Journal of Spine
ISSN: 2165-7939

Voigt and Anderson, J Spine 2019, 7:6
DOI: 10.4172/2165-7939.1000430

Research Article | Open Access

Cost Effectiveness Analysis-Cryopreserved Amniotic Membrane's (cAM) Use in Lumbar Micro Discectomy-A Modeling of the Costs and Outcomes from a Randomized Controlled Trial

Jeffrey Voigt[1*] and David Greg Anderson[2]

[1]Medical Device Consultants of Ridgewood, LLC, 99 Glenwood Rd., Ridgewood, NJ, USA
[2]Department of Orthopaedic and Neurological Surgery, Thomas Jefferson University, Clinical Director of Spine Section, Orthopaedic Research Laboratory, Rothman Institute, 925 Chestnut St, Philadelphia, USA

Abstract

Objective: Few studies have evaluated the cost effectiveness associated with lumbar microdiscectomy. The outcome data used in this analysis was from a prior randomized controlled trial (RCT) demonstrating that the use of a cryopreserved amniotic membrane (cAM) reduced the incidence of repeat procedures and improved outcomes vs. the standard of care (SOC). The purpose of this analysis was to cost out the procedural data associated with the outcomes from this RCT for cAM and then to evaluate the cost effectiveness of this alternative compared to every day practice.

Methods: The direct costs of care for patients undergoing lumbar microdiscectomy were modeled using Medicare 2017 national average reimbursement. TreeAge Pro 2018 software was used for the decision tree analysis over a 2 year period. The assumed cost of cAM was $500 US. The probabilities of events were derived from the published literature, including repeat surgery from recurrent disc herniation. The effectiveness outcome evaluated was the Ostwestry Disability Index, as evaluated in the RCT and from published literature. One-way sensitivity analysis was conducted along with Monte Carlo simulation.

Results: The use of cAM was the least costly alternative over 2 years by $343 vs. SOC ($12,417 vs. $12,760). One-way sensitivity analyses found the following variables had the greatest effect on the decision to use SOC vs. cAM (based on costs alone): incidence of revision surgery due to recurrent disc herniation for cAM (>6.8%) and SOC (<7.5%); cost of cAM (>$843); cost of an inpatient repeat procedure of <$8,408. In Monte Carlo simulation, cAM dominated 53% of the time.

Conclusion: Based on a lower incidence of repeat procedures and an improved ODI, cAM can be a cost effective alternative when compared to SOC. In today's environment of US value based reimbursement, the use of cAM may hold promise.

Keywords: Cost effectiveness; Lumbar micro discectomy; Cryopreserved amniotic membrane

Abbreviations: APC: Ambulatory Payment Classification; C: Cost; cAM: Cryopreserved Amniotic Membrane; EV: Expected Value; DRG: Diagnostic Related Group; E: Effectiveness; LDH: Lumbar Disc Herniation; LMD: Lumbar Micro Discectomy; NMB: Net Monetary Benefit; ODI: Oswestry Disability Index; SF-12: Short Form 12; SOC: Standard Of Care; RCT: Randomized Controlled Trial; WTP: Willingness to Pay; VAS: Visual Analog Pain Scale

Introduction

Lumbar micro discectomy (LMD) is a treatment alternative for lumbar disc herniation (LDH). However, complications such as lumbar radiculopathy and recurrent disc herniation can occur in up to 25% of patients [1] with reoperation rates reported in the 7% - 25% range [2-6] commonly over a 2 year period. Residual back pain and lumbar radiculopathy have been reported more frequently for patients requiring revision surgery [3]. Additionally, revision LMD's have been associated with a higher rate of adverse events and complications compared to initial surgery [7]. Thus, recurrent disc herniation following LMD continues to remain an issue.

Cryopreserved amniotic membrane (cAM) is derived from placental tissue from healthy caesarian births post-delivery. The tissue origin of cAM is isolated from the amniotic membrane layer of the placenta which surrounds the fetus during fetal development [8]. cAM has anti-inflammatory properties which have made it useful in wound healing [9,10], ophthalmology [11], and in burn treatment [12]. cAM's application to burns and radiation therapy (radiation burns) has also demonstrated reductions in pain [12-14].

Recently, a randomized controlled trial (RCT) reported the use of cAM in LMD [15]. In this study, cAM tissue was placed into the annular defect at the conclusion of LMD surgery for patients randomized to this treatment group. This study demonstrated that cAM-treated patient had improved outcomes vs. control patients treated with standard of care (SOC) as measured by various instruments which included: the Oswestry Disability Index (ODI) [a specific instrument measuring a patient's functional disability [16], the Short Form-12 (SF-12) health survey questionnaire, and the 10 cm Visual Analog Pain Scale (VAS) at various time points over a 24 month time period [15]. At the 2-year follow up time point, none of the patients treated with cAM had sustained a recurrent disc herniation at the same level; whereas 7.5% of those in the SOC group had required revision surgery for recurrent herniation at the level of initial treatment [15].

***Corresponding author:** Jeffrey Voigt, Medical Device Consultants of Ridgewood, LLC, 99 Glenwood Rd., Ridgewood, NJ, USA, Tel: + 2012518204; E-mail: meddevconsultant@aol.com

Received December 03, 2018; **Accepted** December 28, 2018; **Published** January 04, 2019

Citation: Voigt J, Anderson DG (2019) Cost Effectiveness Analysis-Cryopreserved Amniotic Membrane's (cAM) Use in Lumbar Micro Discectomy-A Modeling of the Costs and Outcomes from a Randomized Controlled Trial. J Spine 7: 430. doi: 10.4172/2165-7939.1000430

It is the intention of this analysis to examine the cost effectiveness over 2 years between SOC and cAM treatment following LMD using data derived from this RCT and from published systematic reviews and meta-analyses (for SOC). A two year timeframe was chosen, as the recurrent operation rates for LMD have been the most widely reported in Dohrmann and Mansour study [17] and; from which the RCT was evaluated.

