## Title

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ORIGINAL RESEARCH

# The Comparison of Cost-Effectiveness Between Magnetic Resonance Spectroscopy and Provocative Discography in the Identification of Chronic Low Back Pain Surgery Candidates

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**Background/Context:** Chronic low back pain (CLBP) is a significant US healthcare burden with millions of lumbar spine procedures annually. Diagnostic tests are essential to guide treatment but provocative discography (PD), the most common diagnostic procedure, is without robust evidence of its value. A non-invasive alternative using Magnetic Resonance Spectroscopy (MRS) offers a potential solution.

**Context/Purpose:** We assess cost-effectiveness of MRS with NOCISCAN diagnostic algorithm compared to PD for identifying lumbar discs requiring surgical intervention.

**Study Design/Setting:** We conducted cost-effectiveness analysis using modelling.

**Patient Sample:** We used data from a clinical study of 139 CLBP patients who met criteria for and received PD of lumbar spine and presented with an ODI score ≥40; comparing PD and MRS-based diagnostics.

**Outcome Measures:** We considered diagnostic costs, adverse events, surgical costs and outcomes based on a 15-point improvement on the Oswestry Disability Index.

**Methods:** Incremental cost-effectiveness ratios (ICERS) and probabilistic sensitivity analyses were determined. Some authors have consulted for Aclarion.

**Results:** Mean total cost per PD patient was $59,711, and $57,998 for MRS, demonstrating $1712 cost savings per MRS diagnosed patient. Diagnostic costs ($1950 for PD; $1450 for MRS), saved $500 per MRS patient. PD incurred adverse event costs ($57,323) for 1% of patients, which MRS eliminated. MRS-based diagnosis showed 78% surgical success, whereas PD achieved 68%. MRS was the dominant diagnostic strategy, with better clinical outcomes and cost savings. Probabilistic sensitivity analysis confirmed MRS dominance and was cost-effective across a wide range of willingness-to-pay thresholds and across 2 different scenarios which vary base-case outcomes and surgical rates.

**Conclusion:** This study demonstrates cost-effectiveness dominance of MRS with the Nociscan diagnostic algorithm over PD for identifying CLBP surgical candidates. MRS provides significant cost savings and leads to better surgical outcomes, making it a preferred choice for insurers and health systems.

**Plain Language Summary:** Chronic low back pain (cLBP) is experienced by 20% of the US population. It is difficult to determine the best treatment, and many have unnecessary surgery. Discography is the currently available diagnostic but is invasive, of limited value and with serious adverse events. MRS+Nociscan, a new non-invasive diagnostic uses MR Spectroscopy and an algorithm to identify painful discs, is FDA registered. Our aim is to conduct a cost-effectiveness analysis (CEA) to compare the economic value of these two diagnostic procedures. Subjects were part of a multicenter study of 139 patients who received MR imaging and PD for chronic low back pain. The intervertebral disc MRS data post-processing was performed using the NOCISCAN-LS software algorithm. We developed a decision tree model comparing provocative discogram (PD) with an MRS+ Nociscan diagnostic algorithm using a health system perspective over 12-months. The primary endpoint was surgical ODI success or failure. Costs were from the

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Medicare Fee Schedule. We calculated in incremental cost-effectiveness ratio (ICER), in terms of the additional cost or savings per additional treatment success gained. The mean total PD group cost per patient was $59,711 and $57,998 in the MRS+Nociscan group demonstrating that MRS-based diagnosis saved $1712 per patient diagnosed. Clinical success with MRS-based diagnosis was 78%, and 68% with PD diagnosis. The cost-effectiveness demonstrated strong MRS-Nociscan dominance, meaning it was both cost saving and a better clinical success. The strong cost-effectiveness dominance for MRS+Nociscan diagnosis answers the budgetary questions for insurers and health systems considering adoption of this new diagnostic tool.

**Keywords:** cost, cost-effectiveness, lumbar spine, diagnostics, outcomes, discography

## Introduction

Approximately 634,355 lumbar spine fusions are performed annually in US., with as many as 80% experiencing post-surgery discomfort and 10–40% experiencing persistent post-surgical pain, leading to a high rate of additional treatment with emotional stress and increased healthcare costs.[1]

Diagnostic tests are essential to clinical decision-making when they facilitate accurate identification of patients, stratify them to the correct treatment strategy and are affordable.

Currently, in addition to careful physician assessment, the only available diagnostic tests for identification of painful lumbar discs are Computed Tomography (CT), Magnetic Resonance (MR) imaging and discography. Discography is an invasive test using an injected contrast agent to determine the integrity of the intervertebral discs and whether or not they are painful.[2,3] Discography may be used alone or with CT for cross-sectional evaluation.[2,3] Despite the relatively common use of discography, there is limited data to demonstrate its value based on surgical success,[4–6] and with its documented adverse effects, clinical practice guidelines for the use of discography in the evaluation of low back pain prior to surgery are mixed.[7–9] Given the lack of any alternatives, however, many clinicians continue to perform and rely on discography for establishing a diagnosis of discogenic back pain when surgery is being considered.[10,11] Additionally, there is some evidence that discography can pre-dispose the intervertebral disc to additional degenerative disc disease.[10,11] A more optimal solution and one that could avoid this possibility would be a non-invasive diagnostic technique that utilizes MR Spectroscopy to assess the chemical composition of the intervertebral disc in order to differentiate painful from non-painful spine discs. This single voxel MR spectroscopy platform is FDA registered and available for use in the US. This imaging technique also has a CE Mark allowing use throughout the European Union.[12–14]

