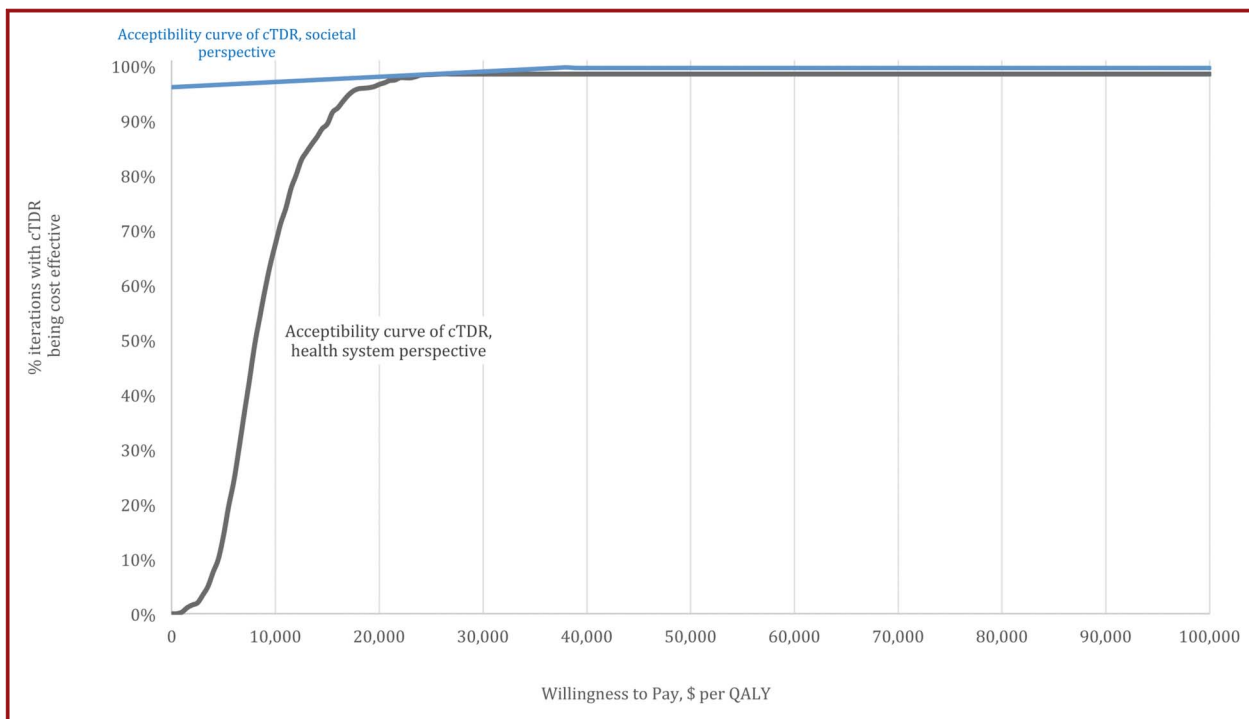


FIGURE 2. Probabilistic sensitivity analysis: cost-effectiveness acceptability curve of cervical total disc replacement (cTDR) in comparison with anterior cervical discectomy and fusion (ACDF) from a societal perspective and a health system perspective. The curve shows the probability that cTDR is cost-effective in comparison with ACDF for a range of maximum willingness to pay per quality-adjusted life year (QALY) gained. The probability was derived from 3000 rounds of simulation that randomly sample parameter values from the parameter distributions assigned. Societal perspective includes both direct medical cost and productivity loss. Health system perspective includes only direct medical cost. Color version available online only.

DISCUSSION

In this study, we derived the ICER of cTDR compared with ACDF by using 5-year trial data and conducted a robust sensitivity analysis to assess generalizability. Similar to the previous 2-year review, CE was again established based on the commonly accepted

WTP threshold of \$50 000 per QALY. This remains true while varying input parameters in multiple sensitivity analyses, reaffirming the stability of the model, and establishing the sustainability of the result. From a societal perspective, cTDR imparts greater quality of life at less cost than ACDF, suggesting that it is the dominant intervention. For the base case analysis, the

TABLE 6. Threshold Analysis^a

Parameter	Base Case Value	cTDR Cost-Ineffective, ^b Societal Perspective	cTDR Cost-Ineffective, ^b Health System Perspective
cTDR DRG	\$17 965	>\$62 637	>\$26 217
ACDF DRG	\$13 025	Nonexistent ^c	<\$5079
QALY for mild disability	0.849	Nonexistent ^c	<0.635
QALY for moderate disability	0.689	Nonexistent ^c	Nonexistent ^c
cTDR adverse events ^d	100% of baseline rates	>6281% of baseline rates	>1192% of baseline rates
ACDF adverse events ^d	100% of baseline rates	Nonexistent ^c	Nonexistent ^c

^aACDF, anterior cervical discectomy and fusion; cTDR, cervical total disc replacement; DRG, diagnosis-related group; QALY, quality-adjusted life year.