Materials and Methods

A Markov model analysis (using TreeAge Pro 2018) was undertaken comparing the direct treatment costs over time, outcomes (using the ODI) and probabilities of recurrent herniation using cAM vs. control for patients requiring LMD (Figure 1). The ODI was used as an outcome measure as it is condition specific to the lower back, has been well validated, is reliable, a responsive measure to functional score and is used frequently in the management and assessment of spinal disorders [16,18]. Patient outcomes were assessed over a 24-month follow up period [15]. Direct costs for revision surgery were estimated using Medicare 2017 national average reimbursement rates and were discounted at 3%/year [19]. ODI scores were also discounted similarly [19]. The probabilities of events such as surgical complications and recurrent disc herniation requiring surgery were derived from published systematic reviews and meta-analyses [20-23] and were used even though the RCT demonstrated no recurrent herniation with the cAM group [15]. The estimate/probability for recurrent surgery at 2 years in the cAM group was assumed to have a low end of 0% (based on the previously mentioned RCT demonstrating no recurrent surgeries [15]) and the average rate for recurrent surgery at 2 years as identified in the literature. For the non-cAM group (SOC), the low end was assumed to be 7.5% (as demonstrated in the RCT [15]) and the average rate for recurrent surgery at 2 years as identified in the literature. For both cAM and SOC the average rate of recurrent surgery, based on a systematic review, was assumed to be 10.5% [23]. Therefore the recurrent surgery ranges for cAM and SOC were: 0%-10.5% and 7.5% - 10.5% respectively over the 2 year period. The systematic reviews and meta-analyses were identified using the following search terms: Lumbar AND Microdiscec* AND Outcome* AND Systematic AND meta-analysis. Search engines/digital repositories were searched on June 10, 2018 and included: Pubmed and Google (first 4 pages of hits for Google).

Probabilities, direct costs, and outcomes are found in Appendix 1. These variables include: cost for acute care (i.e., micro discectomy procedure), rehabilitation/physical therapy, surgical complications (a weighted cost of complications based on the incidence of the complication; costs for treating pain; costs for treating recurrent disc herniation surgery); and ODI scores at baseline, 1 year and 2 years.

Data sources for the model are identified in Appendix 1 for each variable and distribution used in the model. The direct costs for treatment were based upon 2017 Medicare national average reimbursement rates. The cost of revision surgery for recurrent disc herniation was based on 2017 Medicare costs and included a blended mix from outpatient (Ambulatory Payment Classification [APC] 5114 with a reimbursement of $6,132) and lumbar fusion (Diagnostic Related Group [DRG] 440 with a reimbursement of $28,971) which were reflective of current practice related to site of service [24]. The perspective of this study was from a direct healthcare cost perspective. Lastly the CHEERS check list [25] was followed and appears as Appendix 2.

Running the model and outcomes derived

The assumed health states used in the model for both cAM and for SOC were as follows:

- Patient well post initial procedure and for 2 years.
- Patient has complications with initial procedure (approximating one year) and then well thereafter;
- Patient well post initial procedure but reoperation (recurrent herniation) required within 2 years of initial surgery and patient well post reoperation.
- Patient well post initial procedure but reoperation (recurrent herniation) required within 2 years of initial surgery and patient has complications with 2nd procedure for recurrent herniation.

The main outcomes of interest were the aggregate direct costs of treating patients undergoing LMD with and without cAM over a 24-month period and; the difference in the ODI score for each arm over 2 years between baseline ODI score and score at 2 years. Further the net monetary benefit (NMB) of each alternative was calculated as follows: NMB=E *WTP-C where E equals the effectiveness as measured under ODI; WTP equals a person's willingness to pay for the alternative; and C equals the cost. Since, WTP equaled zero ("0") for each alternative; the NMB was calculated as the total cost (i.e., a negative value) of each alternative over the 2 year period. Thus, the least costly alternative had a lower negative value (or total cost). Lastly each alternative was evaluated for dominance; with dominance referring to an improved ODI score (outcome) and a lower cost.

A stochastic element to the analysis using the Monte Carlo technique was also introduced where the model was run numerous times, each time varying the unit value of a particular variable. The ranges of values used in the Monte Carlo simulation can be found in Appendix 1.

One-way sensitivity analysis was evaluated on those variables which had the greatest effect on the model (i.e., value at which one therapy would be used over another based on lower costs) using Tree Age Pro 2018.

Results

The base scenario using the variables and distributions found in Appendix 1, demonstrated that the use of cAM resulted in lower overall costs of care by $343 vs. SOC ($12,417 vs. $12,419) as well as improved outcomes as measured via ODI (Figure 1). Using sensitivity analysis, it was determined that the following variables had the greatest effect on the use of cAM vs. SOC (Table 1 and Figure 2 [Tornado sensitivity analysis]): cost inpatient reoperation with lumbar fusion (evaluated over a range of $0 - $17,500); rate of recurrent disc herniation requiring surgery cAM (0 – 205%); rates of recurrent disc herniation requiring surgery SOC (0 -20%); list price of cAM (0-$1,000)

In one way sensitivity, and at a price of $500 for cAM, in order for cAM to be the more expensive alternative its price would need to be >$843 in treating disc herniation (Figure 3). Additionally, in order for cAM to be the more expensive alternative in treating recurrent disc herniation, the incidence of repeat surgery using cAM would need to occur >6.8% of the time (Figure 4). As well, in order for SOC to be the lower cost alternative, revision surgeries for recurrent disc herniation using SOC would need to occur <7.5% of the time (Figure 5). Figure 6 shows that the cost (reimbursement) for an inpatient lumbar fusion procedure would need to be <$8,408 in order for SOC to be the less costly alternative. Using Monte Carlo simulation (run 10,000 times), cAM was the dominant therapy (least costly/improved ODI [change from baseline to 2 years out]) in patients undergoing LMD the majority of time (53%; Quadrant IV; Figure 7). Additionally, 30% of the time, cAM was more costly but ODI improved (Quadrant I).

