Washington State Health Care Authority

Artificial disc replacement – Re-review

Clinical Expert

Rod J. Oskouian, Jr. MD

Chief of Spine
Co-Director, Complex and Minimally Invasive Spine Fellowship Program
Swedish Neuroscience Institute

President and CEO
Seattle Science Foundation

Affiliate Faculty
Institute for Systems Biology

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000.	\	
2.	Equity interests such as stocks, stock options or other ownership interests.		\
3.	Status or position as an officer, board member, trustee, owner.		\
4.	Loan or intellectual property rights.		\
5.	Research funding.		\
6.	Any other relationship, including travel arrangements.		\

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

Globus (<25k)

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		\

If yes to #7, provide name and funding Sources: _____

*If you believe that you do not have a conflict, but are concerned that it may appear that you do, you may **attach additional sheets** explaining why you believe that you should not be excluded.*

I certify that I have read and understand this Conflict of Interest form and that the information I have provided is true, complete, and correct as of this date.

X [redacted] 12/29/16 Rod Oskoian MD

Signature *Date* *Print Name*

So we may contact you regarding your presentation, please provide the following:

Email Address: [redacted]

Phone Number: 206.320.2990

Rod J. Oskouian, Jr. MD, FAANS

Personal Information

Chief of Spine
Co-Director, Complex and Minimally Invasive Spine Fellowship Program

SWEDISH NEUROSCIENCE INSTITUTE
James Tower
550 17th Ave, Suite 500
Seattle WA 98122

President and CEO

SEATTLE SCIENCE FOUNDATION
James Tower
550 17th Ave, Suite 600
Seattle WA 98122

Affiliate Faculty

INSTITUTE FOR SYSTEMS BIOLOGY
401 Terry Ave N
Seattle WA 98109

Office: 206.320.2990
rod.oskouian@swedish.org

Education

1991 – 1996	University of Washington Seattle, Washington	BS
1997 – 2001	UCLA School of Medicine Los Angeles, CA	MD
2001 – 2002	University of Virginia Department of Surgery Charlottesville, VA	Surgical Internship
2001 – 2008	University of Virginia Department of Neurological Surgery Charlottesville, VA	Neurosurgical Residency
2006 - 2007	New Zealand National Hospital Auckland City Hospital	New Zealand Brain & Spine Fellowship

Hospital Privileges

Active Medical Staff	Swedish Medical Center	Seattle, WA
Courtesy Staff	Evergreen Hospital	Kirkland, WA
Courtesy Staff	Overlake Medical Center	Bellevue, WA

Honors

1999 – 2001	UCLA Iris Cantor School of Medicine Research Grant
2001	Edith and Carl Lasky Research Award, UCLA School of Medicine
2001	Leonard Marmor Surgical Arthritis Foundation Memorial Award
2001	Medial Student Thesis Program, UCLA School of Medicine
2001	Deans Scholar Award for Research, UCLA School of Medicine
2001	CNS Award for Clinical Paper, San Antonio Annual Meeting
2004 – 2005	University of Virginia Commonwealth Neurotrauma Fellowship for Spinal Cord Injury
2016	Seattle Met Magazine “Top Doc”

Board Certifications/Licensing

	USMLE Steps 1, 2 & 3
2005	American Board of Neurological Surgery Written Board Examination
2012	Board Certified for the American Board of Neurological Surgery
MD 00049085	Washington State Department of Health
0116014119	Commonwealth of Virginia Medical License

Organizational Participation & Membership

Member	Christopher and Dana Reeve Paralysis Foundation
Member	Neurofibromatosis Foundation
Member	American Association of Neurological Surgeons
Member	Congress of Neurological Surgeons
Member	American Medical Association
Member	North American Spine Association
Board Member	One Spine
Chairman	One Spine Annual Fellows Meeting
Board Member	Puget Sound Spine Interest Group
Member	Seattle Science Foundation Advisory Board
Member	AOSpine

Editorial Responsibilities

2012	European Spine Journal Ed Board
2013	Journal Neurological Surgery – Minimally Invasive Spine Surgery Issue

Research Funding

1999	Cerebral vasospasm and endovascular therapy. Neil A. Martin, MD UCLA, Irish Cantor School of Medicine, Division of Neurosurgery *Research Grant*	$ 2,500
2001	Vascular complications and anterior spinal surgery. J. Patrick Johnson, MD UCLA Spine Center, UCLA School of Medicine, Edith and Carl Lasky Research Award	$ 1,500
2003-2005	Adenosine A2a agonist in the treatment of acute spinal cord injury: University of Virginia School of Medicine. Commonwealth Neurotrauma Initiative	$233,702
2006-2007 Submitted	Adult Stem Cells Processing and Delivery Technology. NIH STTR Grant #00069088	$150,000

Clinical & Research Interests

- Mesenchymal stem cell and regeneration of the nucleus pulposus and annulus
- Degenerative disc disease mouse model
- Tissue engineering with nanoscaffolds and stem cells
- The role of adenosine agonist therapy in spinal cord injury
- Minimally invasive neurosurgery
- Minimally invasive surgical techniques in the management of degenerative, traumatic, and degenerative spinal disorders
- Stereotactic radiosurgery for the spine
- Co-founded a Biotechnology/Stem Cell Company, NanoSpine LLC

Teaching Experience

Spine Fellowship – Trained Fellows

2016 – Present	Jonathan York MD Tarush Rustagi MD Marat Grigorov MD Peter Grunert MD Doniel Drazin MD Daniel DiLorenzo MD

2015 – 16	Marc Moisi MD David Paulson MD Shiv Jeyamohan MD Alireza Shoakazemi MD
2014-15	Dan DiLorenzo MD Emil Pastrana Ramirez MD Ryan Urbonas MD
2013-14	Elizabeth Fontanta MD Shahnawaz Qureshi MD
2012-13	Bret Ball MD Noojan Kazemi MD Fotis Souslian MD
2011-12	Sandeep Bhangoo MD Namath Hussein MD
2010-11	Ali Murad MD Florin Tanase MD Mark Winder MD
2009-10	David Westra MD
2008-09	Michael Higgins MD
2007-08	Abhi Chaturbedi MD
2006-07	Bob Shafa MD
2005-06	Dennis Velex MD

Publications

1. Kelly DF, Oskouian RJ Jr, Fineman I. Collagen sponge repair of small cerebrospinal fluid leaks obviates tissue grafts and cerebrospinal fluid diversion after pituitary surgery. *Neurosurgery.* 2001;49(4):885-889.

2. Oskouian RJ Jr, Johnson JP, Regan JJ. Thoracoscopic microdiscectomy. Operatíve Nuances Section: *Neurosurgery.* 2002;50(1):103-109.

3. Oskouian RJ Jr, Johnson JP. Vascular complications in anterior thoracolumbar spinal reconstruction. *J Neurosurg.* 2002;96(1):1-5.

4. Oskouian RJ Jr, Jane JA Sr, Laurent JJ, Dumont AS, Levine PA. Esthesioneuroblastoma: Clinical presentation, radiology, pathology, treatment, and review of the literature. *Neurosurg Focus*. 2002;12(5)1-9.

5. Oskouian RJ Jr, Martin NA, Lee JH, Glenn TC, Guthrie D, Gonzalez N, Afari A, Vinũela F. Multimodal quantitation of endovascular therapy for vasospasm: TCD, CBF and arterial diameters. *Neurosurgery.* 2002;51(1):30-41.

6. Dumont AS, Oskouian RJ Jr, Chow MM, Kassell NF. Surgical management of unruptured basilar artery bifurcation aneurysms: Technical note. *Neurosurg Focus.* 2002;13(3):e3.

7. Dumont AS, Dumont RJ, Oskouian RJ Jr. Will improved understanding of the pathophysiological mechanisms involved in acute spinal cord injury improve the potential for therapeutic intervention? *Curr Opin Neurol.* 2002;(6):713-20.

8. Oskouian RJ Jr, Samii A, Whitehill R, Shaffrey Me, Johnson R, Shaffrey CI. The future of spinal arthroplasty: A biomaterial perspective. *Neurosurg Focus*. 2004;17(3):E2.

9. Laws ER, Sheehan JP, Sheehan JM, Jaganathan J, Jane JA Jr, Oskouian JR Jr. Stereotactic radiosurgery for pituitary adenomas: a review of the literature. *Journal of Neuro-Oncology.* 2004;69: 257–272.

10. Oskouian RJ, Johnson PJ. Endoscopic thoracic discectomy. *Neurosurg Focus.* 2005;3(6):459-464.

11. Kanter AS, Dumont AS, Asthagiri AR, Oskouian RJ Jr, Sansur C, Jane JA Jr, Laws ER Jr. The transsphenoidal approach: A historical perspective*. Neurosurg Focus.* 2005;18(4):e6.

12. Villavicencio AT, Oskouian RJ Jr, Roberson C, Stokes J, Park J, Shaffrey CI, Johnson JP. Thoracolumbar vertebral reconstruction of metastatic spinal tumors: Long-term outcomes. *Neurosurg Focus.* 2005;19(3):E8.

13. Johnson JP, Stokes JJ, Oskouian RJ Jr, Choi W. Image-guided thoracoscopic spinal surgery: A merging of two technologies. *Spine* 2005;30(19):E572-8.

14. Kanter AS, Diallo AO, Jane JA Jr., Sheehan JP, Asthagiri AR, Oskouian RJ Jr, Okonkwo DO, Sansur CA, Vance ML, Rogol AD, Laws ER Jr. Single-center experience with pediatric Cushing's disease. *J Neurosurg.* 2005;103(5):413-20.

15. Jagannathan J, Dumont AS, Prevedello DM, Lopes B, Oskouian RJ Jr, Jane JA Jr, Laws ER Jr. Genetics of pituitary adenomas: Current theories and future implications. *Neurosurg Focus.* 2005;19(5):E4.

16. Oskouian RJ Jr, Johnson JP. Endoscopic thoracic microdiscectomy. *J Neurosurg Spine.* 2005;3(6):459-64.

17. Li Y, Oskouian RJ Jr, Day Y-J, Kewrn JA, Linden JM. Evaluation of a compression-derived mouse spinal cord ischemia/reperfusion (SCIR) injury model. *J Neurosurg Spine.* 2006;4(2):165-73.

18. Pouratin N, Oskouian RJ Jr, Jensen ME, Kassell NF, Dumont AS. Endovascular management of unruptured intracranial aneurysms. *J Neurol Neurosurg Psychiatry.* 2006;77:572-578.

19. Li Y, Oskouian RJ Jr, Day YJ, Rieger JM, Liu L, Kern JA, Linden J. Mouse spinal cord compression injury is reduced by either activation of the adenosine a(2a) receptor on bone marrow-derived cells or deletion of the a(2a) receptor on non-bone marrow-derived cells. *Neuroscience.* 2006;141(4):2029-2039.

20. Oskouian RJ Jr, Samii A, Laws ER. The craniopharyngiomas. Pituitary surgery. *Front Horm Res.* 2006;34:256-278.

21. Li Y, Oskouian RJ, Day YJ, Ker Ja, Linden J. Optimization of a mouse locomotor rating system to evaluate compression-induced spinal cord injury: Correlation of locomotor and morphological injury indices. *J Neurosurg Spine.* 2006;4(2):165-173.

22. Oskouian RJ Jr, Kelly DF, Laws ER. Vascular Injury and transsphenoidal surgery. Pituitary surgery. *Front Horm Res.* 2006;34:105-126.

23. Li Y, Oskouian RJ, Shaffrey CI, Day Y-J, Bumpass DB, Roy RJ, Berr SS, Kern JA, Linden J. Novel and reproducible murine spinal cord ischemia/reperfusion injury mode. *Top Spinal Cord Inj Rehabil.* 2006;12(1):1-10.

24. Oskouian RJ Jr, Shaffrey CI. Degenerative lumbar scoliosis. *Neurosurg Clin N Am.* 2006;17(3):299-315, vii.

25. Aslan H, Zilberman Y, Kandel L, Liebergall M, Oskouian RJ Jr, Gazit D, Gazit Z. Osteogenic differentiation of noncultured immunoisolated bone marrow-derived CD105+ cells. *Stem Cells.* 2006;24(7):1728-1737.

26. Oskouian RJ Jr, Shaffrey CI, Whitehill R, Sansur CA, Pouratian N, Kanter AS, Asthagiri AR, Dumont AS, Sheehan JP, Elias WJ, Shaffrey ME. Anterior stabilization of three-column thoracolumbar spinal trauma. *J Neurosurg Spine.* 2006;5(1):18-25.

27. Li Y, Oskouian RJ Jr, Day YJ, Rieger JM, Liu L, Kern JA, Linden J. Mouse spinal cord compression injury is reduced by either activation of the adenosine A2A receptor on bone marrow-derived cells or deletion of the A2A receptor on non-bone marrow-derived cells. *Neuroscience.* 2006;141(4):2029-2039.

28. Elias WJ, Pouratian N, Oskouian RJ, Schrimer B, Burns T. Peroneal neuropathy following successful bariatric surgery. Case report and review of the literature. *J Neurosurg.* 2006;105(4):631-635.

29. Oskouian RJ Jr, Sansur CA, Shaffrey CI. Congenital abnormalities of the thoracic and lumbar spine. *Neurosurg Clin N Am.* 2007;18(3):479-498.

30. Sansur CA, Frysinger RC, Pouratian N, Fu K-M, Bittl M, Oskouian RJ, Laws ER, Elias JW. Incidence of symptomatic hemorrhage after stereotactic electrode placement. *J Neurosurg.* 2007;107(5):998-1003.