The process of adoption of a new diagnostic technique into the health care system not only requires strong efficacy evidence but also assessment of the economic effects on the health care system and on insurers. This impact is most often determined by a cost-effectiveness analysis (CEA) or a budget impact analysis. The standard CEA allows for a comparison of one method of diagnosis to another by estimating how much it will cost to gain a unit of outcome such as a surgery prevented, or a surgical success achieved.[15]

Historically there are few cost-effectiveness studies comparing diagnostic techniques used for back pain, and none comparing the use of MR imaging or discography for the identification of painful intervertebral discs leading to surgical intervention. This paucity of data is primarily due to comparatively less evidence underpinning pricing and reimbursement policies of diagnostics and the scientific evidence facilitating the market-entry of diagnostics is much more limited than that of treatment-based methods. Additionally, there is frequently a lack of a "gold standard" for diagnostic comparison, limiting the amount of evidence available for an economic evaluation of a diagnostic. Another limiting factor is that randomized controlled trials (RCTs) comparing outcomes of a test and treat scenario are uncommon due to the challenges and ethical appropriateness of conducting such trials. Decision modeling is recognized as a valuable alternative to randomized controlled trial evidence for conducting cost-effectiveness analyses with a focus on including the best evidence available and exploring all analytical uncertainties. Decision analytic modeling allows the synthesis of evidence from multiple sources to allow an evaluation of the cost-effectiveness of a particular diagnostic technique or modality.

The aim of this study was to use a decision analytic model and current literature evidence base to determine the costs and cost-effectiveness of a new non-invasive Magnetic Resonance Spectroscopy (MRS) plus algorithm interpreted diagnostic test compared to existing provocative discography (PD) testing for identification of painful intervertebral discs.

# Materials and Methods

## Sample

Subjects were part of an already published multicenter, indirect comparative clinical study of 139 enrolled adult patients who received MR imaging and PD as part of their standard workup for chronic low back pain. These subjects also met accepted criteria for PD of the lumbar spine and presented with an ODI score ≥40 and <80 and a VAS score improvement of 2 points.[16] Patients were excluded if they had undergone prior lumbar spine surgery, spondylolisthesis with more than 2mm of translation, scoliosis greater than 15 degrees, evidence of prior fracture, a lumbar disc extrusion, or lower extremity motor strength deficit as previously described.[17] The intervertebral disc MRS data post-processing was performed using the NOCISCAN-LS software algorithm as described by Gornet et al.[17] The clinical utility of the optimized MRS software protocols and the Nociscan diagnostic algorithms were independently assessed by correlating the results of the imaging modalities with the outcomes of the surgical procedures at 6 and 12 months. Surgical success was determined as an ODI improvement of 15 points. Patients were classified based on their MRS disc diagnosis in comparison to whether the discs were also PD+ or PD –. We assumed that all patients who had a PD diagnosis and then had surgery, were PD+ patients. The following MRS classifications included:

1) MRSmatch patients, defined as those who were both PD+ and who had surgery only at discs that were MRS+ or MRSmild (patients without an MRS+ disc), or 2) MRSmiss patients defined as those who were PD+ surgical patients treated at only an MRS- disc or who had an MRS+ disc left untreated.[17] All surgeries described in the Gornet et al trial "were performed independently of the MRS algorithm scores since most MRS scans were performed prior to the discography results and surgical decision".[17] This eliminated any assignment bias when making the MRS classification and surgical decision. Seventy-three of the 139 CLBP patients received lumbar spine surgery and reached 6-month outcomes (62 patients at 12 months). Diagnostic results could identify either single or multiple positive discs. Patients had either fusion or total disc replacement or both (with multiple disc procedures). Published literature was sought for probability estimates that were not included in the Gornet (2019) study and therefore had to be modeled from other studies. Since all patients in the Gornet (2019) study had surgery, other studies were used to estimate the models branch probabilities for those who did not have surgery, as described in more detail below.[5,9,16,18–22]

## Cost-Effectiveness Modeling

### Model

We developed a base-case decision tree model comparing provocative discogram (PD) with an MRS+ Nociscan diagnostic algorithm obtained after routine MRI. The health care system perspective over a 12-month time horizon was used, based on the data available for this comparison.[17] A bubble diagram (Figure 1) shows the algorithmic pattern of our decision tree with variables including: Surgery or no surgery, number of disc levels (1- or 2-levels), type of surgery (spinal fusion or total disc replacement), occurrence of any PD and surgical complications, delayed surgery, PD results, and MRSmatch and MRSmiss sensitivities for MRS+ Nociscan diagnosis. The primary endpoint was defined as either success or failure based on reaching a 15-point increase in ODI from baseline (Supplement: Figure 1).

We calculated an incremental cost-effectiveness ratio (ICER), in terms of the additional cost or savings per additional treatment success gained, by dividing the difference in 12-month effectiveness outcome into the difference of 12 months costs of the two diagnostic interventions being compared. The ICER indicates the difference in costs per added effect unit gained using the MRS diagnosis of a painful disc as compared to using a provocative discogram diagnosis. ICER is defined as:

$$ICER = (COST_{(MRS+NOCISCAN)}) - (COST_{(Inc.ODI\ success/fail)}) / (ODI\ SUCCESS_{(MRS+NOCISCAN)}) - (ODI\ SUCCESS_{(Inc.ODI\ success/fail)}).$$

We performed univariate and probabilistic Monte Carlo sensitivity analyses. We calculated an acceptability curve based on a willingness to pay (WTP) amount of $150,000. A WTP of from $50,000 to $150,000 are standard WTP for acceptability of new treatments being introduced in the United States for each quality adjusted-life-year-saved (QALYs).[23] The acceptability curve is generated from 1000 random sampling of the distributions of all variables at the same time to determine the proportion of the calculations that are cost-effective for each alternative. We also