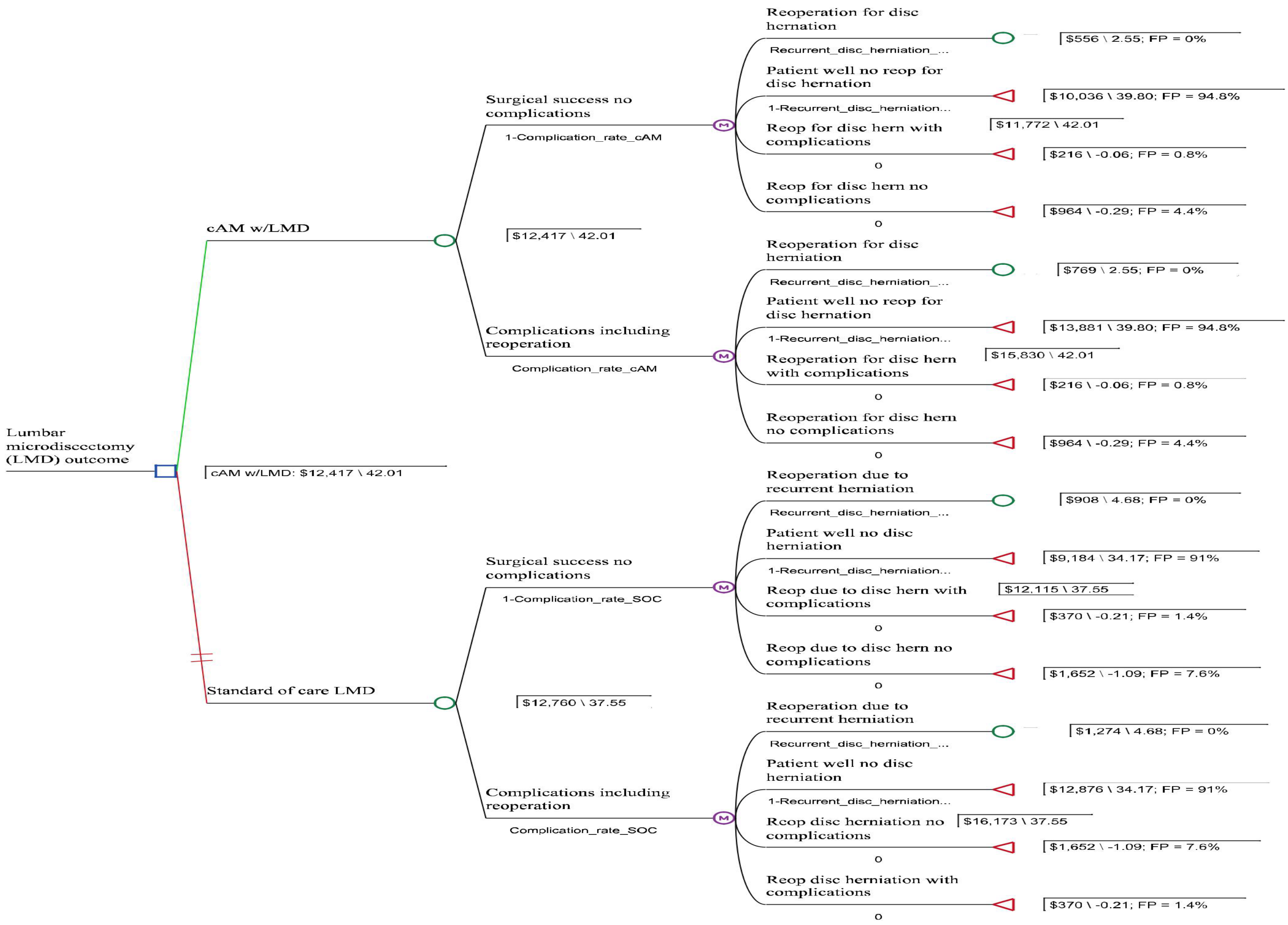

Figure 1: Decision tree model – compares overall costs and effectiveness of cAM vs. SOC.