31. Jagannathan J, Oskouian RJ, Yeoh K, Dumont AS. Molecular biology of unreresectable meningiomas: Implications for new treatments and review of literature. *Skull Base.* 2008;18(3):173-187.

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33. Jagannathan J, Oskouian RJ Jr, Dumont AS, Shaffrey CI, Jane JA Sr. Radiographic and clinical outcomes following single level anterior cervical diskectomy and allograft fusion without plating or cervical collar. *J Neurosurg Spine.* 2008;8(5):420-428.

34. Hamilton DK, Jones-Quaidoo SM, Sansur C, Shaffrey CI, Oskouian R, Jane JA Sr. Outcomes of bone morphogenetic protein-2 in mature adults: Posterolateral non-instrument-assisted lumbar decompression and fusion. *Surg Neurol.* 2008;69(5):457-461.

35. Furneaux CE, Marshall ES, Yeoh K, Monteith SJ, Mews PJ, Sansur CA, Oskouian RJ, Sharples KJ, Baguley BC. Cell cycle times of short-term cultures of brain cancers as predictors of survival. *Br J Cancer J.* 2008;99(10):1678-1683.

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39. Hussain NS, Hanscom D, Oskouian RJ Jr. Chyloretroperitoneum following anterior spinal surgery. Report of 4 cases. *J Neurosurg Spine.* 2012;17(5):415-421.

40. Ahmadian A, Verma S, Mundis GM Jr, Oskouian RJ Jr, Smith DA, Uribe JS. Minimally invasive lateral retroperitoneal transpsoas interbody fusion for L4-5 spondylolisthesis: clinical outcomes. *J Neurosurg Spine*. 2013 Sep;19(3):314-20.

41. Oskouian RJ Jr, Uribe JS. Introduction: Minimally Invasive Spine surgery: The Greatest Advance in Medicine? *Neurosurg Focus*. 2013 Aug;35(2):Introduction.

42. Chapman JR, Oskouian RJ Jr. Nonoperative care or noncore for thoracolumbar spine fractures? Questioning the unthinkable. *Spine J.* 2014;14(11):2557-64.

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44. Oskouian, RJ Jr, Chapman, JR Cervicothoracic Spine Fractures. *AOSpine* 2015 (6): 57-75.

45. Hussain, NS, Perez-Cruet, MJ, Oskouian RJ Jr. Thoracolumnbar Osteoporosis. *Spinal Instrumentation*, 2nd Ed., Ch 49.

46. Moisi M, Page J, Paulson D, Oskouian RJ. Technical Note - Lateral Approach to the Lumbar Spine for the Removal of Interbody Cages. *Cureus*. 2015 May 11;7(5):e268. doi: 10.7759/cureus.268. eCollection 2015 May.

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49. Bernard S, Loukas M, Rizk E, Oskouian RJ, Delashaw J, Shane Tubbs R. The Human Orbital Bone: Review and Update of its Embryology and Molecular Development. *Childs Nerv Syst*. 2015 Aug 18

50. Youssef P, Loukas M, Chapman JR, Oskouian RJ, Tubbs RS. Comprehensive Anatomical and Immunohistochemical Review of the Innervation of the Human Spine and Joints with Application to an Improved Understanding of Back Pain. *Childs Nerv Syst*. 2015 Aug 18.

51. Aly I, Chapman JR, Oskouian RJ, Loukas M, Tubbs RS. Lumbar Ribs: a Comprehensive Review. *Childs Nerv Syst*. 2015 Sep 9.

52. R. Shane Tubbs, Christina M. Kirkpatrick, Elias Rizk, Joshua J. Chern, Rod J. Oskouian, W. Jerry Oakes. Do the Cerebellar Tonsils Move During Flexion and Extension of the Neck in Patients with Chiari I Malformation? A Radiological Study with Clinical Implications. *Childs Nerv Syst*

53. R. Shane Tubbs, Amin Demerdash, Anthony D'Antoni, Marios Loukas, Charles Kulwin, Rod J. Oskouian, Aaron Cohen-Gadol.Blockage or Sacrifice of the Middle Meningeal Artery May Lead to Hydrocephalus: A Theory with Cadaveric Support and Case Illustration *Childs Nerv Syst*

54. Seleipiri A, Rizk Em, Loukas M, Chapman JR, Oskouian RJ, Tubbs RS. The Odontoid Process: A Comprehensive Review of its Anatomy, Embryology and Variations. *Childs Nerv Syst*. 31

55. Tubbs RS, Demerdash A, Oskouian RJ, Chern J, Oakes WJ. Evolution of cerebellar tonsillar ischemia to cerebellar tonsillar cysts in the Chiari I malformation: radiological, surgical, and histological evidence. *Childs Nerv Syst*.

56. Tubbs RS, Blour M, Singh, R, Lachman N, D'Antoni A, Loukas M, Hattab E, Oskouian RJ. Relationship Between Regional Atherosclerosis and Adjacent Spinal Cord Histology. *Cureus 329*

57. Endoscopic third ventriculostomy: A historical reviewDemerdash A, Rocque BG, Johnston J, Rozzelle CJ, Yalcin B, Oskouian R, Delashaw J, Tubbs RS. Br J Neurosurg. 2016 Oct 22:1-5. PMID: 27774823

58. The Epidural Ligaments (of Hofmann): A Comprehensive Review of the Literature. Tardieu GG, Fisahn C, Loukas M, Moisi M, Chapman J, Oskouian RJ, Tubbs RS. Cureus. 2016 Sep 13;8(9):e779. Review PMID: 27752405

59. Detethering of the C2 nerve root and avoidance of transection and injury during C1 screw placement: A cadaveric feasibility study. Fisahn C, Johal J, Moisi M, Iwanaga J, Oskouian RJ, Chapman JR, Tubbs RS.
World Neurosurg. 2016 Oct 12. pii: S1878-8750(16)30994-9. doi: 10.1016/j.wneu.2016.10.007. PMID: 27744083

60. Innervation of the blood vessels of the spinal cord: a comprehensive review. Montalbano MJ, Loukas M, Oskouian RJ, Tubbs RS. Neurosurg Rev. 2016 Oct 6. Review. PMID: 27709410

61. Cervical fracture from chronic steroid usage presenting as a stroke: A case report. Fisahn C, Moisi MD, Jeyamohan S, Wingerson M, Tubbs RS, Cobbs C, Oskouian RJ, Chapman JR. Int J Surg Case Rep. 2016 Sep 29;28:135-138. doi: 10.1016/j.ijscr.2016.09.042. PMID: 27701004

62. The Chiari 3.5 malformation: a review of the only reported case. Fisahn C, Shoja MM, Turgut M, Oskouian RJ, Oakes WJ, Tubbs RS. Childs Nerv Syst. 2016 Sep 27. Review. PMID: 27679454

63. The superior petrosal sinus: a review of anatomy, embryology, pathology, and neurosurgical relevance.

Mortazavi MM, Cox MA, Saker E, Krishnamurthy S, Verma K, Griessenauer CJ, Loukas M, Oskouian RJ, Tubbs RS. Neurosurg Rev. 2016 Sep 19. Review. PMID: 27647276

64. A history of the autonomic nervous system: part II: from Reil to the modern era. Oakes PC, Fisahn C, Iwanaga J, DiLorenzo D, Oskouian RJ, Tubbs RS. Childs Nerv Syst. 2016 Sep 9. Review. PMID: 27613641

65. A history of the autonomic nervous system: part I: from Galen to Bichat. Oakes PC, Fisahn C, Iwanaga J, DiLorenzo D, Oskouian RJ, Tubbs RS. Childs Nerv Syst. 2016 Sep 9. Review. PMID: 27613639

66. A New Landmark for Localizing the Site of the Subdental Synchondrosis Remnant: Application to Discerning Pathology from Normal on Imaging. Tubbs RS, Kirkpatrick CM, Fisahn C, Iwanaga J, Moisi MD, Hanscom DR, Chapman JR, Oskouian RJ. World Neurosurg. 2016 Aug 30. pii: S1878-8750(16)30780-X. doi: 10.1016/j.wneu.2016.08.096. PMID: 27591099

67. Clinical Anatomy of the Most Common Dementias. Usman S, Oskouian RJ, Loukas M, Tubbs RS. Clin Anat. 2016 Sep 2. doi: 10.1002/ca.22784. Review. No abstract available. PMID: 27588364

68. The Neuroanatomy of Depression: A Review. Oakes P, Loukas M, Oskouian RJ, Tubbs RS. Clin Anat. 2016 Aug 31. doi: 10.1002/ca.22781. Review. PMID: 27576673

69. Auscultation of the heart: The Basics with Anatomical Correlation. Voin V, Oskouian RJ, Loukas M, Tubbs RS. Clin Anat. 2016 Aug 31. doi: 10.1002/ca.22780. Review. PMID: 27576554

70. Hip fractures in the elderly-: A Clinical Anatomy Review. Collin PG, D'Antoni AV, Loukas M, Oskouian RJ, Tubbs RS. Clin Anat. 2016 Aug 31. doi: 10.1002/ca.22779. Review. PMID: 27576301

71. Five Common Clinical Presentations in the Elderly: An Anatomical Review. Collin PG, Oskouian RJ, Loukas M, D'Antoni AV, Tubbs RS. Clin Anat. 2016 Aug 25. doi: 10.1002/ca.22771. PMID: 27560007

72. Lateral Thoracic Osteoplastic Rib-Sparing Technique Used for Lateral Spine Surgery: Technical Note. Moisi M, Fisahn C, Tubbs RS, Page J, Rice R, Paulson D, Kazemi N, Hanscom D, Oskouian RJ. Cureus. 2016 Jul 5;8(7):e668. doi: 10.7759/cureus.668. PMID: 27551648

73. Johann Gaspar Spurzheim (1775-1832) and his contributions to our understanding of neuroanatomy. Sanders FH, Fisahn C, Iwanaga J, Oskouian RJ, Tubbs RS. Childs Nerv Syst. 2016 Jul 30. No abstract available. PMID: 27476037

74. George J. Garceau (1896-1977) and the first introduction of the "filum terminale syndrome". Saker E, Cox M, Loukas M, Oskouian RJ, Tubbs RS. Childs Nerv Syst. 2016 Jul 30. No abstract available. PMID: 27476036

75. The Italian Giuseppe Muscatello (1866-1951) and his contributions to our understanding of childhood spina bifida aperta and occulta. Tardieu GG, Loukas M, Fisahn C, Shoja MM, Oskouian RJ, Tubbs RS. Childs Nerv Syst. 2016 Jul 28. No abstract available. PMID: 27469456

76. Bergmann's ossicle (ossiculum terminale persistens): a brief review and differentiation from other findings of the odontoid process. Johal J, Loukas M, Fisahn C, Oskouian RJ, Tubbs RS. Childs Nerv Syst. 2016 Sep;32(9):1603-6. doi: 10.1007/s00381-016-3199-7. Review. PMID: 27465675

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Johal J, Loukas M, Fisahn C, Chapman JR, Oskouian RJ, Tubbs RS. Childs Nerv Syst. 2016 Jul 23. Review. PMID: 27449768

78. The ancient Syrian physician Archigenes and his contributions to neurology and neuroanatomy. Montalbano MJ, Sharma A, Oskouian RJ, Loukas M, Tubbs RS. Childs Nerv Syst. 2016 Jul 23. No abstract available. PMID: 27449767

79. Venous air embolus during prone cervical spine fusion: case report. Cruz AS, Moisi M, Page J, Shane Tubbs R, Paulson D, Zwillman M, Oskouian R, Lam A, Newell DW. J Neurosurg Spine. 2016 Jul 22:1-4. PMID: 27448172

80. The intriguing history of vertebral fusion anomalies: the Klippel-Feil syndrome. Saker E, Loukas M, Oskouian RJ, Tubbs RS. Childs Nerv Syst. 2016 Sep;32(9):1599-602. doi: 10.1007/s00381-016-3173-4. Review. PMID: 27444288

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83. Unilateral Laminotomy with Bilateral Spinal Canal Decompression for Lumbar Stenosis: A Technical Note. Moisi M, Fisahn C, Tkachenko L, Tubbs RS, Ginat D, Grunert P, Jeyamohan S, Reintjes S, Ajayi O, Page J, Oskouian RJ, Hanscom D. Cureus. 2016 May 27;8(5):e623. doi: 10.7759/cureus.623. PMID: 27433402

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85. Variations of the accessory nerve: anatomical study including previously undocumented findings-expanding our misunderstanding of this nerve. Tubbs RS, Ajayi OO, Fries FN, Spinner RJ, Oskouian RJ. Br J Neurosurg. 2016 May 24:1-3. PMID: 27216244

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89. Enigmatic human tails: A review of their history, embryology, classification, and clinical manifestations.