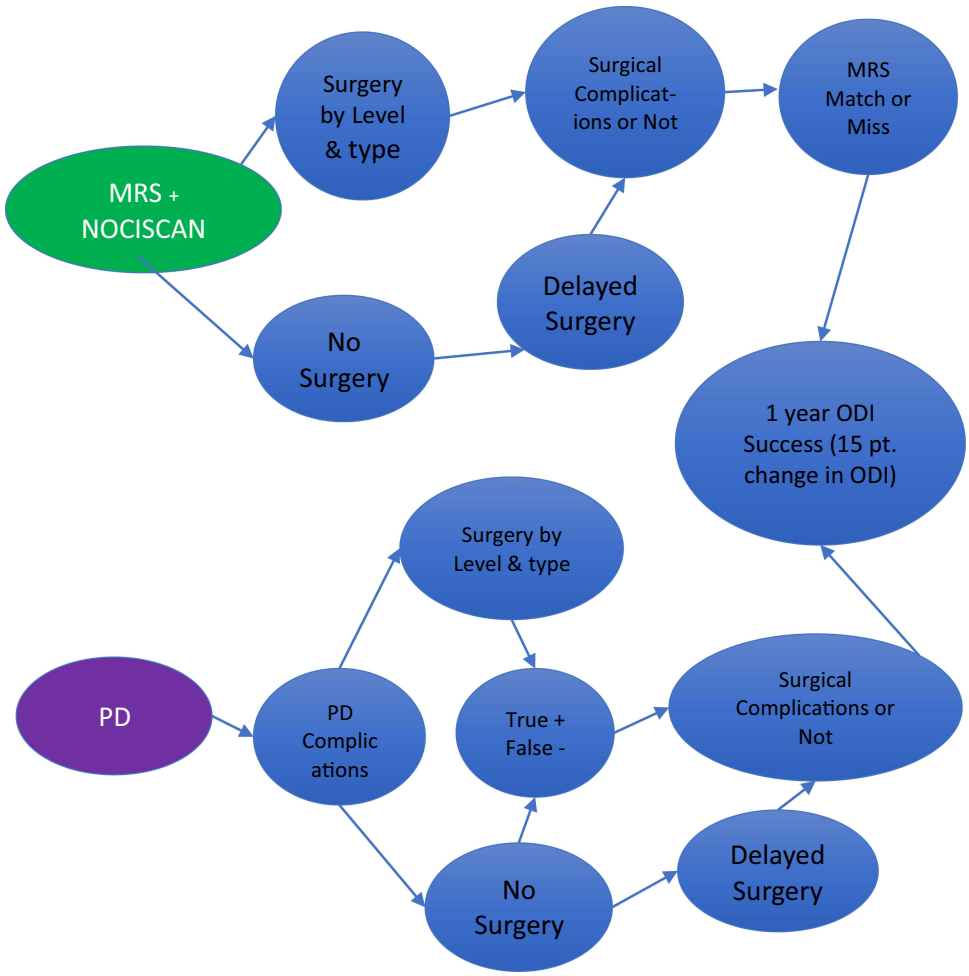


**Figure 1** Bubble diagram comparing MRS+ Nociscan vs provocative discography.

calculated the net monetary benefit (NMB) which is defined as: NMB = (alpha $_{(WTP)}$*Effectiveness$_{(Inc.ODI\ success/fail)}$)– Cost $_{(Inc.\$)}$. A positive NMB indicates a cost-effective diagnostic intervention. There was no discounting given our short-term perspective.

## Clinical Outcome Data

In order to calculate a cost-effectiveness ratio comparing this new non-invasive Magnetic Resonance Spectroscopy (MRS) plus algorithm interpreted diagnostic test compared to existing provocative discography (PD) testing for identification of painful intervertebral discs, we have to determine both costs and a utility-based outcome. Our primary outcome used in our CEA model was based on the Oswestry Disability Index main outcome from Gornet et al, where a change of at least 15 points was considered a clinically significant improvement.[17] In the CEA surgical treatment was considered a success with at least a 15-point improvement in ODI or a non-success if not attained. Outcomes for PD negative patients without surgery and not included in the Gornet et al study were based on other, less stringently defined measures of success and failure.[18] Patients who were MRS-negative were also assumed not to have surgery in the base-case decision branches and were given the same outcomes of those who are PD negative without surgery (52% success for Level-1 and 33% success for Level-2 surgeries).[5] Clinical treatment success with a PD true negative rate is 41%.[20] Success rates for PD false negatives (those not having surgery and should have had surgery) was 12% for level-1 discs and 10.5% for level-2 discs.[18]

### Cost Data

Costs were estimated in 2022 US dollars and included costs of diagnostic tests, diagnostic test adverse event treatments, surgery (including hospital, surgeon and instrumentation fees), physician visits, medications, lab tests, diagnostic tests, hospitalizations weighted by type of surgery (fusion or total disc replacement), surgery adverse events treatments, and costs of negative surgical outcomes (pain medication, physician visits, physical therapy, and repeat surgery) for a period of 1 year.

Costs were collected by the Centers for Medicare and Medicaid Services (CMS) National Drug Codes (NDC), Current Procedural Terminology (CPT) procedure and visit codes, and/or International Classification of Diseases (ICD)-10 diagnosis codes based on type and amount of cost, using Medicare payment rates. Indirect costs such as work loss and pain and suffering were not included. This modeling study using only already published data was exempt from IRB approval.

# Results

## Decision Model

The decision model had 8 main branches: including: 1. Diagnostic procedure, 2. Positive or negative diagnosis result, 3. Diagnostic accuracy, 4. Single or multiple discs, 5. Side-effects of diagnostic procedure, 6. Surgery performed, 7. Surgery type, 8. Adverse events, and 9. Outcomes at 12 months (Figure 1).