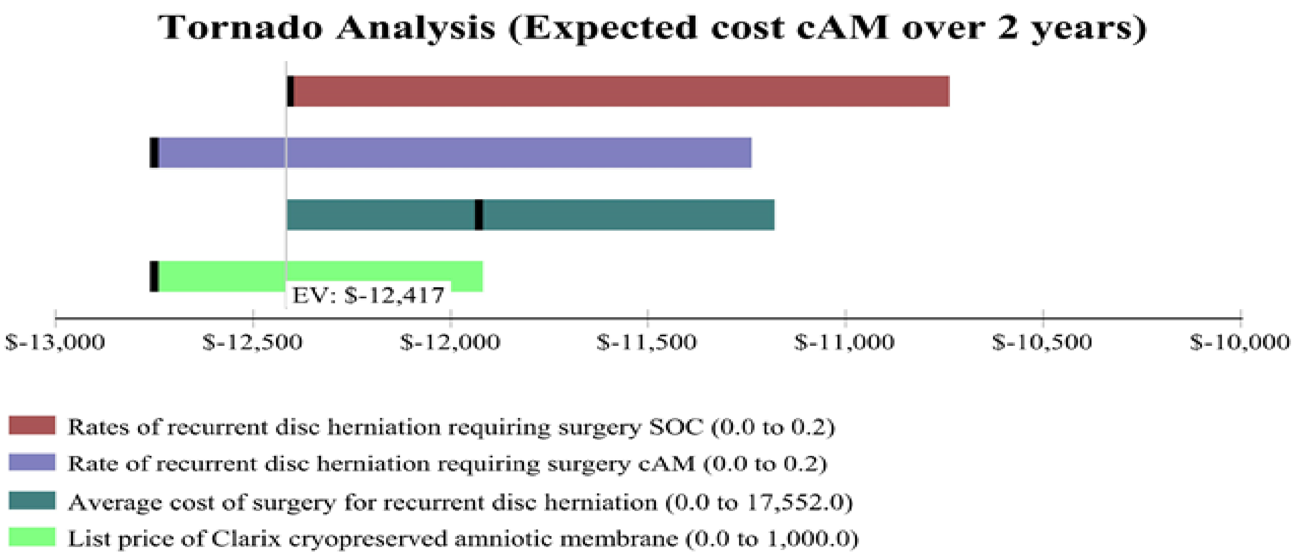

Figure 2: Tornado analysis – identifies which variables had the greatest effect on the model.

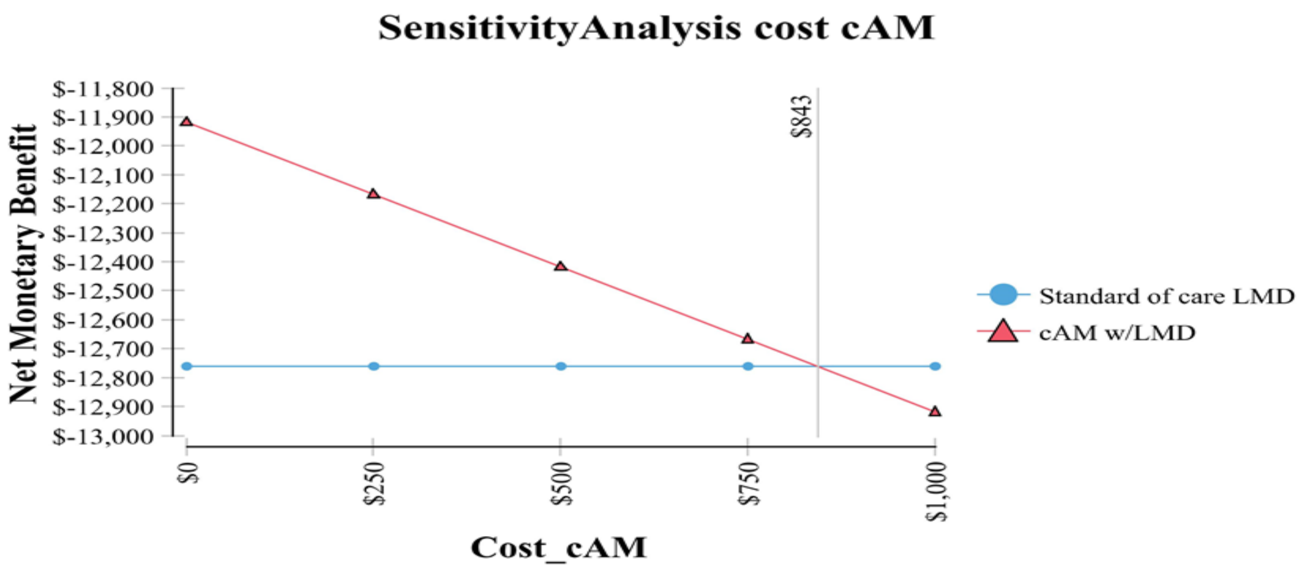

Figure 3: Sensitivity analysis – cost of cAM – identifies cost for cAM above which SOC becomes less the less expensive alternative.