Tubbs RS, Malefant J, Loukas M, Jerry Oakes W, Oskouian RJ, Fries FN. Clin Anat. 2016 May;29(4):430-8. doi: 10.1002/ca.22712. PMID: 26990112

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Manuscripts Submitted for Publications

1. *The Atlas: A Comprehensive Review of Its Molecular Development, Embryology, Comparative Anatomy and Variations* R. Shane Tubbs, Olaide O. Ajayi, Sloan Dickerson, Jens R. Chapman, Rod J. Oskouian. Childs Nerv Syst

2. *The Vertebral Artery Cave at C2: Anatomical Study with Application to C2 Pedicle Screw Placement* R. Shane Tubbs, Andre Granger, Marios Loukas, Marc Moisi, David Paulson, Shiveindra Jeyamohan, Jens R. Chapman, Rod J. Oskouian Spine Journal

3. *Craniocervical Dissociation in the Pediatric Population: Do Children Have Better or Worse Outcomes than Adults? A Narrative Review* R. Shane Tubbs, Chirag Patel, Marios Loukas, Rod J. Oskouian, Jens R. Chapman. Childs Nerv Syst

4. *Extraforaminal Compression of the L5 Nerve: An Anatomical Study with Application to Failed Posterior Decompressive Procedures* R. Shane Tubbs, Islam Aly, Marc D. Moisi, David R. Hanscom, Jens R. Chapman, Marios Loukas, Rod Oskouian. Spine Journal

5. *Intracranial Connections of the Vertebral Venous Plexus: Anatomical Study with Application to Neurosurgical and Endovascular Procedures at the Craniocervical Junction* R. Shane Tubbs, Amin Demerdash, Marios Loukas, Joel Curé, Rod J. Oskouian, Shaheryar Ansari, Aaron A. Cohen-Gadol. Neurosurgery

6. *Mapping the Internal Anatomy of the Lateral Brainstem: Anatomical Study with Application to Far Lateral Approaches to Intrinsic Brainstem Tumors* R. Shane Tubbs, Andre Granger, Payman Vahedi, Marios Loukas, Rod J. Oskouian, Johnny Delashaw, W. Jerry Oakes. Childs Nerv Syst

7. *Relationship of the Lumbar Plexus Branches to the Lumbar Spine: Anatomical Study with Application to Lateral Approaches* R. Isaiah Tubbs, Brandon Gabel, Shiveindra Jeyamohan, Marc Moisi, Jens R. Chapman, R. David Hanscom, Marios Loukas, Rod J. Oskouian, R. Shane Tubbs. Spine Journal

8. *Variations of the Accessory Nerve: Anatomical Study Including Previously Undocumented Findings-Expanding our Misunderstanding of this Nerve* R. Shane Tubbs, Olaide O. Ajayi, Robert J. Spinner, Rod J. Oskouian. Brit J Neurosurg

9. *Endoscopic Third Ventriculostomy: A Historical Review* Amin Demerdash, Brandon G. Rocque, James Johnston, Curtis J. Rozzelle, Rod J. Oskouian, Johnny Delashaw, R. Shane Tubbs. Brit J Neurosurg

10. *Enigmatic Human Tails: A Review of their History, Embryolgy and Classification* R. Shane Tubbs, Marios Loukas, Jason Malefant, Rod J. Oskouian. Clin Anat

11. *A New Landmark for Localizing the Site of the Subdental Synchondrosis Remnant: Application to Discerning Pathology from Normal on Imaging* R. Shane Tubbs, Christina M. Kirkpatrick, Marc D. Moisi, David R. Hanscom, Jens R. Chapman, Rod J. Oskouian. Spine

12. *Arterial Variations in the Territory of the Atlas: A Comprehensive Review* Galyna Ivashchuk, Marios Loukas, David Paulson, Stephen J. Monteith, Jens R. Chapman, Rod J. Oskouian, R. Shane Tubbs. Spine

13. *A Novel Method of Lengthening the Accessory Nerve for Anterior Neurotization and Primary Repair Procedures* R. Shane Tubbs, Yolanda Stoves, Rong Li, Rod J. Oskouian, Robert Spinner. Neurosurg

Articles in Preparation

1. Complications of sacroiliac screw placement
2. Notochord remnants in the apical ligament
3. Trabecular patterns of the atlas
4. Internal morphology of the odontoid process
5. Movement of the dens in flexion and extension of the cervical spine
6. Ectopic dorsal root ganglion cells
7. Anatomical study of the iliolumbar ligament
8. Landmarks for the lumbosacral trunk
9. Landmarks for the lumbar sympathetic trunk
10. Immunohistochemistry of the nuchal ligament
11. New theory of os odontoideum formation
12. C2 pedicle screw teaching model
13. Redefining the odontoid process
14. The sacroiliac ligaments: a Review
15. A new finding of the spinal dura mater
16. A new finding of the sinuvertebral nerves
17. Lumbar tropism: a review
18. Coronal imaging of the Chiari I malformation
19. The falciform ligament and relation to the optic nerve
20. Intracranial arteries that pierce cranial nerves: a review

Book Chapters

1. Bhattacharjee S, Oskouian RJ Jr, Shaffrey CI. Fixed versus flexible deformity. In: Henry RF, Albert TJ, eds. *Spinal Deformity: The Essentials*. New York, NY: Thieme Medical Publishers; 2007.

2. Oskouian RJ, Sansur CA, Shaffrey I. Posterior correction of thoracolumbar deformity. In: Mummaneni P, Lenke LG, Haid RW Jr, eds. *Spinal Deformity: A Guide to Surgical Planning and Management.* St. Louis, MO*:* Quality Medical Publishing; 2008.

3. Battacharjee S, Oskouian RJ, Shaffrey CI. Lumbar pedicle subtraction osteotomy. In: Mummaneni P, Lenke LG, Haid RW Jr, eds. *Spinal Deformity: A Guide to Surgical Planning and Management*. St. Lous, MO: Quality Medical Publishing, Inc; 2008.

4. Okonkwo D, Oskouian RJ, Shaffrey CI. Management of cervical spine injuries. In: Jallo J, Vaccaro AR, eds. *Neurotrauma and Critical Care of the Spine*. New York, NY: Thieme Medical Publishers; 2008.

5. Jagannathan J, Oskouian RJ, Jr, Pouratian N, Jane JA, Jr, Laws ER, Vance MA, Sheehan JP. Sterotactic radiosurgery for pituitary adenomas. In: Lunsford LD, Sheehan JP, eds. *Intracranial Sterotactic Radiosurgery*. New York, NY: Thieme Medical Publishers; 2009.

6. Crowley RW, Yeoh HK, McKisic MS, Oskouian RJ Jr, Dumont AS. Osteoporotic fractures: Evaluation and treatment with vertebroplasy/kyphoplasty. In: Winn HR, ed. *Youmans Neurological Surgery.* 6th ed. St. Louis, MO: Elsevier Saunders; 2012.

7. Hamilton DK, Oskouian RJ Jr, Shaffrey CI. Flat back and sagittal plan deformity. In: Winn HR, ed. *Youmans Neurological Surgery.* 6th ed. St. Louis, MO: Elsevier Saunders: 2012.

Books in Preparation

1. *The Intracranial Venous Sinuses: Anatomy, Embryology, Imaging, Pathology and Surgery* R. Shane Tubbs, Mohammadali M. Shoja, Marios Loukas, Steven J. Monteith, Rod J. Oskouian, Johnny Delashaw

2. *The Lumbar Plexus: Anatomy, Comparative Anatomy, Embryology, and Surgical Approaches* Tubbs RS, Chapman JR, Oskouian RJ

Other Publications

1. Oskouian RJ Jr. Spinal Cord Abscess: eMedicine. eMedicine Web Site. http://emedicine.medscape.com/article/248030-overview. Published 2009.

2. Oskouian RJ Jr. Spinal Hematoma: eMedicine Neurosurgery. eMedicine Web Site. http://emedicine.medscape.com/article/247957-overview. Published 2009.

3. Oskouian RJ Jr, Sansur CA, O'Brien M, Shaffrey CI. Untreated Late-onset Idiopathic scoliosis and revision surgery in adults. Harms Study Group Book Project, Depuy Spine

Invited Presentations

1. Oskouian RJ Jr. Avoiding complications in lateral spine surgery. Presented at: John Jane Society Annual Meeting. October 4-6, 2012; Charlottesville, VA.

2. Oskouian RJ Jr. Lateral approaches for deformity-lengthening the spine versus shortening. Presented at: The 18th Spine Workshop, The Chinese University of Hong Kong. October 13-15, 2012; Hong Kong, China.

3. Oskouian RJ Jr. Complication avoidance in lateral surgery. Presented at: The 18th Spine Workshop, The Chinese University of Hong Kong. October 13-15, 2012; Hong Kong, China.

4. Oskouian RJ Jr. Lateral Spine Surgery. Presented at the 9th Annual Mazama Spine Summit. February 7-10, 2013; Winthrop, WA.

5. Oskouian RJ Jr. Cadaveric Lab Session. Presented at the 4th Spine Deformity Solutions: A Hands-On Course. April 9-11, 2015; Houston, TX.

6. Oskouian RJ Jr. MIS Deformity Correction & MIS techniques for maximizing lumbar lordosis. Presented at 22nd Scoliosis Research Society (SRS) International Meeting on Advanced Spine Techniques - IMAST 2015. July 8-11, 2015; Kuala Lumpur, Malaysia.

7. Oskouian RJ Jr. Special Course: SOLAS: Advanced Lateral Access Challenges and solutions: A Case Based Approach & the Latest and Greatest in Spine Navigation. Presented & Moderated at the 32nd Annual

Meeting of the Section on Disorders of the Spine and Peripheral Nerves Spine Summit 2016. March 16-19, 2016: Orlando, Florida.

Active Studies

1. Stand-Alone Cage versus Conventional ACDF.
    - Principle Investigator
    - IRB Number: 5929S-16
2. Unplanned Reoperation after Intradural Spinal Tumor Resection.
    - Principle Investigator
    - IRB Number: 5898S-15
3. Duraseal Exact Spine Sealant System: Post Approval Study.
    - Primary Investigator
    - IRB Number: 5684W-14
    - Protocol Number: COV-DRSS--0002
4. SNI Frality Index Study: A prospective evaluation of the influence of patient frailty and their eventual disposition.
    - Primary Investigator
    - Protocol in Progress with IRB
5. RISCIS: The effect of Riluzole on outcomes of acute spinal cord injury
    - Primary Investigator
    - IRB Number: 5910W-15
    - Protocol Number: SPN-12-001
6. I-Spondi: An assessment of outcomes of surgical treatment of isthmic spondylolistheses.
    - Primary Investigator
    - Protocol in Progress with IRB
7. Neurologically controlled intrinsic neuromuscular feedback therapy in the treatment of incomplete spinal cord disease: A pilot study using the HAL system.
    - Primary Investigator
    - Protocol in Progress with IRB
8. Stand-Alone Cervical Fusion Cage Systems: Long Term Results and Complications
    - Sub Investigator
    - IRB Number: 5618S-14
9. Osteocel Bone Grafting Results in Spinal Fusions: Long Term Review of Outcomes and Complications
    - Sub Investigator
    - IRB Number: 5619S-14
10. Spinal Fusion With Local Boneback Autograft: Preliminary Clinical Results and Cost Analysis Retrospective Chart Review
    - Sub Investigator
    - IRB Number: 5405S-13
11. Lateral Spine Interbody Fusion: Long Term Results and Complications
    - Sub Investigator
    - IRB Number: 5302S-12

Washington State Health Care Authority

Agency medical director comments

Artificial Disc Replacement

Gary Franklin, MD, MPH
Medical Director
Washington State Department of Labor & Industries
January 20, 2017

Background – Lumbar ADR

- Degenerative Disc Disease (DDD) may be a somatic pain source in the lumbar spine
- Treatments for symptomatic DDD may include medications, PT, intensive rehabilitation program, spinal fusion and ADR
- The HTCC reviewed the evidence of lumbar fusion in 2016 and concluded that fusion is not more effective, is less safe and is more costly than an intensive rehabilitation program. Fusion is not covered for DDD uncomplicated by comorbidities
- ADR has been intended as an alternative surgical approach, but it is not better than lumbar fusion for treating lumbar DDD

2

Background – Lumbar ADR (cont.)

The HTCC reviewed the short-term evidence of lumbar ADR available in 2008 and determined that L-ADR is a covered benefit for patients who meet FDA approved indications for use

- **Lumbar ADR**
  - Patients must first complete a structured, intensive, multi-disciplinary program for management of pain, if covered by the agency;
  - Patients must be 60 years or under;
  - Patients must meet FDA approved indications for use and not have any contra-indications. FDA approval is device specific but includes:
    - Failure of at least six months of conservative treatment
    - Skeletally mature patient
    - Replacement of a single disc for degenerative disc disease at one level confirmed by patient history and imaging

The effectiveness and safety of the procedure remain a concern due to the lack of long-term evidence. Some mid-term evidence of L-ADR has become available

3

Background – Cervical ADR

- Surgery may be indicated when non-operative conservative treatments fail to prevent neurologic progression.
- ACDF is a surgical option for the treatment of radiculopathy or myelopathy as a result of central or paracentral disc herniations, or osteoarthritis of the facet or uncovertebral joint.

4

Background – Cervical ADR

- In 2008, HTCC reviewed the topic and determined cervical ADR is a covered benefit when patients meet FDA approved indications for use
  - Cervical ADR
    - Patients must meet FDA approved indications for use and not have any contra-indications. FDA approval is device specific but includes:
      - Skeletally mature patient
      - Reconstruction of a disc following single level discectomy for intractable symptomatic cervical disc disease (radiculopathy or myelopathy) confirmed by patient findings and imaging.
    - Artificial Disc Replacement FDA general contra-indications

5

Background – Cervical ADR

- Since 2008, a total of eight ADR devices were approved by the FDA. The effectiveness and safety of the procedure remain a concern due to the lack of long-term evidence.
- In 2013, the FDA approved a device for 2-level arthroplasty. The Mobi- C cervical disc prosthesis is intended to replace two adjacent cervical discs (from C3-C7).
- Now some mid-term evidence of ADR has become available.