## Probability Estimates

Table 1 shows the model probabilities. In our CLBP population with symptom severity sufficient to deem them eligible for PD, it was assumed that 88% (63/73) of MRS-tested patients would have surgery and the 10% who were MRS-negative were assumed to not have surgery, Gornet et al.[17] It was also assumed that 88% of the PD-tested patients would have surgery. After removing those patients not undergoing surgery, 76% of MRS-diagnosed patients (48/63) had level-1 surgery and 23% had 2 or more levels. Surgical complication rates were 11% regardless of diagnosis method and 6% of patients undergoing surgery were assumed to require additional surgery. Complications from PD were conservatively estimated at 1%.[19]

The diagnostic accuracy of MRS was described in comparison to PD results from Gornet et al, and classified first as either level-1 or 2 and then as 1) MRSmatch (77% or 37/48 for level-1) which are those that are PD+ (and undergoing surgery) and are also MRS+ (70% or 26/37 for level-1) or 2) MRS mild (30% or 11/37 for level-1), or 3) MRSmiss (23% or 11/48 for level-1) which are those that are PD+ surgical patients and treated at an MRS- disc or with an MRS- disc that is left untreated.[17] The probability of success or failure based on the ODI scores was identified based on these MRS designations and on the number of surgical levels. Single-level surgeries on MRS + only patients had 100% success (26/26). The MRSmild patients undergoing a single-level surgery had an 81.8% success rate and the MRSmiss patients (after non-surgical patients were removed) had a 54.5% success rate (Table 2).

Probabilities for the 10% of MRS-negative patients assumed to not have surgery were based on the 67% surgical success rate seen in Gornet et al but were reduced to the PD-negative rate of 52% obtained from Colhoun et al for single-level PD surgical success, which was reduced to 33% for 2-levels, based on the % reduction in success between 1 and 2-level disc patients.[5,17]

Accuracy of PD diagnosis for those who had surgery was based on the 81% true positive rate (TPR) and 19% false-negative rate (FNR) from Willems et al for discography.[20] The single-level surgical success rate for the PD true positives was 89%.[5] The success rate of the false negatives (those that should have surgery, but did not, based on the PD results) seen in the evaluation by Derby et al was 12%.[18] Calhoun et al showed a success rate of 80% for 2-disc levels that were classified as true positives, and Derby et al showed a success rate of 10.5% for discs classified as false negatives.[5,18] The accuracy of PD diagnosis for those who did not have surgery was 41% (TNR) and 52% for those who are MRS-negative without surgery for level-1 and 33% for level-2 discs without surgery.[5,20]

## Costs

### Diagnostics

Total cost of discography was obtained from the 2022 Medicare Fee Schedule, using CPT codes 62290 for the injection, and 72295 for clinical supervision one time and for interpretation for each level.[25] The total cost of an MRS+Nociscan was $1450, the

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**Table 1** Probability Inputs

| | Mean | High | Low | SD | Comments | References |
|---|---|---|---|---|---|---|
| **p_MRSSurg** | 0.86 | 1.075 | 0.645 | 0.08875 | Assume same as for PD as Gornet does not include PD- pts. | Manchikanti, 2009[22] and Wolfer, LR,2018[16] (averaged) |
| **p_SurgComplications** | 0.11 | 0.1375 | 0.0825 | 0.01375 | | Fairbanks J, 2005[19] |
| **p_MRSmatchLevel1Surg** | 0.77 | 0.9625 | 0.5775 | 0.09625 | | Gornet, MG, 2019[17] |
| **p_MRSmatchLevel2Surg** | 0.67 | 0.8375 | 0.5025 | 0.08375 | | Gornet, MG, 2019[17] |
| **p_MRSnegNosurgeryLevel1** | 0.60 | 0.75 | 0.45 | 0.075 | | Gornet, MG, 2019[17] |
| **p_MRSNoSurgeryLevel1ODISucccess** | 0.52 | 0.65 | 0.39 | 0.065 | | Colhoun, E. 1988[5] |
| **p_MRSNoSurgeryL2ODISuccess** | 0.33 | 0.4125 | 0.2475 | 0.04125 | | Gornet, MG, 2019[17] |
| **p_MRSposOnly** | 0.70 | 0.875 | 0.525 | 0.0875 | | Gornet, MG, 2019[17] |
| **p_MRSSurgeryLevel1MatchMildODISuccess** | 0.818 | 1.0225 | 0.6135 | 0.096625 | | Gornet, MG, 2019[17] |
| **p_MRSSurgeryLevel1MatchPosOnlyODISuccess** | 0.96 | 1.2 | 0.72 | 0.07 | | Gornet, MG, 2019[17] |
| **p_MRSSurgeryLevel1MissPosOnlyODISuc** | 0.545 | 0.68125 | 0.40875 | 0.068,125 | | Gornet, MG, 2019[17] |
| **p_MRSSurgeryL2MatchPosOnlyODISuc** | 0.90 | 1.125 | 0.675 | 0.08125 | | Gornet, MG, 2019[17] |
| **p_MRSSurgeryLevel2PosMixODISuccess** | 0.80 | 1 | 0.6 | 0.1 | | Gornet, MG, 2019[17] |
| **p_MRSSurgery** | 0.86 | 1.075 | 0.645 | 0.08875 | | Calhoun, E, 1997 |
| **p_MRSsurgeryLevel1** | 0.76 | 0.95 | 0.57 | 0.095 | same as for PD | Gornet, MG, 2019[17] |
| **p_PDCompl** | 0.01 | 0.0125 | 0.0075 | 0.00125 | | Gornet, MG, 2019[17] |
| **p_PDnegFPRSuccess** | 0.33 | 0.4125 | 0.2475 | 0.04125 | | Colhoun, E, 1988 |
| **p_PDnegTNRSuccess** | 0.50 | 0.65 | 0.39 | 0.065 | | Gill, K & Blumenthal, SK, 1976[6] |
| **p_PDpositive** | 0.86 | 1.075 | 0.645 | 0.08875 | Averaged, and Assume all had surgery | Manchikanti, L, 2009[22] and Wolfer, LR, 2008[24] (averaged) |
| **p_PDSurgeryLevel1FNRSuccess** | 0.12 | 0.15 | 0.09 | 0.015 | | Derby, R, 1999[18] |
| **p_PDSurgeryLevel1TPRSuccess** | 0.89 | 1.1125 | 0.6675 | 0.083125 | | Colhoun, E, 1988[5] |
| **p_PDSurgeryLevel2FNRSuccess** | 0.105 | 0.13125 | 0.07875 | 0.013,125 | | Derby, R, 1999[18] |
| **p_PDSurgeryLevel2TPRSuccess** | 0.80 | 1 | 0.6 | 0.1 | averaged from Gornet, 2019 but account for # disc levels | Gornet, MG, 2019[17] and Colhoun, 1988[5] |
| **p_PDsurgeryLevel1** | 0.76 | 0.95 | 0.57 | 0.095 | same as for MRS | Gornet MG, 2019[17] |
| **p_PDTNR** | 0.41 | 0.5125 | 0.3075 | 0.05125 | | Willems, PC, 2014[20] |
| **p_PDTPR** | 0.81 | 1.0125 | 0.6075 | 0.098125 | | Willems, PC, 2014[20] |