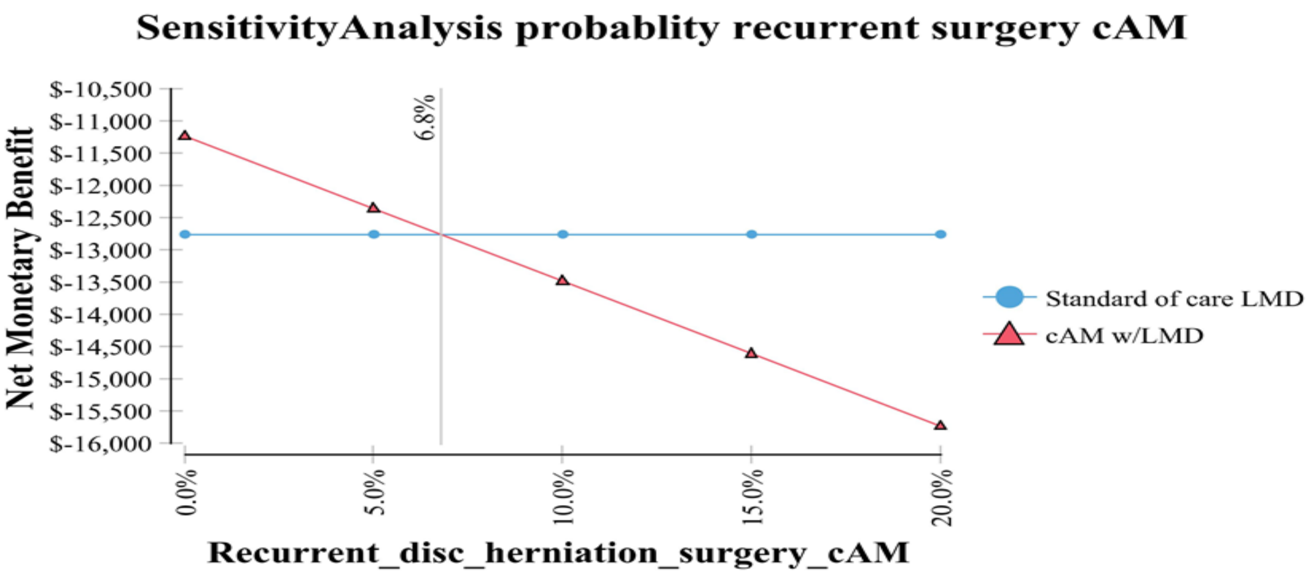

Figure 4: Sensitivity analysis – probability recurrent surgery with cAM – identifies percentage of recurrent surgeries when using cAM below which SOC become the less expensive alternative.

Discussion

Based on the above analysis which modeled out assumed complication rates and repeat LMDs, cAM was more cost effective compared to the SOC over a 2-year time horizon. This finding was primarily driven based on an assumption of a lower rate of revision surgery (and its associated costs) following LMD surgery.

The model found that in order for SOC to be the lower cost alternative, revision surgery would need to occur less than 7.5% of the time, a rate that seems unlikely given the published literature which demonstrates in meta-analyses a recurrent herniation rate at 2 years to be in excess of 10% [20,23,26]. Additionally, longitudinal analyses of large series of patients showed a mean rate of reoperation at 4 years at 13.2% (95% CI: 11.3% to 15.5%) [27]. At 8 years, reoperation rates for recurrent disc herniation were found to be 15% [28]. If one were to assume correspondingly higher rates of reoperation over time (up through 8 years) with both cAM and SOC, then reoperation with cAM would need to be >9% and <9.7% for SOC at year in order for SOC to be the least costly alternative (analysis not shown). Thus, a product that can prevent revision surgery should be a welcome addition to the clinical armamentarium.

Further, the model found that the cost of inpatient revision surgery would need to be <$8,408 in order for SOC to be the less expensive alternative. This amount of <$8,408 is unlikely to occur in everyday practice considering a recent analysis of a national insurance database also showed the average insurance reimbursement for recurrent disc herniation to be $49,192 [23].

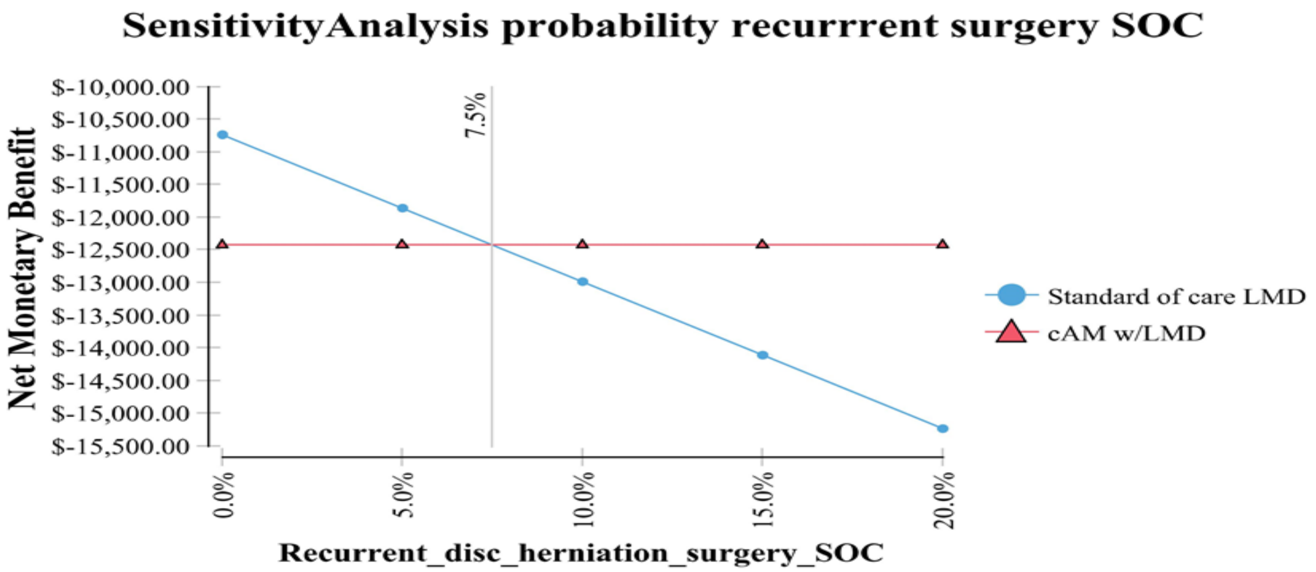

Figure 5: Sensitivity analysis – probability recurrent surgery with SOC – identifies percentage of recurrent surgeries when using SOC above which cAM becomes the less expensive alternative.