6

Agency Medical Director Concerns

- Safety = Medium/High
- Efficacy = High
- Cost = Medium

7

Current State Agency Policy

PEBB	Covered; requires PA
Medicaid FFS and Managed Care	Covered; requires PA
Labor and Industries	Covered; requires PA
Dept. of Corrections	Covered; requires PA

8

Agency Utilization and Cost

Count of Cervical and Lumbar Procedures	2013		2014		2015	
	Cervical	Lumbar	Cervical	Lumbar	Cervical	Lumbar
PEBB/UMP	7	0	8	0	11	0
LNI	41	9	36	10	36	5
Medicaid MCO	6	2	24	1	33	4
Medicaid FFS	1	0	2	0	2	0

Total Dollars Paid and Average Paid Per Procedure

Measure	Total Paid Dollars 2013 - 2015	2013		2014		2015	
		Paid dollars	Paid/ Procedure	Paid dollars	Paid/ Procedure	Paid dollars	Paid/ Procedure
PEBB/UMP	$561,688	$176,125	$25,161	$150,815	$18,852	$234,748	$21,341
LNI	$1,783,520	$796,686	$15,934	$551,033	$11,979	$435,801	$11,778
Medicaid MCO[b]	$628,064	$44,747	$5,593	$158,217	$6,329	$428,100	$11,570
Medicaid FFS	$22,676	$2,286[a]	$2,286	$14,802	$7,401	$6,398	$3,199

9

Key Questions

- What is the evidence of efficacy and effectiveness of ADR compared with comparative therapies (including non-operative therapy; spinal fusion; other surgery)?
- What is the evidence related to the ADR safety profile? (including device failure, reoperation)
- What is the evidence of differential efficacy or safety issues amongst special populations (including but not limited to the elderly and workers compensation populations)?
- What are the cost implications and cost effectiveness for ADR?

10

Effectiveness of Lumbar ADR

- Lumbar ADR appears to be comparable to lumbar fusion in the short-term and the mid-term (24 – 60 months) based on low quality evidence.
- However, the efficacy of the comparator - lumbar fusion, is not established as compared with non-operative care for degenerative disc disease.
- The HTCC reviewed the evidence of lumbar fusion in 2016 and concluded that fusion is no better than an intensive rehabilitation program, and is not covered for DDD uncomplicated by comorbidities.

11

Effectiveness of Lumbar ADR (cont.)

- Lumbar ADR vs. multidisciplinary rehabilitation *(Hellum 2011)*
  - Though ADR appears to result in greater improvement in ODI than intensive rehabilitation (-8.4), it didn't exceed the pre-specified minimally important clinical difference (10 points).
  - Randomization procedure still left imbalance in baseline factors with greater pain and more sick leave in rehab group
  - There was no difference in return to work, SF-36 mental component score, EQ-5D, fear avoidance beliefs, Hopkins symptom check list, drug use, and the back performance scale.
- High risk of surgery; substantial amount of improvement experienced by the rehabilitation group;

12

Effectiveness of Lumbar ADR (cont.)- Return to Work

Study	F/U	L-ADR % (n/N)	Fusion %(n/N)
Work status: proportion of patients working **full-time**			
Charite IDE trial (Blumenthal 2005)	0 months	44.9% (92/205)	49.5% (49/99)
	24 months	55.9% (104/186)	52.5% (42/80)
Work status: proportion of patients working **part-time**			
Charite IDE trial (Blumenthal 2005)	0 months	8.3% (17/205)	8.1% (8/99)
	24 months	6.5% (12/186)	12.5% (10/80)

13

Safety of Lumbar ADR

- The risks of lumbar ADR are real
- Lumbar ADR vs. multidisciplinary rehabilitation *(Hellum et al 2011)*
  - 34% of L-ADR recipients experienced at least one complication
    (e.g., intimal lesion in left common iliac artery, arterial thrombosis of dorsalis pedis artery, and sensory loss at two follow-up.)
  - The complications resulted in impairment in 8% of L-ADR patients at two year follow-up
  - 6.5% reoperation rate at the index level.

14

Long-term Safety and Longevity of ADR

- The long-term outcomes of patients with a lumbar disc arthroplasty need to be followed carefully.
- The longevity of an artificial lumbar disc is not known
- A revision lumbar arthroplasty may be more difficult and risky than the initial surgery because of intraabdominal scar formation and adhesion of the great vessels.

Inamasu J and Guiot BH. 2006. Vascular injury and complication in neurological spine surgery. Acta Neurochir 148: 375-387

15

Cost-Effectiveness of Lumbar ADR

- Lumbar ADR vs. Fusion
  - No evidence for 1-level or 2-levels
  - Inconsistent evidence for mixed levels: results across the two moderate quality studies are mixed with regard to the cost-effectiveness of L-ADR versus fusion.
- Lumbar ADR vs. Rehabilitation
  - Inconsistent evidence: one cost-effectiveness analysis suggests that L-ADR may be a cost effective alternative to rehabilitation given a willingness to pay greater than $49,132 based on utilities derived from the EQ-5D. The same was not true with SF-6D was used.

16

Evidence for Cervical ADR

- The quality of evidence for Cervical ADR is better than that for lumbar ADR
- C-ADR appears to be superior or comparable to ACDF in both effectiveness and safety at 24, 24-36 and 48-60 months.
- C-ADR may be more cost-effective than ACDF.

17

National Coverage Decision (NCD)

- The CMS has a National Coverage Decision (NCD) for L-ADR but not C-ADR
- For services performed on or after August 2007, CMS has found that L-ADR is not reasonable and necessary for the Medicare population over 60 years of age; therefore, L-ADR is non-covered for Medicare beneficiaries over 60 years of age.
- For Medicare beneficiaries age 60 and younger, there is no NCD for L-ADR.

18

Agency Medical Director Recommendations

Lumbar

- Artificial disc replacement is **not covered** for degenerative disc disease

Cervical

- Artificial disc replacement **is covered** for treatment of degenerative disc disease resulting in cervical radiculopathy or myelopathy when patients meet 2013 HTCC criteria for ACDF
- Cervical ADR **is not covered** for chronic neck pain without evidence of radiculopathy or myelopathy.
- Cervical ADR **is covered** for a two level FDA approved device when radiculopathy or myelopathy is demonstrated by objective evidence of radiculopathy or myelopathy at both levels

19

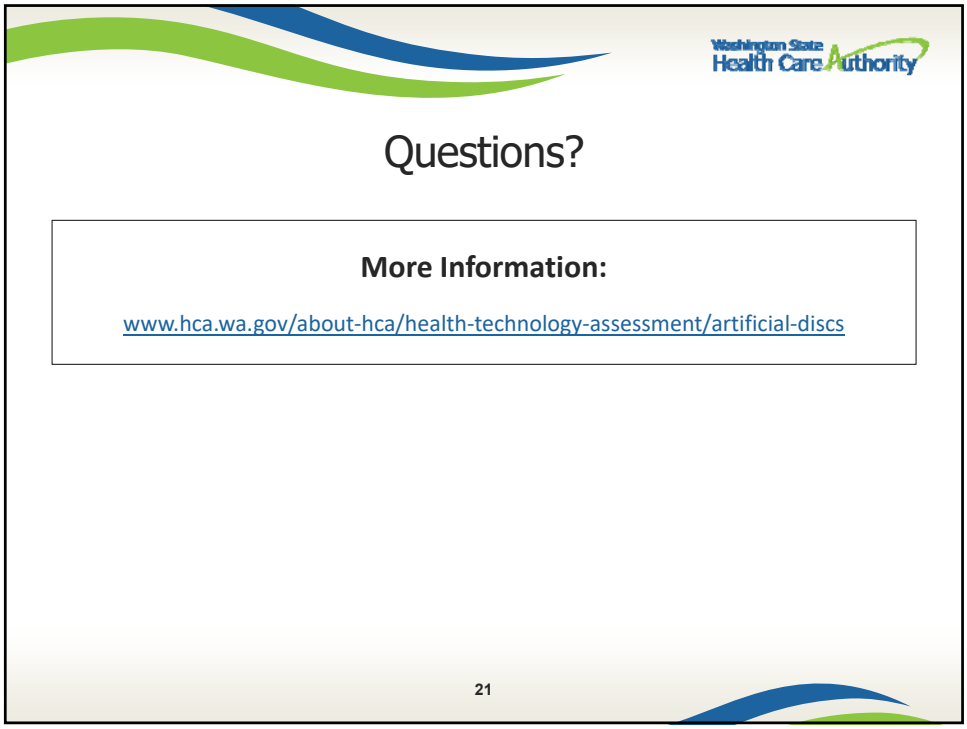
2013 HTCC ACDF Decision

HTCC Reimbursement Determination: Limitations of Coverage Cervical Spinal Fusion is covered when the following conditions are met:

1. Patients with signs and symptoms of radiculopathy; and
2. Advanced imaging evidence of corresponding nerve root compression; and
3. Failure of conservative (non-operative) care.

Non-Covered Indicators: Cervical Spinal Fusion is not a covered benefit for neck pain without evidence of radiculopathy or myelopathy.

20


Washington State Health Care Authority
Questions?
More Information:
www.hca.wa.gov/about-hca/health-technology-assessment/artificial-discs
21

Washington State Health Care Authority

Order of scheduled presentations:

Artificial disc replacement – re-review

	Name
1	Jens Chapman, MD
2	Daniel Elskens, MD
3	Catherine Hill, Senior Manager, Regulatory Affairs, American Association of Neurological Surgeons / Congress of Neurological Surgeons

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000.		
2.	Equity interests such as stocks, stock options or other ownership interests.		
3.	Status or position as an officer, board member, trustee, owner.		
4.	Loan or intellectual property rights.		
5.	Research funding.		
6.	Any other relationship, including travel arrangements.		↓

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		X

If yes to #7, provide name and funding Sources: _____

*If you believe that you do not have a conflict, but are concerned that it may appear that you do, you may **attach additional sheets** explaining why you believe that you should not be excluded.*

I certify that I have read and understand this Conflict of Interest form and that the information I have provided is t[redacted] this date.

X [redacted] 3/17 Jens F. Chapman

Signature *Date* *Print Name*

So we may contact you regarding your presentation, please provide the following:

Email Address: Jens.Chapman@Swedish.org

Phone Number: (206) 320-3373

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000.		✓
2.	Equity interests such as stocks, stock options or other ownership interests.		✓
3.	Status or position as an officer, board member, trustee, owner.		✓
4.	Loan or intellectual property rights.		✓
5.	Research funding.		✓
6.	Any other relationship, including travel arrangements.		✓

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

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	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		✓

If yes to #7, provide name and funding Sources: _____

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*If you believe that you do not have a conflict, but are concerned that it may appear that you do, you may **attach additional sheets** explaining why you believe that you should not be excluded.*

I certify that I have read and understand this Conflict of Interest form and that the information I have provided is true, complete, and correct as of this date.

X [redacted] 1/5/2016 Daniel P. Elskens, M.D.

Signature *Date* *Print Name*

So we may contact you regarding your presentation, please provide the following:

Email Address: [redacted]

Phone Number: [redacted]

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000.	X	
2.	Equity interests such as stocks, stock options or other ownership interests.		X
3.	Status or position as an officer, board member, trustee, owner.		X
4.	Loan or intellectual property rights.		X
5.	Research funding.		X
6.	Any other relationship, including travel arrangements.		X

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

No conflicts with device or companies.
Full time staff with the Am. Assoc. of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) DC office as Senior Manager for Regulatory Affairs

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).	X	

If yes to #7, provide name and funding Sources:

full time staff with AANS/CNS Washington DC office.

If you believe that you do not have a conflict, but are concerned that it may appear that you do, you may ***attach additional sheets*** *explaining why you believe that you should not be excluded.*

I certify that I have read and understand this Conflict of Interest form and that the information I have provided is true, complete, and correct as of this date.