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**Table 2** Cost Inputs in 2022 US Dollars

| Variable | Probability | Total Cost | SD | Refs |
|---|---|---|---|---|
| **Diagnosis** | | | | |
| **MRI** | 1 | $2208 | 276 | https://www.medicare.gov/procedure-price-lookup/cost/72158 |
| **PD** | 1 | $1950 | 181 | https://www.aapc.com/discuss/threads/billing-for-disscogram.39343/[25] and https://prairiesurgicare.com/get-pricing/ |
| **MRS+ Nociscan** | 1 | $1450 | 244 | Personal communication Bond, R, August, 2022 |
| **CT** | 1 | $467 | | https://www.evicore.com/-/media/files/evicore/provider/network-standard/cigna_spine-imaging-guidelines_v20_eff10012021_pub06292021.pdf[24] http://www.ic.nc.gov/ncic/pages/70000.htm[26] |
| **Surgery including hospital, surgeon (wted by type of surgical approach), instrumentation** | | | | |
| **Fusion/TDR (wted) for Level 1 Discs** | 0.76 | $52,493 | 6562 | https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Wynn0307.pdf[27] |
| **Fusion/TDR (wted) for Level 2 Discs** | 0.24 | $71,027 | 8878 | file:///C:/Users/WilsonL/Downloads/1547-5654-article-p546.pdf<br>https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/Wynn0307.pdf[27]<br>https://www.gohealthcarellc.com/blog/coding-and-billing-orthopedic-spinal-fusion[28]<br>2020 AMA's CPT Guidelines[29] |
| **Adverse Events/Complications: (hosp, MD visits, Labs, Meds, PT)** | | | | |
| **PD Adverse events** | 0.01 | $57,323 | 7165 | Peh WCG, 2005[4] and Willems PC, 2004[30] |
| **Surgical Adverse Events** | 0.11 | $45,382 | 5673 | RedBook/Micromedex,[31] Center for Medicare/Medicaid Services: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Clinical-Laboratory-Fee-Schedule-Files,[32] and 2019 medical fee schedule,[33] and https://www.bls.gov/data/inflation_calculator.htm[34] |
| **Long-term complication treatments (PT, MD visits, re-surgery, labs, meds)** | | | | |
| **ODI failure for 2nd 6 mos** | 1 | $5056 | 632 | Peh WCG, 2005[4] and Willems PC, 2004.[30]<br>RedBook/Micromedex,[31] Center for Medicare/Medicaid Services: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Clinical-Laboratory-Fee-Schedule-Files,[32] and 2019 medical fee schedule,[33] and https://www.bls.gov/data/inflation_calculator.htm[34] |

current payment in clinical practice R. Bond (personal communication, July 2022). Temporary codes available for billing of a Nociscan are 0609T (payment to imaging center), 0611T (Nociscan-LS payment to company), 0610T (process of transmitting raw spectroscopy data from MRI scanner to software for analysis and back to the imaging center, and 0612T (physician interpretation/reporting). Total CT cost was $467 (tech and professional fees) for CPT 72131 (CT lumbar without contrast (post discography CT)).[24,26]

The total MRI cost was $2208 using CPT code 72158 and AMA Radiology Medicare payment (professional and technical component).[35]

## Surgery

Surgical cost was estimated as the APR-DRG cost for hospitalization as determined by the Medi-caid payment from the DRG Calculator (2021–2022) plus the physician-specific procedure payment by CPT code from the 2021 CMS Medicare fee schedule. Surgical costs were weighted by procedure type (fusion or total disc replacement (TDR)) and levels treated. Fusion cost was $57,180, including severity-weighted hospitalization group classifications (DRGs 023–1 to 4),[27] surgeon

fees by surgical approach (PLIF, TLIF, ALIF, DLIF) (CPTs 22630–2263, 22,558, 22585 depending on interspaces included),[28] and instrumentation (CPT22845). Total cost for TDR was $38,431. This amount included DRGs 310–1 to 4,[28] surgeon fees by type of surgical approach and interspaces included (CPTs 22856–22,858),[29] and instrumentation (CPT code 22845).