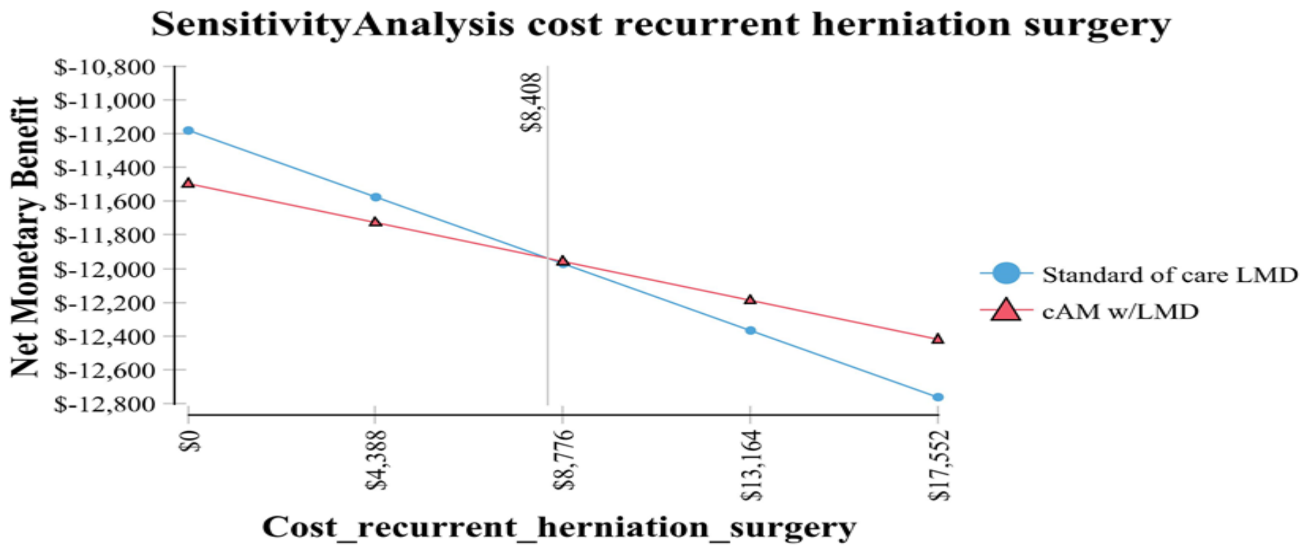

Figure 6: Sensitivity analysis – cost surgery recurrent herniation – identifies cost for recurrent surgery below which SOC becomes the less expensive alternative.

Other investigators such as Sherman and coauthors have performed economic analyses similar to the current study [29]. In their investigation, longitudinal insurance claims were analyzed for patients up to 18 months after LMD surgery. It was found that 137 patients (28%) had additional lower back claims with 52 patients (11%) requiring additional surgery and 85 (17%) requiring medical management. The costs for surgical treatment found in the Sherman study were substantially higher than costs used in the current model (adjusted for inflation; revision microdiscectomy cost was $11,360 vs. $6,130; fusion cost was $43,320 vs. $28,970). The main reason for this cost difference is the use of the commercial/private payment data in the Sherman study vs. the use of 2017 Medicare national average reimbursement data in the current analysis. In addition, the cost of medical therapies for patients having recurrent disc herniation was substantial in the Sherman study with an average medical treatment costs of $3,365 in 2006; ($4,770; 2016 $). The cost of medical therapies for patients with recurrent disc herniation was not captured by the current model and thus the findings herein may under-estimate the true costs of sustaining a recurrent disc herniation.

As mentioned, an important finding in the recent RCT [15] is the statistically significantly lower ODI and improved SF-12 physical composite scores at 2 years with cAM. Although the exact mechanism of action of cAM in achieving these findings has not been demonstrated, it may be related to either the anti-inflammatory effects [30,31], anti-scarring properties [32-35] or perhaps a regenerative response within the intervertebral disc that is responsible for the observed benefits.

Reimbursement policy has begun to shift towards a value-driven model, where better outcomes with more durable results are financially incentivized in the reimbursement algorithms. A good example of this

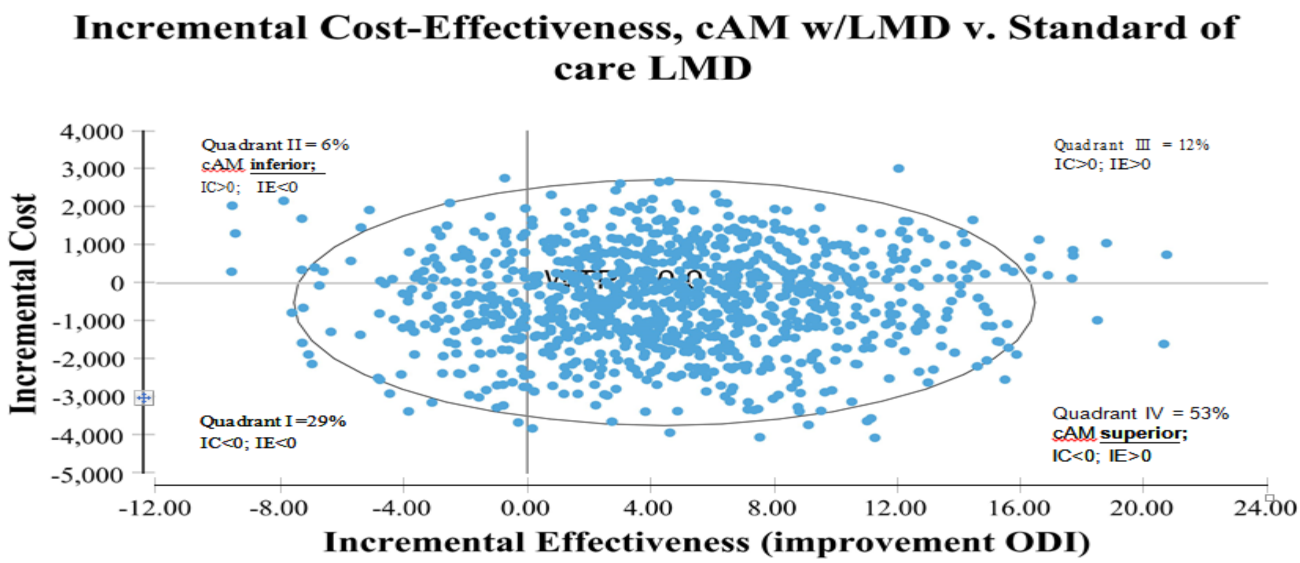

Figure 7: Incremental cost effectiveness scatter plot – identifies percentage of time in using Monte Carlo simulation when cAM would be the superior (53% of the time) and inferior (6% of the time) alternative (superior meaning cAM costs less overall and improves effectiveness; inferior meaning cAM costs more overall and is less effective than SOC.