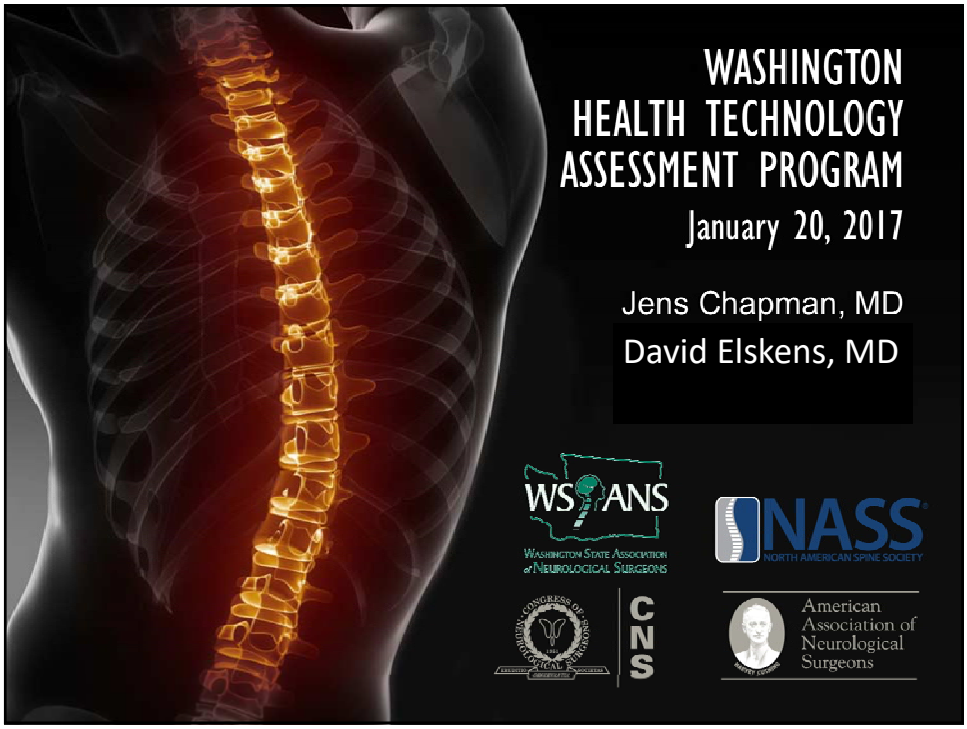
X [redacted] 1/3/17 Catherine J. Hill

Signature *Date* *Print Name*

So we may contact you regarding your presentation, please provide the following:

Email Address: chill@neurosurgery.org

Phone Number: 202-446-2026



Purpose of re-review

- "selected for re-review based on new literature identified which may invalidate aspects of the previous 2008 report "

Key Questions

1: Efficacy of ADR over comparative therapy

2: Safety profile for ADR

3: Differential efficacy or safety in special populations

4: Cost effectiveness of ADR

Cervical ADR

Since 2008,

- 8 additional RCTs for 1-level, CDR vs ACDF
- 2 RCT for 2-level, CDR vs ACDF
- 0 RCT for CDR vs rehab

Lumbar ADR

Since 2008,

0 addition RCTs for 1-level, LDR vs fusion

1 RCT for 2-level, LDR vs fusion

1 RCT for LDR vs rehab

Re-review of CDR warranted

- Numerous new RCTs, including RCTs addressing key questions that had not had any evidence in 2008
- New technology since 2008 in CDR devices

CDR results

- Benefit (moderate-low) of CDR over ACDF for both 1- and 2-level cases in terms of efficacy and safety
- Cost effectiveness was greater with CDR over ACDF, especially for 2-level cases

Re-review of LDR unwarranted

- No new RCT since 2008 to suggest change in coverage needed
  - No demonstration of lack of effectiveness
  - Safety profile unchanged even with longer-term followup
  - No additional adverse events

Re-review of LDR unwarranted

- When comparing LDR vs rehab (new since 2008)
  - Improvement in efficacy over rehab
    - Change in ODI > 15, improvement in VAS
    - Cost effective compared to rehab with EQ-5D analysis

LDR Safety Data

- Complication rate data from 5 studies, encompassing 1525 patients (1025 LDR, 500 fusion)
  - 5.8% complication rate in LDR
  - 10.8% complication rate in fusion group
  - 5.2% reoperation rate in LDR
  - 6% reoperation rate in fusion group

Comparison of artificial total disc replacement versus fusion for lumbar degenerative disc disease: a meta-analysis of randomized controlled trials
Wei, J., Song, Y., Sun, L. et al. International Orthopaedics (SICOT) (2013) 37: 1315.

Conclusion

- C-ADR offers advantages over ACDF for both 1- and 2-level cases
- L-ADR evidence is overall unchanged since 2008, and continues to demonstrate equivalence to lumbar fusion
  - Only new study comparing L-ADR to nonoperative rehab demonstrated advantage for L-ADR

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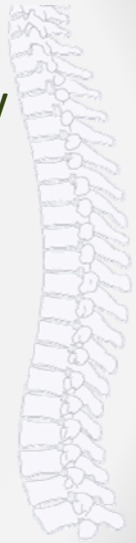
Safety of LDR Study (Meta-analysis)

- Comparison of artificial total disc replacement versus fusion for lumbar degenerative disc disease: a meta-analysis of randomized controlled trials. Wei, J., Song, Y., Sun, L. et al. International Orthopaedics (SICOT) (2013) 37: 1315.

Artificial Disc Replacement: Re-Review

Presentation to
Washington State Health Care Authority
Health Technology Clinical Committee
Andrea C. Skelly, PhD, MPH
January 20, 2017



Report prepared by:
Robin E. Hashimoto, PhD
Andrea C. Skelly, PhD, MPH
Erika D. Brodt, BS
Mark Junge, BS

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Update to 2008 HTA

2008 Report: Lumbar and cervical artificial disc replacement (ADR) (arthroplasty)

- 2 RCTs comparing L-ADR vs. fusion to a maximum of 24 months for single-level DDD; 2 FDA approved devices
- 5 RCTs comparing C-ADR vs. ACDF to 24 months for single-level DDD; only 2 FDA approved devices

Since the 2008 report:

- New FDA approved devices (C-ADR)
- FDA approval for expansion of C-ADR to 2 levels (1 device)
- Longer term follow-up for earlier RCTs of L-ADR and C-ADR
- New evidence comparing L-ADR with non-operative treatment
- Additional RCTS comparing C-ADR with ACDF

An update was commissioned to systematically review and evaluate:

- Longer term evidence on FDA-approved devices
- Impact of new RCT evidence, new devices, new comparators
- New cost-effectiveness studies

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Background

Disease Burden

- Low back pain is the leading cause of pain and disability in adults in the United States (~2.4 million at any given time)
  - 25%-58% of cases resolve spontaneously with conservative care
- Neck pain is also prevalent, with ~15-20% of adults reporting ≥1 episode each year.
  - Cervical spine surgery has increased significantly since 2002 (~307,188 procedures between 2002 and 2011)
- Degenerative disc disease (DDD) may cause pain
- Surgery (e.g., fusion, ADR) may be considered in cases refractory to conservative treatment ; 10%-20% with lumbar DDD, up to 30% with cervical DDD may be unresponsive to conservative treatment

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Background: DDD

Spondylosis

- Umbrella term describing spinal degeneration; natural consequence of aging:
  - Degenerative disc disease (DDD)
  - Spinal stenosis
  - Herniated disc
  - Osteoarthritis
- May cause low back or neck pain
- May result in *radiculopathy* (peripheral nerve root impingement) or *myelopathy* (compression of spinal cord)
- Over 90% of spinal procedures are performed because of DDD

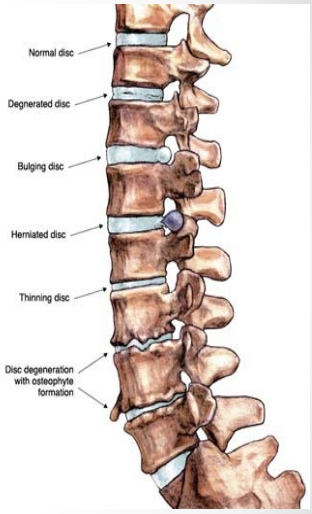

Image: www.spineuniverse.com

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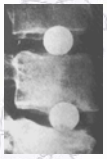
SRI

Background

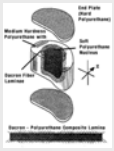
- Over 50 years of research into artificial disc replacement
- Early attempts to replace nucleus
  - Methyl-acrylic into disc space (1955-Cleveland)
  - Self-curing silicone (1962-Nachemson)
  - Swedish Ball Bearings (1964- Fernström)
  - Research continues in nucleus replacement

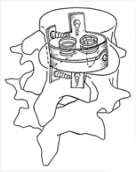


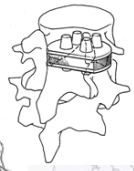
SRI

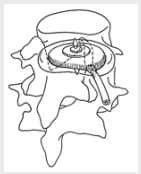
Background

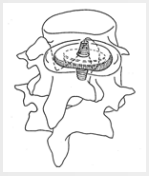
- Early attempts to replace entire disc
  - Numerous design types
    - Hinged
    - Spring loaded
    - Low friction sliding surfaces
    - Constrained fluid filled chambers
    - Elastic disc prostheses











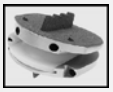
SRI

Contemporary L-ADR Designs

Current FDA-approved

- InMotion (formlerly SB Charité, DePuy Spine, Raynham, MA)

- ProDisc-L (also called ProDisc II, Synthes, Paoli, PA)



- Activ-L (Aesculap Implant Systems, Center Valley, PA)

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SRI

Contemporary C-ADR Designs

Current FDA approved (6)

- Prestige ST and Prestige LP (Medtronics, Memphis, TN
- Prodisc-C (Synthes, Paoli, PA)

- Secure-C (Globus Medical, Audubon, PA)

- Mobi-C 1-level, Mobi-C 2-level (LDR Spine, Austin, Tx)
- PCM (NuVasive, San Diego, CA),

- Bryan disc (Medtronics, Memphis, TN)

Current IDE trial

- Discover (DePuy Spine, Raynham, MA)

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FDA Indications, Contraindications: C-ADR

Indications

- Skeletally mature
- Single-level SCDD in C3-C7; Consecutive 2-levels for Mobi-C 2-level; radiculopathy and/or myelopathy, radiographic evidence
- Progressive symptoms despite non-operative care
- Failure 6 weeks non-surgical care (except ProDiscCT, Prestige LP)

Contraindications

- Infection (systemic, site of implantation), osteoporosis, osteopenia (except Prestige CT), allergy/sensitivity to components (except ProDisc-C)
- Severe spondylolisthesis (ProDisc-C, Prestige LP, Secure C); moderate to advanced for Bryan
- Cervical instability (except Prestige CT, Mobi-C 2-level, Bryan); Spinal stenosis (PCM)

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FDA Indications, Contraindications: L-ADR

Indications

- Skeletally mature
- Confirmed single-level DDD
- ≤ Grade1 spondylolisthesis (Prodisc-L, Activ-L); ≤ 3 mm (Charité)
- No relief from pain after 6 months of non-surgical care

Contraindications

- Infection (systemic, site of implantation), osteoporosis, osteopenia, allergy/sensitivity to components,
- Charité, Prodisc-L: bony lumbar spinal stenosis, pars defect
- Prodisc-L: Isolated radicular compression, trauma-related vertebral body compromise, lytic or > grade 1 spondylolisthesis; endplate smaller than 34.5 mm

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ADR – Key Questions

1. What is the evidence of efficacy and effectiveness of ADR compared with comparative therapies?
2. What is the evidence related to the ADR safety profile? (including device failure, reoperation)
3. What is the evidence of differential efficacy or safety issues amongst special populations?
4. What are the cost implications and cost effectiveness for ADR?

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PICO Scope: Inclusion Criteria

Population

- **Lumbar**: primary L-ADR for DDD without neurological compromise or prior surgery at instrumented level
- **Cervical:** primary C-ADR for DDD with radiculopathy or myelopathy without prior surgery at instrumented level

Intervention

- Lumbar or cervical ADR with FDA approved device or phase III device with ≥ 1 year of follow-up.

Comparator(s)

- Non-operative care, fusion, other spine surgery

Study design

- RCTs, observational studies (concurrent controls), full economic studies published subsequent to 2008 report ; focus on studies with least potential for bias

Publication

- Full-length studies published in English in peer-reviewed journals, FDA reports (no meeting abstracts, proceedings)

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Outcomes

- **Efficacy and Safety**
  - Primary: (studies must report at least one)
    - Function/disability (overall clinical success, ODI (L-ADR), NDI (C-ADR); focus on "success"
    - Pain reduction
    - Device failure (re-op at index level including revision, reoperation or removal)
    - Complications
  - Secondary:
    - Quality of life
    - Symptomatic adjacent segment disease (e.g. Surgery at index level)
- **Economic:**
  - Cost-effectiveness outcomes (e.g. ICER)

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Appraisal of *Individual Studies* – Risk of Bias (Appendix D, E)

Risk of Bias Description	Studies of Therapy	
	Study design	**Criteria**
Low risk: Study adheres to commonly held tenets of high quality design, execution and avoidance of bias	**Good quality RCT**	• **Random sequence generation** • **Allocation concealment** • **Intent-to-treat analysis** • **Blind or independent assessment -author's primary outcomes*** • **Co-interventions applied equally** • **F/U of 80%+ and<10% difference between groups** • **Controlling for possible confounding†**
Moderately low risk: Potential for some bias; study does not meet all criteria for a good quality RCT, but deficiencies not likely to invalidate results or introduce significant bias	**Moderate quality RCT**	• Violation of one or two of the criteria for good quality RCT
	Good quality cohort	• Blind or independent assessment in prospective study, or use of reliable data‡ in a retrospective study • Co-interventions applied equally • F/U 80%+ and<10% difference between groups • Controlling for possible confounding†
Moderately High risk: Study has significant flaws in design and/or execution that increase potential for bias that may invalidate results	**Poor quality RCT**	• Violation of three or more of the criteria for a good quality RCT
	Moderate, poor quality cohort	• Violation of any of the criteria for good quality cohort
	Case-control	• Any case-control design
High risk: Study has significant potential for bias; lack of comparison group precludes direct assessment of important outcomes	**Case series**	• Any case series design

Strength of Evidence (SoE)

SoE for overall body of evidence for primary outcomes was assessed *across included studies* based on:

- **Risk of bias**: the extent to which the included studies protect against bias
- **Consistency**: degree to which estimates are similar in terms of range and variability.
- **Directness**: whether the evidence is directly related to patient health outcomes.
- **Precision**: level of certainty surrounding the effect estimates.
- **Publication/report bias**: selective reporting or publishing.