### Adverse Event Costs

Adverse event costs for PD and for surgical procedures were included in our model. Adverse events from MR imaging examinations or MRS were sufficiently rare to be excluded. Surgical adverse events were estimated at 11% and included infection/inadequate wound healing (16%), pulmonary embolism (2.5%), deep venous thrombosis (17.5%), and spinal nerve compression with weakness, pain, bowel/bladder problems requiring decompression surgery (30.7%). Costs included one hospitalization (MS-DRGs 175 and 176, 30, 458, 294, 856 and 857, 61.62 and 63, 101, 103, and 916 depending on the AE), drug costs (PO and IV antibiotics, pain meds, and warfarin/coumadin) were included out to 40 or 180 days, physician visits (CPT codes 99204,99,219,99,217,99,225,99,244), and laboratory tests and physical therapy (CPT codes 97163,97,164) ($1675) were also included out to 6 months. The repeat surgery rate was 6% and costs included the surgical intervention, pain medications, and physician visits.[31–34]

The AEs from PD included discitis, nerve damage, post-procedural headache, intrathecal hemorrhage, meningitis, arachnoiditis, and osteomyelitis. The baseline estimate for the incidence of AEs associated with PD was 1%. Costs included all appropriate treatment categories as described above for surgical AEs.[4,30]

## Total Cost and Cost-Effectiveness

### Total Cost by Diagnostic Approach

The mean total cost per patient in the PD group was $59,711 and was $57,998 in the MRS group demonstrating that MRS-based diagnosis on average saved $1712 per patient diagnosed. Diagnostic costs alone were $1950 per person for PD and $1450 per person for MRS, a savings of $500 per person. In addition, PD has an additional adverse event cost of $57,323 for 1% of patients which is not present for patients undergoing MRS to achieve a diagnosis (Table 3).

### Clinical Outcomes

Clinical success was attained in both groups, with MRS-based diagnosis demonstrating an overall success in 78% of patients and PD showing success in 68%. This is a 10% advantage to MRS-based diagnosis compared with PD (Table 3).

### Incremental Cost-Effectiveness Ratio

The ICER for MRS as compared to PD demonstrated strong MRS dominance, meaning that an MRS diagnostic approach was both cost saving and had a better clinical success (Table 3). In this scenario, an ICER is not calculated because of this dominance. The net benefit was $20,489 for MRS and $8762 for PD (an $11,712 difference) showing that MRS is the cost-effective strategy when compared to PD (Table 3). The incremental net monetary benefit demonstrates a preference for MRS at all WTP levels (Supplement: Figure 2). The scatterplot in Figure 3 shows the mean ICER is in the lower right quadrant, also indicating MRS was both cost saving and associated with improved ODI outcome. The dotted area represents the uncertainty in all 4 quadrants and thus in the calculations.

**Table 3** Cost-Effectiveness Analysis Results: Incremental Cost-Effectiveness Ratio

| Strategy | Cost | Incr Cost | Effect | Inc Effect | ICER | NMB |
|---|---|---|---|---|---|---|
| | (US $'s) | | (Success= 15 point improvement in ODI) | | | |
| MRS+ Nociscan | $57,998 | | 0.78 | | Dominant | $20,489 |
| Provocative Discogram | $59,711 | $1712 | 0.68 | −0.10 | −17,100 | $ 8762 |