Variables	Sensitivity range evaluated	Value above (if >) or below (if<) which resulted in SOC being least costly
Price cAM (Figure 3)	$0 - $2,000	>$843
Incidence recurrent disc herniation surgery w/cAM (Figure 4)	0% – 15%	>6.8%
Incidence recurrent disc herniation surgery w/SOC (Figure 5)	0% - 25%	<7.5%
Cost recurrent disc herniation surgery (Figure 6)	$0 - $17,550	<$8,408

Table 1: Variables affecting decision tree model and ranges evaluated.

is Medicare's bundled payment program for hip and knee implants. The bundled payment compensates a provider (commonly clinician plus facility) for 30-60 days of care post procedure [36]. Under bundled payments, if a patient requires readmission to a facility during this timeframe, the facility is not paid additionally for the readmission but out of the existing bundled payment. This form of payment encourages providers to ensure a good overall and durable outcome for the patient. A product such as cAM, which may be able to reduce the risk of future medical care and; improve outcomes is likely to be viewed favorably in the era of value-based healthcare.

Limitations

Because costs in the current study were modeled rather than prospectively captured, certain direct costs for care were likely missed. However, the effects of this limitation would likely be to increase the value of cAM, given the likelihood that the actual costs were higher for patients requiring medical care for recurrent disc herniation compared to that used in the current model.

Also, it is possible that the cost effectiveness was underestimated by the 2-year follow up time of the Anderson study [15]. As others have shown, the rate of recurrent disc herniation increases over time (~10% at 2 years [20,23,26], 12%+ at 4 years [27,37], 14% at 5 years [38], and 15% at 8 years [28]. Therefore, it is important that this recurrent surgery rate for both cAM and SOC be followed up on over time in a high quality study design (e.g. RCT). One of the authors of this study (DGA) continues to follow the patients reported on [15] over time.

Another limitation is that costs in the current model were estimated using 2017 Medicare reimbursements. Medicare reimbursements have been noted to be approximately 93% of the actual costs [39].

A two hear time horizon was used in the analysis. Over time the costs and effects could differ between the two groups (cAM vs. SOC). Further, the incidence of recurrent disc herniation surgery with cAM has only been followed out 2 years. The observe 0% recurrent surgery rate in the RCT with cAM may change over time.

ODI was used in this analysis versus the short form health form health survey questionnaire, even though both outcomes were evaluated in the analysis from which much of the outcome data was derived from [15].

Conclusion

As mentioned above, ODI is specific to lower back functionality (i.e., disability) and it was felt the analysis should be from this condition specific perspective, considering the evaluation of the treatments and costs were also from this specific perspective. Finally, the costs for medications and other medical therapies were not captured in this analysis. These likely would have made the SOC costs higher in treating the higher rate of recurrent herniation and associated pain.

References

1. Berjano P, Pejrano M, Damilano M (2013) Microdiscectomy for recurrent L5-S1 disc herniation. Eur Spine Jrl. 22: 2915-2917.

2. Ambrossi GLG, McGirt MJ, Sciubba DM, Witham TF, Wolinsky JP, et al. (2009) Recurrent lumbar disc herniation after single-level lumbar discectomy: Incidence and health care cost analysis. Neurosurgery 65: 574-578.

3. Aichmair A, Du JY, Shue J, Evangelisti G, Sama AA, et al. (2014) Microdiscectomy for the treatment of lumbar disc herniation: An evaluation of reoperations and long-term outcomes. Evid Based Spine Care Jrl 5: 77-86.

4. Soliman J, Harvey A, Howes G, Seibly J, Dossey J, et al. (2014) Limited

microdiscectomy for lumbar disc herniation: a retrospective long-term outcome analysis. J Spinal Disord Tech 27: E8-E13.