^bcTDR is no longer considered as being cost-effective when the ICER for cTDR > \$50 000 per QALY.

^cNonexistent = the value beyond which cTDR is no longer effective does not exist within any possible range. For probability parameters, the possible range is 0% to 100%; for cost parameters, the possible range is \$0 to positive infinite; for multiplier, the possible range is 0 to positive infinite.

^dBecause the complication rates for revision, fixation, or reoperation and for removal are time specific. For the purpose of threshold analysis, we varied all complication rates by a certain percentage of the baseline rate at the same time.

ICER for cTDR at 5 years ($-\$165\,103$ per QALY) far exceeded the previous 2-year result ($\$24\,594$ per QALY). This is not surprising because the QALY improvement between cTDR and ACDF increased from 0.087 at 2 years to 0.198 at 5 years, respectively. Similarly, cTDR was $\$2139$ more costly than ACDF at 2 years compared with a cost savings of $\$32\,690$ at 5 years. Again, this highlights how cTDR appears to provide patients with better quality of life at a savings over time. Our results also appear consistent with recent publications. In an article by McAnany et al,⁸ authors analyzed the CE of cTDR vs ACDF for single-level DDD using the ProDisc-C trial data. They found that cTDR also dominates ACDF at 5 years for single-level disease ($-\$557\,849$ per QALY).

The dramatic difference in the 2- and 5-year data was believed to be secondary to a more comprehensive RTW analysis than was previously conducted. Unlike the 2-year analysis, RTW data were available and not assumed. Furthermore, we calculated both the associated health state-specific and time-specific probabilities to inform the model and work status persistence. When comparing surgical cohorts, the overall difference in RTW rates was found to be significantly different. At 6 months, the cTDR and ACDF RTW rates were 47.6% and 36.5%, respectively. At 3 years, the RTW rates were 80.6% compared with 65.4%, respectively. Health status-specific RTW probabilities suggested that patients with less postoperative disability were more likely to return to and sustain work. However, the results cannot be explained by the enhanced RTW analysis alone. This is because the majority (68.1%) of patients who worked before surgery were able to return to work within 6 weeks postoperatively. More importantly, 50% of patients whose condition prevented them from working before surgery were able to return to work within 6 months postoperatively. Furthermore, because the RTW analysis was limited to 3 years, other costs, complications, and/or quality-of-life differences appear to be contributing to sustained CE past this time point. It is unclear how complete 5-year RTW data would affect our results; however, the authors assume the effect to be negligible because the rate of late complications (that could affect productivity) was markedly low and there was no documented change in RTW status between the 2 and 3 years of follow-up periods.

Limitations

This study should be interpreted in the context of several limitations. It was conducted using decision analytical modeling and, as a result, has several inherent limitations. By definition, the Markov model is supposed to be conditional on the present state alone; future and past events are assumed independent. With disease processes, it is rarely plausible to assume that a patient's transition to another health state was not in some way dependent on their previous health state. The model also assumed that surgical cohorts began in similar health states. The authors believed that this was acceptable because the initial patient selection was randomized. Despite the stringent criteria used in the RCT,⁹ however, it is rarely possible to blind patients or surgeons in a surgical trial. Therefore, it is perceivable that patients receiving the *novel* cTDR

intervention may have experienced more subjective improvement compared with the ACDF group. Similarly, surgeons may be biased toward 1 approach and make different intraoperative and postoperative decisions as a result. Although difficult to control, this was addressed by combining multiple outcome measures, such as NDI, VAS, and SF-12, all of which demonstrated reliability and consistency.

We also recognize that some cost data were not ascertainable. For example, because it is problematic to use hospital charge data to conduct a CEA, we used Medicare rates for diagnosis-related groups. As a result, differences in parameters (such as operating room time and length of stay) were not captured. However, it is likely that the marginal increases in operating room time associated with cTDR, and the resultant increased cost, is obviated by the shorter length of stay observed in this same group in comparison with ACDF.⁹ To be able to calculate the medication-related costs, we created estimates from AWP ($\times 0.85$) because updated Medicare average sales prices were not publicly available. Although this estimate was considered appropriate, it is impossible to determine if this actually overestimated or underestimated costs for both groups. Productivity loss also significantly contributed to cost. Although comprehensive, this analysis did not include aspects such as transportation costs, caregiver time/responsibilities, and educational days missed. Furthermore, in monetary terms, productivity loss was calculated by using the 2014 national average wage. It is unclear how these estimates may bias our conclusion. However, we contend that when the direction of the bias was unclear, at least both groups were treated similarly based on sound and collaborative clinical judgment.