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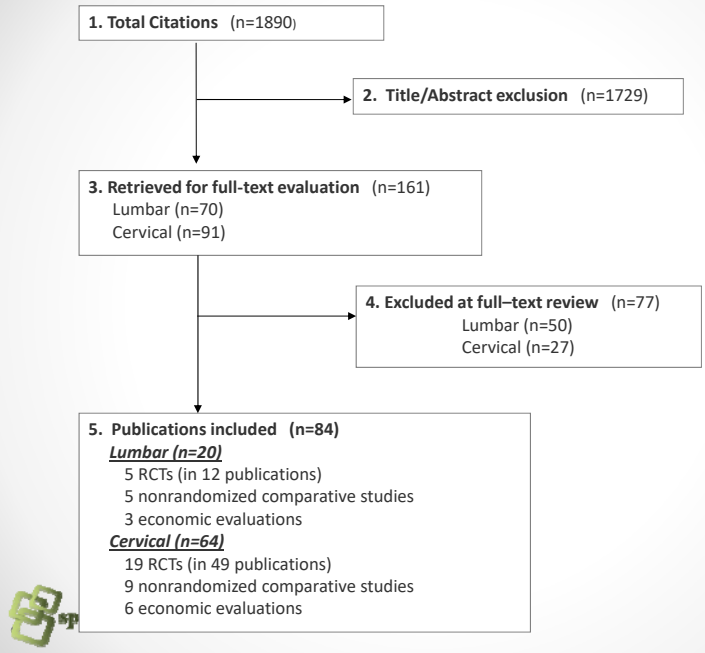
Evaluating Strength of Evidence

AHRQ/GRADE ***Strength of Evidence (SOE)*** approach is based on risk of bias, consistency of results across studies, directness of the evidence linking the intervention and health outcomes, and precision of the effect estimate

Strength of Evidence Ratings and Interpretation	
High	Very confident that the estimated effect is true
Moderate	Moderate confidence that estimate is likely to be close to true effect; possible that it is substantially different from true effect
Low	Limited confidence; effect may be substantially different
Insufficient	No evidence; little confidence in effect; effect likely to be substantially different

Literature Search Results



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Noninferiority Studies

- FDA trials employed a noninferiority study design
- Noninferiority is intended to show that the effect of a new treatment is not worse than that of an active control by more than a specified margin (Δ)
- Superiority can be evaluated and demonstrated with this type of design
- Interpretation depends on where the CI for the treatment effect lies relative to (1) the margin of noninferiority, Δ and (2) the null effect
- **Assumption:** The reference treatment must have an established efficacy or is in widespread use

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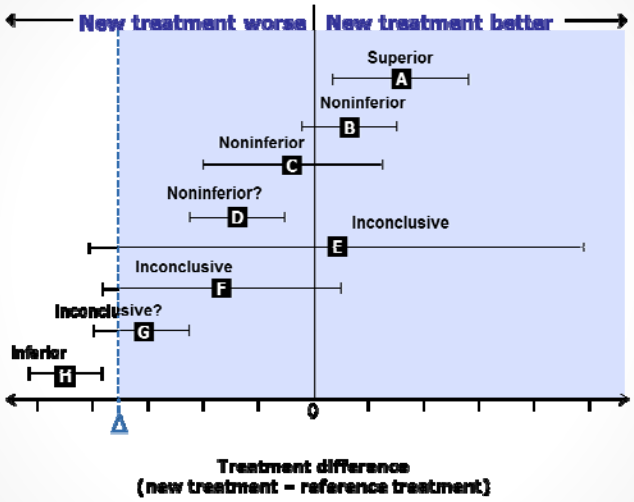
Noninferiority Interpretation



From: Piaggio G, Elbourne DR, Altman DG, et al. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT Statement. *JAMA*. 2006;295(10:1152-1160

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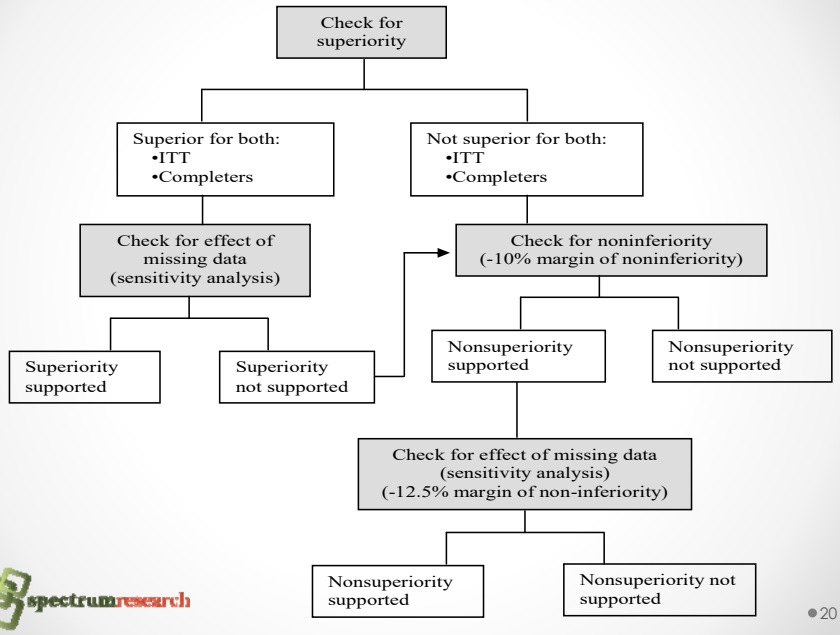
Efficacy Analysis and Interpretation



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Cervical Disc Arthroplasty C-ADR

- Majority of new evidence is for C-ADR
  - New approved devices
  - Additional trials for 1-level
  - New indication: 2-level intervention
- Presentation focus: Overall clinical success, NDI success, neurological success, pain reduction, secondary surgery, AEs

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Cervical Disc Arthroplasty (C-ADR)

- **NCD:** CMS does not have a NCD for C-ADR
- **Guidelines** (Section 2.4)
  - **NASS (2010):** ACDF and C-ADR are suggested to be comparable, similar short term outcomes for single level degenerative cervical radiculopathy
  - **Colorado Department of Labor (2014):**C-ADR is recommended for patients with single-level radiculopathy or myelopathy.
  - **ACOEM (2011):** Recommends C-ADR for sub-acute or chronic radiculopathy and for myelopathy; not recommended for chronic cervicothoracic pain or chronic non-specific cervical pain

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KQ1: Evidence Base for Cervical-ADR

Key Question	Original 2008 Report	Update
C-ADR vs. ACDF (1-level)		
KQ1: Efficacy & Effectiveness	5 RCTs 13 case series*	13 index RCTs (18 additional publications) 3 comparative observational studies
KQ2: Safety	5 RCTs 22 case series	13 index RCTs (23 additional publications) 2 comparative observational studies
KQ3: Differential Effects	0 studies	2 post hoc analyses each summarizing 2 RCTs
KQ4: Cost-effectiveness	0 studies	4 studies
C-ADR vs. ACDF (2-level)		
KQ1: Efficacy & Effectiveness	0 studies	2 Index RCTs[1] (3 additional publications) 2 comparative observational studies
KQ2: Safety	0 studies	2 Index RCTs (4 additional publications) 1 comparative observational study
KQ3: Differential Effects	0 studies	0 studies
KQ4: Cost-effectiveness	0 studies	2 studies
C-ADR vs. ACDF (Mixed levels)		
KQ1: Efficacy & Effectiveness	0 studies	2 RCTs 3 comparative observational studies
KQ2: Safety	0 studies	2 index RCTs (1 additional publication) 4 comparative observational studies
KQ3: Differential Effects	0 studies	1 RCT
KQ4: Cost-effectiveness	0 studies	0 studies
C-ADR vs. ACDF with a zero-profile device (2 non-contiguous levels)		
KQ1: Efficacy & Effectiveness	0 studies	1 RCT
KQ2: Safety	0 studies	1 RCT
KQ3 and KQ4	0 studies	0 studies
C-ADR vs. Nonoperative care		
Any	0 studies	0 studies

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Outcomes efficacy/effectiveness, C-ADR

1. Overall clinical success, FDA–based composite (1- and 2-level intervention trials):
   - NDI improvement (≥15 points from baseline)
   - Neurological success (maintenance or improvement in neurological status)
   - No secondary surgery as a result of device failure
   - No device-related adverse events
   - [Mobi-C 2-level; no intra-operative treatment changes]
2. NDI success;≥15 point improvement from baseline
3. Neurological success
4. Pain reduction success

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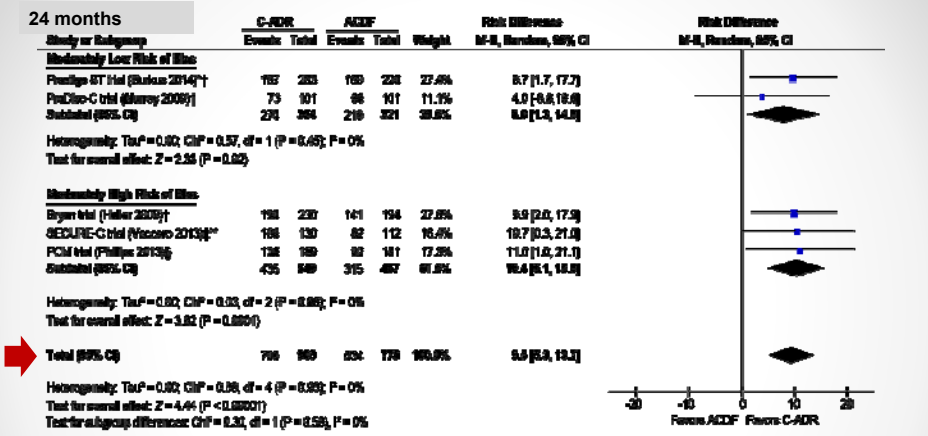
KQ1: Overall Clinical Success, C-ADR vs. ACDF (1-Level)

24 months



MODERATE evidence:

C-ADR is superior to ACDF for achieving clinical success at 24 months; RD 9.5% (95% CI 5.3%, 13.7%)

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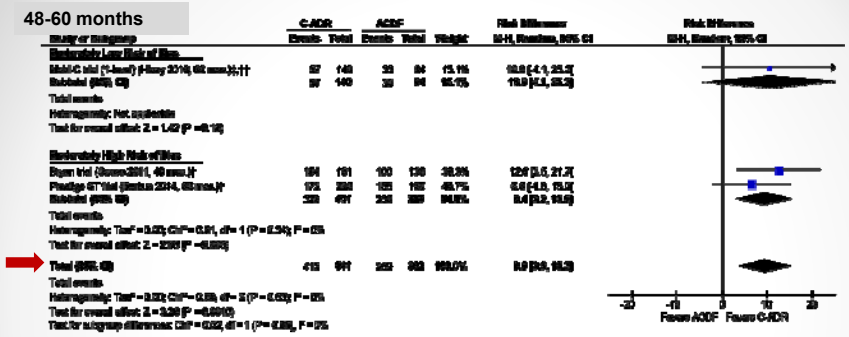
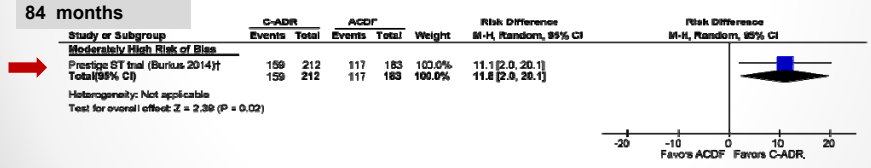
KQ1: Overall Clinical Success, C-ADR vs. ACDF (1-Level)

48-60 months



84 months

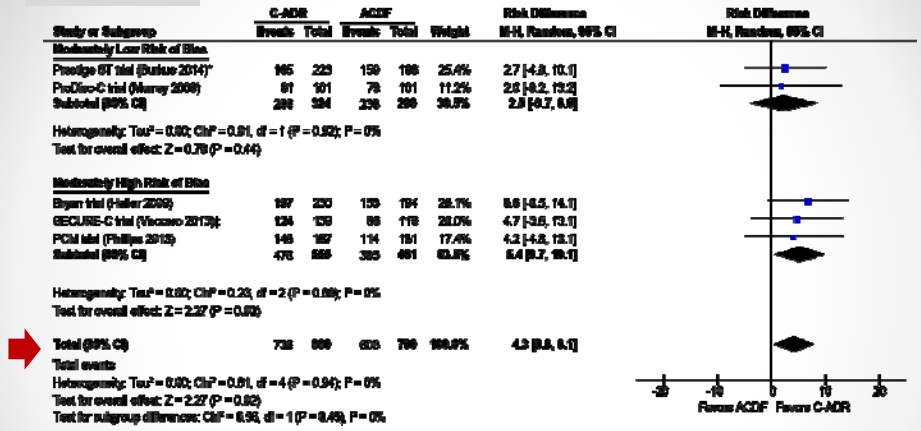


MODERATE evidence: C-ADR is superior to ACDF for achieving clinical success at 48 to 60 months; RD 9.6% (3.9%, 15.3%)

Low evidence: C-ADR superior at 84 months RD 11.8% (2.0%, 20.1%)

NDI Success (≥15-point improvement), C-ADR vs. ACDF (1-Level)

24 months



MODERATE evidence:

C-ADR is slightly better or comparable to ACDF for achieving NDI success at 24 months; RD 4.3% (95% CI 0.6%, 8.1%)

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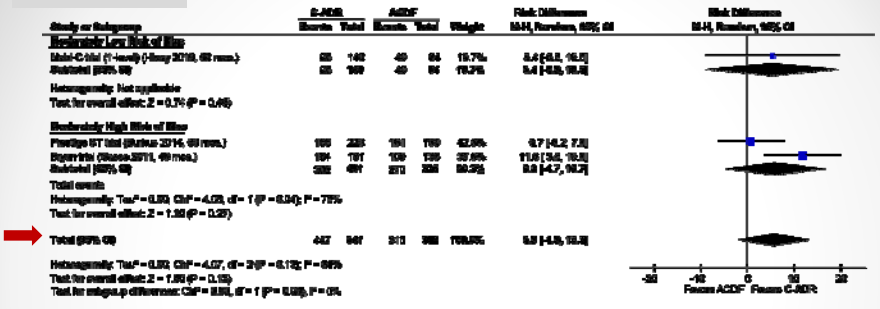
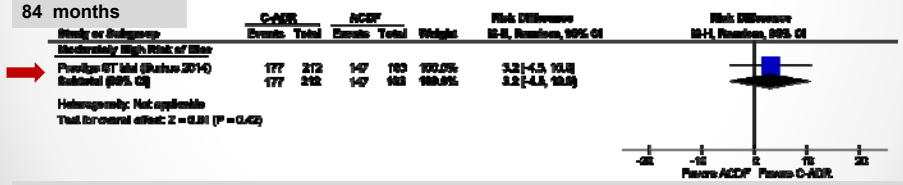
NDI Success (≥15-point improvement), C-ADR vs. ACDF (1-Level)