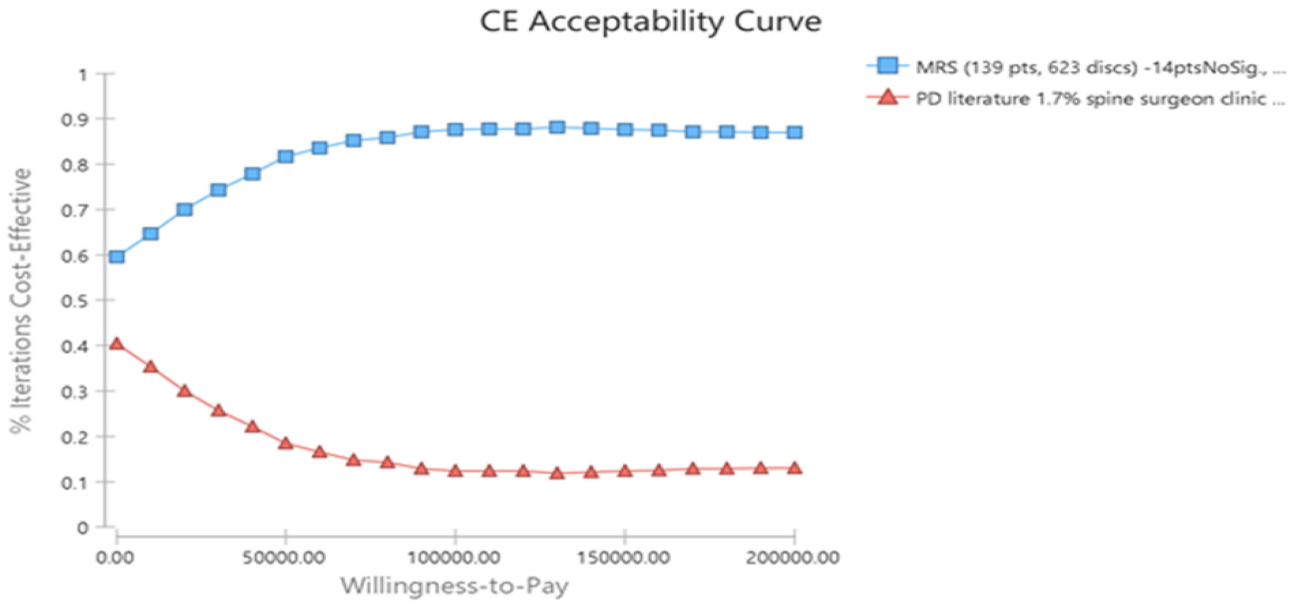


**Figure 2** Monte Carlo acceptability curve.

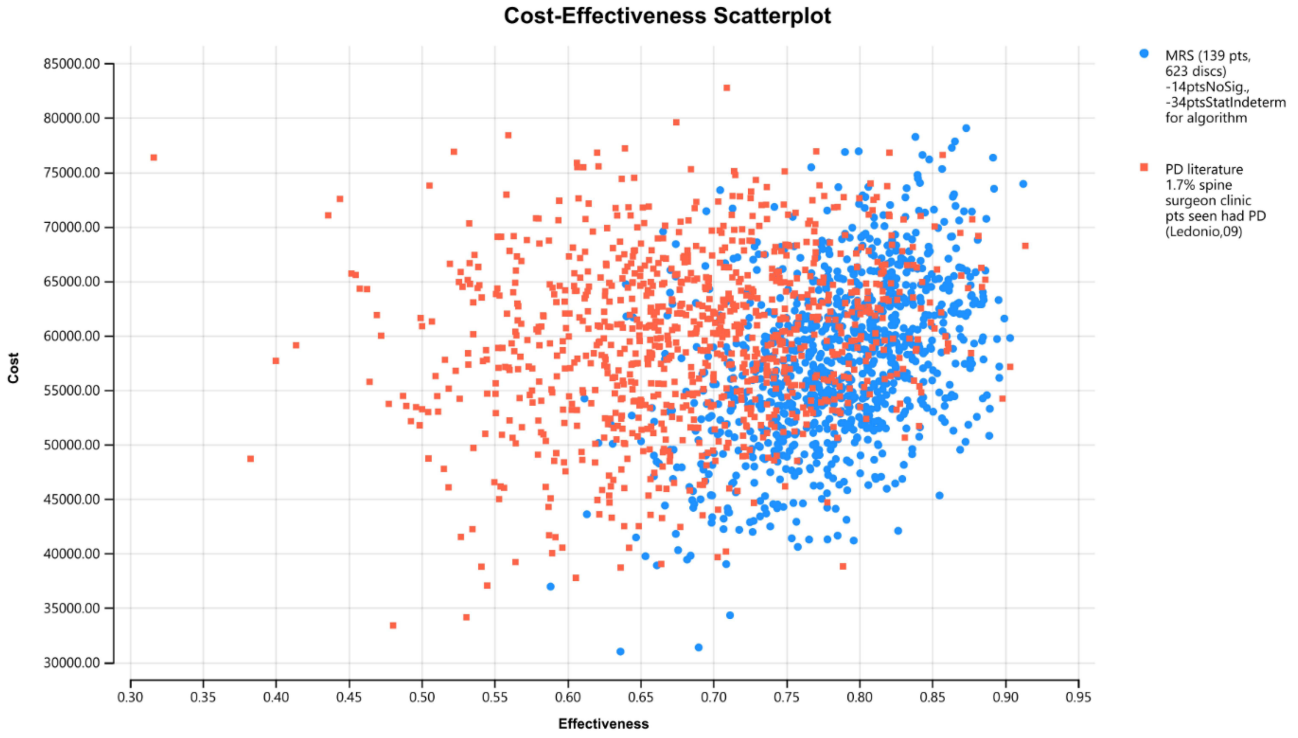


**Figure 3** Cost-effectiveness scatter plot.

## Sensitivity Analysis

A Monte Carlo probabilistic sensitivity analysis, conducted with 1000 simulations demonstrated that MRS is dominant or more cost-effective the majority of time across a wide range of WTP estimates. (Figure 2). Because we elected to use the more accurate study trial endpoint, rather than to estimate a survival difference across these diagnostics, we consider a wider range of possible acceptable thresholds. Additionally, the Cost-effectiveness scatterplot shows that for the


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majority of time, MRS has higher effectiveness at lower costs than does the PD approach (Figure 3). We used univariate sensitivity analysis to specifically examine the effect on the cost-effectiveness ICER of two specific scenarios in addition to the baseline scenario already described. This was especially important because the clinical trials by Gornet et al, did not have comparative data on the outcomes of those who are PD negative, requiring the estimation of these outcomes from other published literature.[17,36]

Initially, we examined the effects of equalizing outcomes for some of the PD and MRS decision branches by reducing the MRS-negative patient's success rates to be the same as those of the PD false-negative patients (those not having surgery and should have). With both MRS-negatives and PD-false negative success rates at 12% for one-level discs and 10.5% for two-Level discs.[18] It resulted in a slightly lower total cost difference between MRS and PD (a $1475 savings with MRS use) and a lower, but still positive gain in effectiveness for MRS over PD (−0.05 success difference). This resulted in the overall ICER still showing the MRS-based diagnosis was dominant over PD diagnosis, thereby showing the robustness of our data even with this most conservative estimate in the MRS-negative group.