5. Parker SL, Mendenhall SK, Godil SS, Sivasubramanian P, Cahill K, et al. (2015) Incidence of low back pain after lumbar discectomy for herniated disc and its effect on patient-reported outcomes. Clin Orthop Relat Res 473: 1988-1999.
6. Fritzell P, Knutsson B, Sanden B, Strömqvist B, Hägg O (2015) Recurrent versus primary lumbar disc herniation surgery. Clin Orthop Relat Res 473: 1978-1984.
7. Papadopoulos EC, Girardi FP, Sandhu HS, Sama AA, Parvataneni HK, et al. (2006) Outcome of revision discectomies following recurrent lumbar disc herniation. Spine 31: 1473-1476.
8. Fetterolf DE, Snyder RJ (2012) Scientific and clinical support for the use of dehydrated amniotic membrane in wound management. Wounds 24: 299-307.
9. 9. Caputo WJ, Vaquero C, Monterosa A, Monterosa P, Johnson E, et al. (2016) A single-center, retrospective study of cryopreserved umbilical cord for wound healing in patients suffering from chronic wounds of the foot and ankle. Wounds 28: 217-225.
10. Raphael A (2016) A single-centre, retrospective study of cryopreserved umbilical cord/amniotic membrane tissue for the treatment of diabetic foot ulcers. J Wound Care 25: S10-S17.
11. Liu J, Sheha H, Fu Y, Liang L, Tseng SC (2010) Update on amniotic membrane transplantation. Expert Rev Ophthal 5: 645-661.
12. Eskandarlou M, Azimi M, Bariee S, Rabiee MAS (2016) The healing effect of amniotic membrane in burn patients. World Jrl Plas Surg 5: 39-44.
13. Kheirkhah A, Johnson DA, Paranjpe DR, Raju VK, Casas V, et al. (2008) Temporary sutureless amniotic membrane patch for acute alkaline burns. Arch Ophthalmol 126: 1059-1066.
14. Finger PT (2008) Finger's amniotic membrane buffer technique protecting the cornea during radiation plaque therapy. Arch Ophthalmol 126: 531-534.
15. Anderson DG, Popov V, Raines AL, O'Connell J (2007) Cryopreserved amniotic membrane improves clinical outcomes following microdiscectomy. Clin Spine Surg 30: 413-418.
16. Fairbank JC, Pynsent PB (2000) The Oswestry Disability Index. Spine 25: 2940-52.
17. Dohrmann GJ, Mansour N (2015) Long-term results of various operations for lumbar disc herniation: Analysis of over 39,000 patients. Med Princ Pract 24: 285-290.
18. Deyo RA (1988) Measuring the functional status of patients with low back pain. Arch Phys Med Rehabil 69: 1044-1053.
19. Gold MR, Siegel JE, Russell LB, Weinstein MC (1996) Cost-effectiveness in health and medicine (2nd edn). Oxford University Press, New York, USA. p: 285.
20. Shriver MF, Xie JJ, Tye EY, Rosenbaum BP, Kshettry VR, et al. (2015) Lumbar microdiscectomy complication rates: A systematic review and meta-analysis. Neurosurg Focus 49: E6.
21. Drazin D, Ugiliweneza B, Al-Khouia K, Yang D, Johnson P, et al. (2016) Treatment of recurrent disc herniation: A systematic review. Cureus 8: e622.
22. McGirt MJ, Ambrossi GLG, Datoo G, Sciubba DM, Witham TF, et al. (2009) Recurrent disc herniation and long-term back pain after primary lumbar discectomy: Review of outcomes reported for limited versus aggressive disc removal. Neurosurgery 64: 338-345.
23. Heindel P, Tuchman A, Hsieh P, Pham MH, D'Oro A, et al. (2017) Reoperation rates after single level lumbar discectomy. Spine 42: E496-E501.
24. Baird EO, Egorova NN, McAnany SJ, Qureshi SA, Hecht AC, et al. (2014) National trends in outpatient surgical treatment of degenerative cervical spine disease. Global Spine J 4: 143-150.
25. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, et al. (2013) Consolidated health economic evaluation reporting standards (CHEERS)-Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. Value Health 16: 231-50.
26. Oh JT, Park S, Jung SS, Chung SY, Kim MS, et al. (2012) Surgical results and risk factors for recurrent of lumbar disc herniation. Kor J Spine 9: 170-175.
27. Martin BI, Mirza SK, Flum DR, Wickizer T, Heagerty PJ, et al. (2012) Repeat surgery following lumbar decompression for herniated disc: The quality implications of hospital and surgeon variation. Spine J 12: 89-97.
28. Leven D, Passias PB, Errioc TJ, Lafage P, Bianco K, et al. (2015) Risk factors for reoperation in patients treated surgically for intervertebral disc herniation. J Bone Joint Surg Am 97: 1316-1325.
29. Sherman J, Cauthen J, Schoenberg D, Burns M, Reaven NL, et al. (2010) Economic impact of improving outcomes of lumbar discectomy. Spine J 10: 108-116.
30. Hao Y, Ma DH, Hwang DG, Kim WS, Zhang F (2000) Identification of antiangiogenic and anti-inflammatory proteins in human amniotic membrane. Cornea 19: 348-352.
31. Niknejad H, Peirovi H, Jorjani M, Ahmadiani A, Ghanavi J, et al. (2008) Properties of the amniotic membrane for potential use in tissue engineering. Europ Cells Materials 15: 88-99.
32. Li W, He H, Chen YT, Hayashida Y, Tseng SCG (2008) Reversal of myofibroblasts by amniotic membrane stromal extract. J Cellular Physiol 215:657-664.
33. Maroon JC, Abla A, Bost J (1999) Association between peridural scar and persistent low back pain after lumbar discectomy. Neurol Res 21(suppl 1) :S43-S46.
34. Ben Debba M, Van Alphen HA, Long DM (1999) Association between peridural scar and activity-related pain after lumbar discectomy. Neurol Res 21(suppl 1): S37-S42.
35. Ross JS, Robertson JT, Frederickson RCA, Petrie JL, Obuchowski N, et al. (1996) Association between peridural scar and recurrent radicular pain after lumbar discectomy: Magnetic resonance evaluation. Neurosurgery 38: 855-863.
36. Centers for Medicare and Medicaid Services (2018) Bundled Payments for Care Improvement (BPCI) Initiative: General Information.
37. Keskimaki I, Seitsalo S, Österman H, Rissanen P (2000) Reoperations after lumbar disc surgery: a population-based study of regional and interspecialty variations. Spine 25: 1000-1508.
38. Kim CH, Chung CK, Park CS, Choi B, Kim MJ, et al. (2013) Reoperation rate after surgery for lumbar herniated intervertebral disc disease: nationwide cohort study. Spine 38: 581-590.
39. MedPAC (2017) Hospital inpatient and outpatient services: Assessing payment adequacy and updating payments.