48-60 months



84 months



LOW evidence: C-ADR is comparable to ACDF for achieving NDI success at 48 to 60 months; RD 5.8% (95% CI -1.8%, 13.3%) and at 84 months; RD 3.2% (95% CI -4.5%, 10.8%)

NDI SCORES (1-100 [worst]), C-ADR vs. ACDF (1-Level)

NDI scores suggest C-ADR may be comparable or slightly better than ACDF (appendix slides); differences are not likely to be clinically meaningful

24 months: MODERATE evidence; WMD 1.11 (95% CI -0.06, 2.27)

48 to 60 months: MODERATE evidence: WMD 4.21 (95% CI 1.67, 6.75); 4 moderately high ROB trials contribute substantially to pooled estimate

84 months: LOW evidence**:** WMD 4.41 (95% CI 0.68, 8.1). One moderately high ROB trial contributes subtantially to pooled estimate

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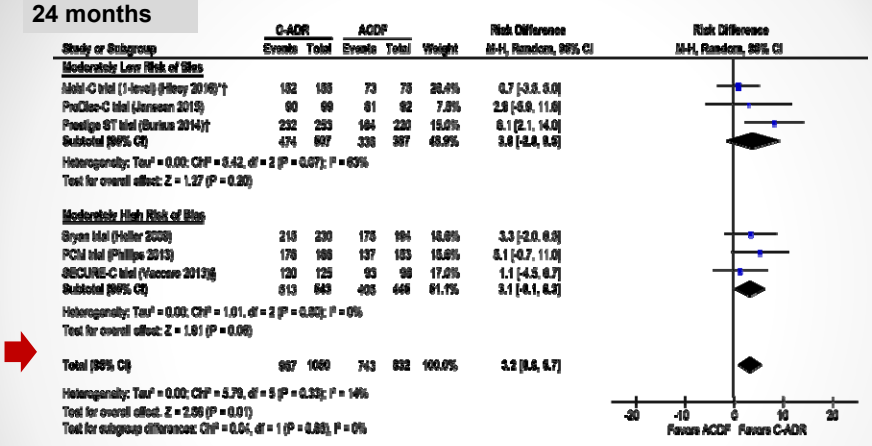
KQ1: Neurological Success, C-ADR vs. ACDF (1-Level)

24 months



MODERATE evidence:

C-ADR may be slightly better than ACDF in terms of neurological success at 24 months; Pooled RD 3.2% (95% CI 0.8%, 5.7%)

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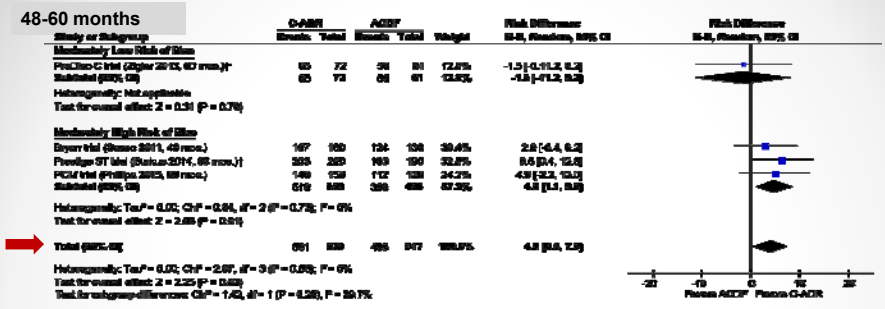
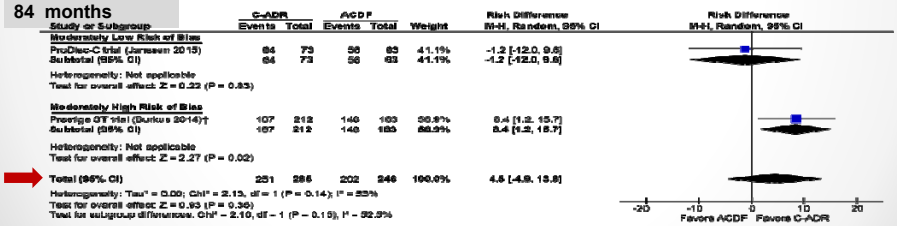
KQ1: Neurological Success, C-ADR vs. ACDF (1-Level)

48-60 months



84 months



MODERATE evidence: C-ADR may be slightly better than ACDF at 48 to 60 months; RD 4.0% (95% CI 0.5%, 7.5%)

LOW evidence: C-ADR comparable at 84 months; 4.5% (-4.9%, 13.8%)

Arm Pain Success (≥20-point improvement), C-ADR vs. ACDF (1-Level)

Outcome	Follo w-up	RCTs	Reasons for Downgrading	Conclusion*	Quality
Arm pain success (≥20-point VAS improvement)	24 mos.	2 RCTs (SECURE-C & PCM IDE trials) N = 578	Risk of bias Imprecision	**C-ADR and ACDF appear to be comparable** • SECURE-C trial: RD 4.7% (95% CI -7.9%, 17.4%) (left arm); RD -2.5% (95% CI -15.1%, 10.1%) (right arm) • PCM trial: RD 3.8% (95% CI -5.2%, 12.8%) (worst arm)	⊕⊕◯◯ LOW
	60 mos.	1 RCT (PCM trial) N= 288	Risk of bias Imprecision	RD 9.5% (95% CI -0.4%, 19.5%) **Conclusion: C-ADR and ACDF appear to be comparable**	⊕⊕◯◯ LOW

‡ Results could not be pooled due to differences in data reporting between the trials.

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ARM Pain: VAS/NRS (1-100 [worst]), C-ADR vs. ACDF (1-Level)

Arm Pain scores (appendix slides):

C-ADR may be comparable or slightly better than ACDF; Statistical differences are not likely to be clinically meaningful

24 months: MODERATE evidence across 9 RCTs: VAS scores slightly better with C-ADR vs. ACDF but not clinically meaningful. WMD 1.60 (95% CI 0.51, 2.70). 2 additional trials, reached similar conclusions but were not included in the pooled analysis

48 to 60 months: MODERATE evidence across 5 RCTs; WMD 3.82 (95% CI 1.15, 6.48); 3 high ROB trials contribute substantially

84 months: LOW evidence across 2 RCTs: C-ADR and ACDF appear to be comparable. WMD 2.21 (95% CI -2.08, 6.50)

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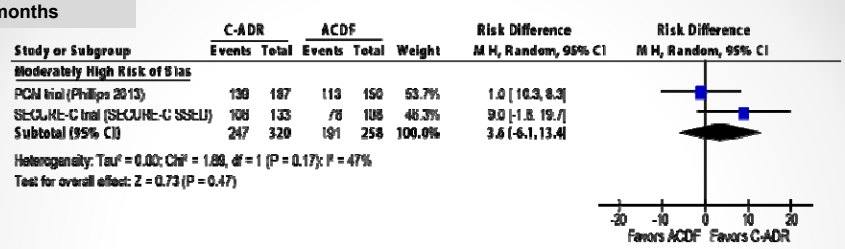
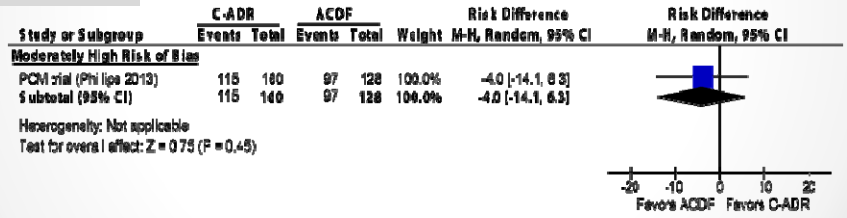
Neck Pain Success (≥ 20-point improvement), C-ADR vs. ACDF (1-Level)

24months



60 months



LOW evidence: C-ADR is comparable to ACDF at 24 months, RD 3.6% (95% CI -6.1%, 13.4%) and 60 months, RD -4.0% (95% CI -14.1%, 6.3%)

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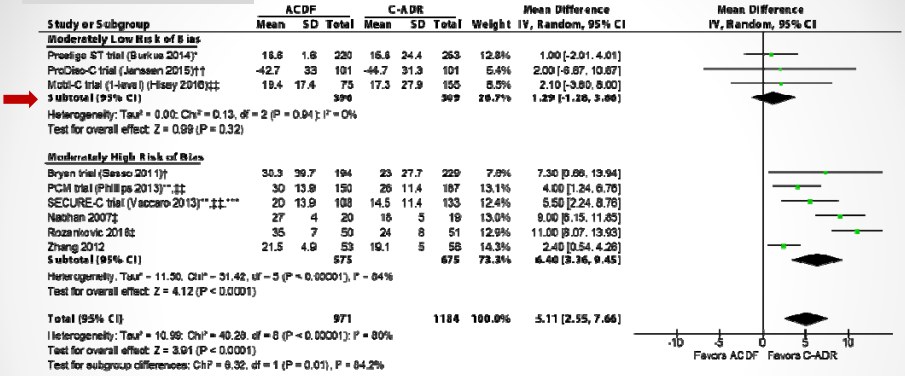
Neck Pain VAS/NRS Scores (0-100); C-ADR vs. ACDF (1-Level)

24 months



MODERATE Evidence:

C-ADR is comparable to ACDF. For trials at lowest risk of bias , WMD 1.29 (95% CI -1.28, 3.86). Substantial heterogeneity noted when high ROB trials included; For all trials WMD 5.11 (95% CI 2.55, 7.66) which may not be clinically meaningful

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Neck Pain VAS/NRS (1-100 [worst]), C-ADR vs. ACDF (1-Level)

Neck Pain scores at later follow-up:

Similar findings to 24 months; C-ADR may be comparable or slightly better than ACDF; Statistical differences are not likely to be clinically meaningful (appendix slides):

48 to 60 months: MODERATE evidence across 5 RCTs; WMD 6.63 (95% CI 3.29, 9.97); 3 Moderately high ROB trial contributes subtantially to pooled estimate

84 months: LOW evidence across 2 RCTs: WMD 5.59 (95% CI 1.31, 9.86); Moderately high ROB trial contributes subtantially to pooled estimate

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Overall, NDI and Neurological Success, C-ADR vs. ACDF (2-Level)

Outcome	Follow-up	RCTs	Reasons for Downgrading	Conclusion	Quality
Overall success†	24 mos. 60 mos.	1 RCT (Mobi-C, 2-level, ST IDE trial)	Risk of bias	**24 months: (N = 320)** RD 23.2% (95% CI 11.6%, 34.8%) **60 months: (n = 297)** RD 29.6% (95% CI 18.1%, 41.2%) **Conclusion: C-ADR was superior to ACDF**	⊕⊕⊕◯ MODERATE
NDI success‡	24 mos. 48 mos.		Risk of bias	**24 months: (N = 320)** RD 16.7% (95% CI 5.7%, 27.7%) **48 months: (N = 285)** RD 26.6% (95% CI 14.6%, 38.6%) **Conclusion: C-ADR was superior to ACDF**	⊕⊕⊕◯ MODERATE
Neurological success	24 mos. 60 mos.		Risk of bias Imprecision	**24 months: (N = 320)** RD 1.6% (95% CI -4.2%, 7.5%) **60 months: (N = 297)** RD -2.4% (95% CI -8.7%, 4.0%) **Conclusion: C-ADR and ACDF appear comparable**	⊕⊕◯◯ LOW

Arm and Neck Pain VAS SCORES, C-ADR vs. ACDF (2-Level)

Outcome	Follow-up	RCTs (N)	Reasons for Downgrading	Conclusion (estimate, 95% CI)	Quality
Arm pain VAS scores (0-100)	24 mos.	2 RCTs (Mobi-C (2-level) ST IDE trial), Cheng 2009) N = 353	Risk of bias Imprecision	**Mobi-C, N=291**: MD -4.3 (-9.5, 0.9,) no difference **Cheng 2009, N=62**: lower scores with C-ADR (14 vs. 27, MD -13 (95% CI NR), p=0.01). **Conclusion: C-ADR is as good as or slightly better; Differences may not be clinically meaningful.**	⊕⊕◯◯ LOW
	48 mos.	1 RCT Mobi-C trial, N = 255	Risk of bias Imprecision	MD in Δ scores: -3.0 (95% CI -11.6, 5.6) **Conclusion: C-ADR and ACDF appear to be comparable;**	⊕⊕◯◯ LOW
Neck pain VAS scores (0-100)	24 mos.	2 RCTs (Mobi-C IDE Cheng 2009) N =353	Risk of bias Imprecision	**Mobi-C, N=291**: MD -3.9 (-10.1, 2.3); no difference **Cheng 2009, N=62)** lower scores with C-ADR than with ACDF (15 vs. 26, MD -11 (95% CI NR), p=0.01) **Conclusion: C-ADR is as good as or slightly better; Differences may not be clinically meaningful**	⊕⊕◯◯ LOW
	48 mos.	1 RCT (Mobi-C IDE) N = 255	Risk of bias Imprecision	MD in Δ scores: -5.0 (95% CI -13.3, 3.3) **Conclusion: C-ADR and ACDF appear to be comparable;**	⊕⊕◯◯ LOW