The second scenario we explored was the potential for a reduction in the number of surgeries that might occur if MRS was more accurate than PD in clinical use. In this scenario, we reduced the number of surgeries in the MRS diagnostic group scenario by 50% (from 86% of those undergoing diagnosis to 43%). One potential value of the use of MRS diagnosis, is that some surgeries would be prevented compared to the current rate in this high-risk group of patients diagnosed by PD. In the base-case analysis, we estimated that both groups undergoing diagnosis had the same surgical uptake (86%).[17] Reducing the rate of surgery after MRS diagnosis reduced the total costs by half resulting in larger savings compared to PD diagnosis ($27,475). The effectiveness of MRS was also reduced, however, because although if this smaller surgical group was more accurately diagnosed it would presumably also have better outcomes in the base-case, as we did not change the outcomes of the surgical or non-surgical groups. Therefore, in this scenario, PD was more effective by 0.07 successes. Despite this situation, MRS still resulted in being the most cost-effective choice, with an ICER of $391,145 additional costs for each added surgical success in subjects that were diagnosed with PD. This ICER is more than double the accepted WTP of $150,000 when using QALYS, so likely also is not cost-effective at our surgical success endpoint. This means, even in this scenario, the PD diagnostic approach is likely not cost-effective and MRS the more efficient diagnostic approach. So even with these two most conservative scenarios, MRS remains the most cost-effective choice. Payers may consider that a non-invasive diagnostic may encourage more patients to undergo diagnosis. This situation may increase the budget needed for diagnostic testing and even the overall number having surgery. However, if the MRS diagnostic rates indicating surgical need, and rates of surgical success remain the same, then the cost-effectiveness results shown here will still hold; and also result in more patients receiving the appropriate care. Further monitoring of the population being tested, the number and condition of those having surgery, and their surgical success rates are essential, just as with any new medical care introduced into a health care system.

## Discussion

We demonstrated a strong cost-effectiveness dominance for MRS as compared with PD in the diagnosis of and subsequent surgical outcomes for patients with lumbar CLBP. This cost-effectiveness dominance was present in the base-case analysis as well as in two more conservative scenarios in our sensitivity analysis. In addition, our probabilistic sensitivity analysis demonstrated an MRS diagnosis as the most cost-effective approach across a wide range of WTP estimates. The MRS diagnosis approach saved $1712 per patient and also was 10% more effective in achieving surgical success.

The availability of comparative data for diagnostics is low, but we were fortunate to have robust comparison data upon which we based this CEA.[17] There are several weaknesses inherent in this CEA model, primarily for the outcomes of PD-negative and nonsurgical patients. We used other non-comparative literature-based data as a basis for the sensitivity and specificity of the PD approach for these outcomes. In addition, we did not have comparative data for MRS-negative and non-surgical patients, so we used literature-based results of PD-negative patients without surgery. To account for the differences in these results that were not directly comparative, we also tested additional scenarios where we equalized these uncertainties. MRS was still the more cost-effective option. Although most outcomes were based on ODI improvement, for a small number of patients (MRS-negatives and PDnegatives not having surgery) it was unclear

the exact measurement of success used which could be important. Our analysis addressed these weaknesses by equalizing the outcomes of these groups for MRS and PD, still demonstrating the cost-effectiveness of the MRS approach. Another limitation of this study is that we did not carry our trial endpoint past its outcome of ODI success to include life expectancy, so we could compare our CEA with a WTP threshold using QALYs. We thought it was not appropriate to extend estimates to survival for a diagnostic test without more evidence. Because of the dominance shown for MRS compared to PD, this is still a strong conclusion for our analysis. Additionally, many researchers and countries using CEA data as evidence for drug/device approvals have begun to move away from a strict QALYs metric of value for dollar, as unable to sufficiently capture societal benefits.[37]

Historically there are few cost-effectiveness studies comparing diagnostics for back pain, and none comparing the use of MRI or discography for identification of discs needing surgical intervention. This is because there is less evidence on the pricing and reimbursement policies of diagnostics and more limited information for market-entry of diagnostic modalities and a lack of a "gold standard" for diagnostic comparison at approval, thereby limiting the evidence needed for robust economic evaluations.

A review article identified 25 model-based CEA analyses assessing diagnostic biomarkers and found CEA results were most sensitive to test accuracy, biomarker costs, relative risk of the event, and proportion adopting the test.[15] A more recent case study example demonstrated the use of modeling to demonstrate the economic value of laboratory testing, stressing the importance of economic information to the acceptance of new diagnostic tests.[38] There are some CEA studies comparing interventions following discography. One study by Maas ET, et al[39] conducted 4 clinical trials to test whether minimally invasive procedures combined with a pain program will be more effective and cost-effective as compared with a pain program alone in patients with chronic mechanical low back pain as identified with discography, finding radiofrequency denervation not cost-effective.[40] A study by Chowdhury et al[41] reviewed seven short-term studies evaluating the economics of a multidisciplinary pain intervention for chronic and subacute low back pain showing mixed cost-effectiveness results.[42] A cost-effectiveness study comparing lumbar fusion with disc replacement for CLBP reported inconclusive results.[43]

## Conclusions

We demonstrate that MRS diagnosis has strongly dominant cost-effectiveness over the use of PD for diagnosis of lumbar chronic low back pain. The cost-effectiveness of new diagnostics is receiving increased attention as new domains of diagnostic testing have grown and use of value-based pricing has become widespread. This study uses the best available data, including comparative data between the new and established diagnostic approaches, to estimate the cost-effectiveness of non-invasive MRS-based diagnostic tool using software protocols and the NOCISCAN-LA algorithm to identify painful intervertebral discs in patients that could be treated with surgical intervention. The strong cost-effectiveness dominance we found for the MRS diagnostic approach should answer some questions regarding the budgetary impact on insurers and health systems who would like to consider adoption of this new diagnostic tool.

## Data Sharing Statement

Materials will be made available on request sent to Leslie Wilson, PhD, the corresponding author. UCSF IRB does not require review for work that only involves information available from published studies, so this study was exempt from a formal IRB review.

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No other acknowledgements. No social media.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

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