Despite numerous limitations, univariate and multivariate sensitivity analyses were conducted in an attempt to test the strength and generalizability of the model. Despite multiple alterations of input parameters and multivariate analysis of thousands of permutations the ICER for cTDR compared with ACDF remained below the US WTP threshold of $\$50\,000$ per QALY. This finding remained true from both health system and societal perspectives. We also reiterate the significance of our threshold analysis. Not only would cTDR need to cost markedly more than its current reimbursement rate, but critical input parameters would have to substantially deviate from their baseline values for a scenario to exist in which ACDF was CE compared with cTDR. For example, the cTDR complication rate would need to increase by $>6281\%$ of the base case value. In several instances, such as with ACDF complication rates or altering QALY values for disability health states, despite maximal modification and/or ranges, (ie, 0-infinity), it was not feasible to create a CE scenario for ACDF vs cTDR. The authors contend that this comprehensive sensitivity analysis provides adequate reassurance regarding the generalizability of our model and conclusion.

CONCLUSION

This study is the first to report the comparative CE of cTDR and ACDF for 2-level DDD at 5 years. It is also the first surgical CUA to include *work persistence* as part of an extensive RTW analysis

for measuring societal impact. The results appear generalizable after an extensive sensitivity analysis demonstrates consistency with similar investigations.^{8,20} Therefore, the authors conclude that for patients with 2-level DDD, cTDR is not only a highly cost-effective surgical modality compared with ACDF, but, at 5 years, it is the dominant modality. In a rapidly changing medical climate with emerging practice paradigms such as *pay for performance* and *value-based purchasing*, surgeons and payers will naturally gravitate toward these analyses. In addition, as the health care system becomes more informed in an established setting of scarce resources and increasing expenses, sustainable surgical technologies that improve quality of life while saving costs require serious attention.

Disclosures

LDR Spine provided a consulting honorarium to analyze their RCT data for the purposes of health care economics and cost-effective analysis and institutional research support for this work. Dr Ament is a consultant for LDR Spine and received funding to support data analysis and preparation of the manuscript. Dr Stone has received institutional funding from LDR for cost data collection for this project and institutional funding for the randomized controlled trial (RCT) and other Mobi-C related research. Dr Nunley received institutional funding from LDR for cost data collection for this manuscript and is a paid consultant for training surgeons in the use of the Mobi-C disc, and is a patent holder for K2M and LDR Spine (specifically for the ROI-A anterior lumbar interbody fusion cage). Dr Kim receives royalties for LDR Spine. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENT

The authors present a cost utility analysis of 2-level artificial disc replacement (ADR) vs fusion with 5 years of follow-up. Decision analytical modeling was utilized with construction of a Markov model. The data were derived from a previously published US Food and Drug Administration Investigational Device Exemption (US FDA IDE) randomized controlled trial for Mobi-C, which included 330 patients. Data from the randomized controlled trial (RCT) was used for the model input parameters.


Direct medical costs favored anterior cervical discectomy and fusion (ACDF) over ADR by \$1687; however, indirect costs favored ADR (\$57 447) over ACDF (\$91 824). The 3-year return-to-work (RTW) rates also favored ADR over ACDF with 80.6% vs 65.4%. The incremental cost-effectiveness ratio (ICER) favored ADR at -\$165 103 per quality-adjusted life years (QALY) at 5 years. All scenario sensitivity analyses favored ADR from the societal perspective (direct and indirect/productivity losses). The limitations of the study derive from both the underlying RCT and the need to simplify a complex course of events into a relatively simple model. For example, the underlying RCT was done in the context of a US FDA IDE trial. The strict inclusion criteria may limit generalizability, and it is possible that the patients who participated in the trial and received the ADR noted greater satisfaction/subjective improvement with the novel treatment option than those who were randomly assigned to fusion. The underlying RCT had limited productivity loss data (indirect cost) of only 3 years and limited direct

medical cost data. For example, an analysis of medication use and unscheduled office visits was used to capture nonsurgical adverse events and adjacent segment disease.

The strengths of the study are that the data were derived from a randomized controlled trial of 330 patients with 5-year follow-up, the use of both direct/indirect costs, discounting to reflect present value, and

sensitivity analysis utilizing various ages and time horizons. With the changing health care landscape, it will be increasingly important for spine surgeons to demonstrate value beyond that of simple statistical significance (ie, P value < .05).

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