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C-ADR vs. ACDF: Mixed levels (1-, 2-, or 3-level)

Outcome	Follow-up	RCTs	Reasons for Downgrading	Conclusion*	Quality
NDI scores	24 mos.	1 RCT (Skeppholm 2015) N = 143	Risk of bias Imprecision	MD -1.0 (95% CI -7.4, 5.4) **Conclusion: C-ADR and ACDF appear to be comparable in radiculopathy patients.**	⊕⊕◯◯ LOW
	24-36 mos.	1 RCT (Cheng 2011) N = 81	Risk of bias Imprecision	**24 months:** (13 vs. 16, MD -3 (95% CI NR), p=0.01 **36 months:** (12 vs. 17, MD -5 (95% CI NR), p<0.01), **Conclusion: C-ADR is as good as or slightly better in myelopathy patients; difference is not likely clinically meaningful.**	⊕⊕◯◯ LOW
Arm pain VAS scores (0-100)	24 mos.	1 RCT (Skeppholm 2015) N = 143	Risk of bias Imprecision	MD 0.4 (95% CI -7.7, 8.5) **Conclusion: C-ADR and ACDF appear to be comparable.**	⊕⊕◯◯ LOW
Neck pain VAS scores (0-100)	24 mos.	1 RCT (Skeppholm 2015) N = 143	Risk of bias Imprecision	MD -1.2 (95% CI -9.9, 7.5) **Conclusion: C-ADR and ACDF appear to be comparable.**	⊕⊕◯◯ LOW

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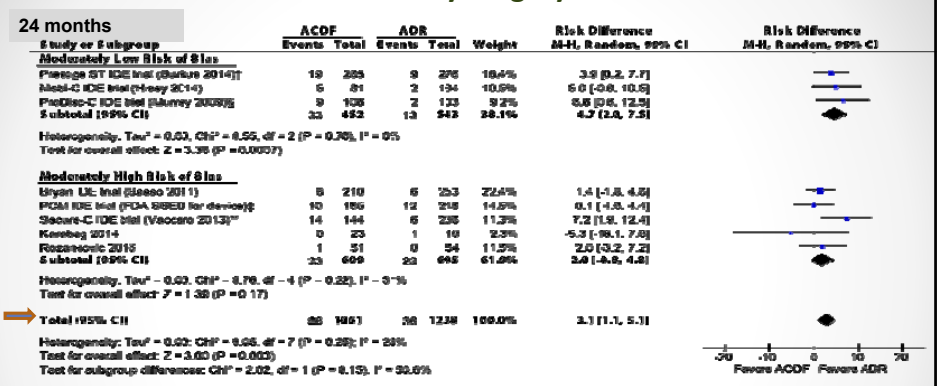
KQ2: Safety C-ADR vs. ACDF (1 level) - RCTs
Secondary Surgery*

24 months



MODERATE evidence at 24 months:
Fewer patients in the C-ADR group had secondary surgery.

C-ADR 2.9%, ACDF 6.2%, RD 3.1% (1.1%, 5.1%)

*index level or both index and adjacent levels; Poor patient tracking noted in many trials

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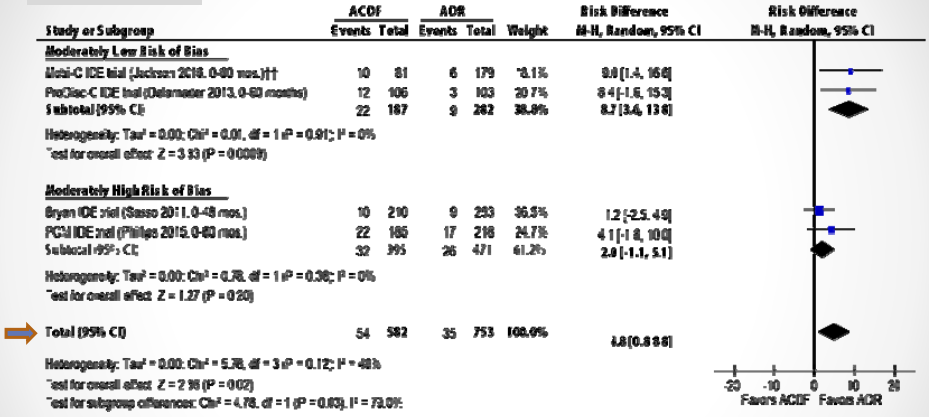
KQ2: Safety C-ADR vs. ACDF (1 level) - RCTs

Secondary Surgery

48-60 months



LOW evidence: Fewer patients in the C-ADR group underwent secondary surgery; C-ADR 4.6%, ACDF 9.3%; Pooled RD 4.8% (95% CI 0.8%, 8.8%)

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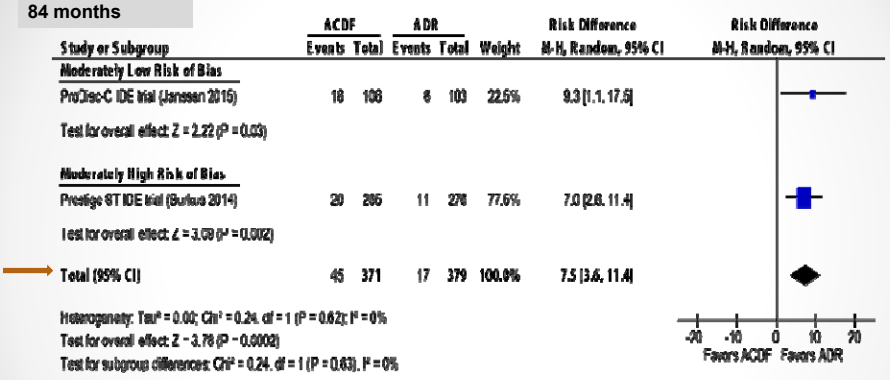
KQ2: Safety C-ADR vs. ACDF (1 level) - RCTs

Secondary Surgery

84 months



LOW evidence: Fewer patients in the C-ADR group underwent secondary surgery; only 2 RCTs

C-ADR 4.5%, ACDF 12.1%
RD 7.5% (95% CI 3.6%, 11.4%)

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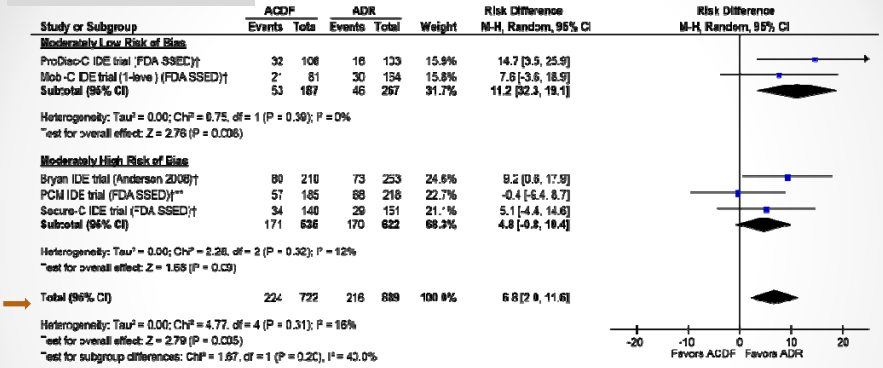
KQ2: Safety C-ADR vs. ACDF (1 level) - RCTs
Serious/Major Adverse Events (as classified by the trial†)

24 months (cumulative)



LOW evidence: Fewer C-ADR than ACDF patients had serious adverse events; C-ADR 24.3%, ACDF 31.0%, Pooled RD 6.8% (95% CI 2.0%, 11.6%)

† Definitions varied across trials

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KQ2: Safety C-ADR vs. ACDF (1 level) - RCTs
Serious/Major Adverse Events at Other Time Frames

Outcome	Follow-up	RCTs	Reasons for Downgrading	Estimates	Quality
Serious/ major adverse events* (as classified by the trial)	24-48 mos.	1 RCT (Bryan ST IDE trial) N = 463	Risk of bias Imprecision	C-ADR 17.4%, ACDF 17.1% RD -0.3% (95% CI -7.2%, 6.7%)	⊕⊕◯◯ LOW
	0-48 mos.	1 RCT (Mobi-C IDE trial) N = 260	Risk of bias Imprecision	C-ADR 10.1%, ACDF 9.9% RD -0.2% (95% CI -8.0%, 7.7%)	⊕⊕◯◯ LOW
	24-84 mos.	1 RCT (PCM ST IDE trial) N = 404	Risk of bias Imprecision	C-ADR 21.0%, ACDF 17.4% RD -3.7% (95% CI -11.3%, 4.0%)	⊕⊕◯◯ LOW

LOW evidence: C-ADR and ACDF are comparable at other times; single studies

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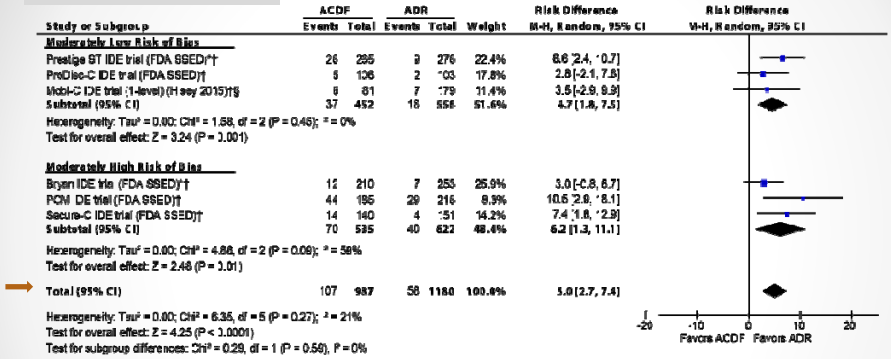
KQ2: Safety C-ADR vs. ACDF (1 level) - RCTs
Device-related Adverse Events (as classified by the trial)

24 months (cumulative)



MODERATE evidence: Device-related adverse events were less common with C-ADR than ACDF;

C-ADR 4.9%, ACDF 10.8%,RD 5.0% (95% CI 2.7%, 7.4%)

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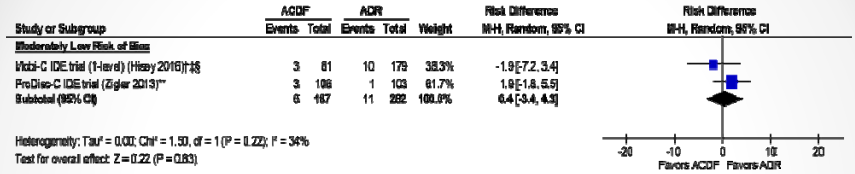
KQ2: Safety C-ADR vs. ACDF (1 level) - RCTs
Device-related Adverse Events (as classified by the trial)

60 months (cumulative)



60 Months, MODERATE evidence: C-ADR comparable to ACDF; C-ADR 3.9%, ACDF 3.2%, RD 0.4% (95% CI -3.4%, 4.3%), 2 RCTs

84 months (cumulative)

Outcome	RCTs	Reasons for Downgrading	Conclusion*	Quality
Device-related AE	1 RCT (ProDisc-C) N = 209	Risk of bias Imprecision	C-ADR 27.2%, ACDF 28.3% RD 1.1% (95% CI -11.0%, 13.3%) **Conclusion: ADR is comparable.**	⊕⊕◯◯ **LOW**

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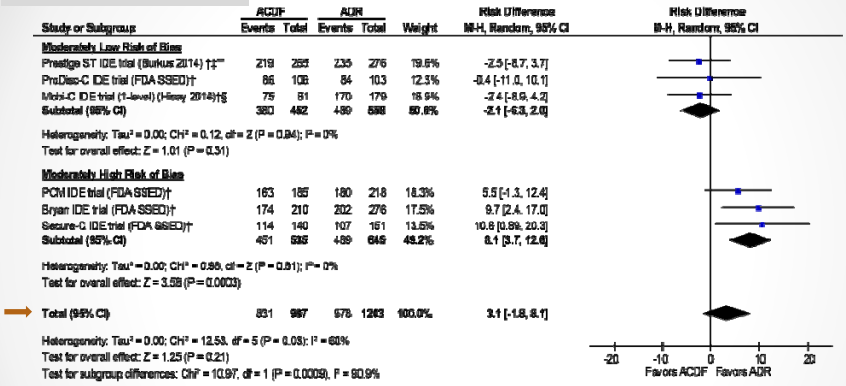
KQ2: Safety C-ADR vs. ACDF (1 level) - RCTs
Any Adverse Event (as reported by the trial)

24 months (cumulative)



INSUFFICIENT evidence: C-ADR and ACDF are comparable with regard to frequency of "any" AE.

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KQ2: Safety C-ADR vs. ACDF (2 level) - RCTs
Secondary Surgery and Adverse Events (as defined in trial)

Outcome	Follow-up	RCTs	Reasons for Downgrading	Conclusion	Quality
Secondary surgery at the index level	24 mos. 60 mos.	1 RCT (Mobi-C (2-level) IDE trial) N = 330	Risk of bias Imprecision	**24 months:** C-ADR 3.1%, ACDF 11.4% RD -8.3% (95% CI -14.8%, -1.8%) **60 months:** C-ADR 4.7%, ACDF 12.4% RD -7.7% (95% CI -14.5%, -0.8%) **Conclusion: Fewer patients in the C-ADR group underwent secondary surgery**	⊕⊕◯◯ **LOW**
Serious, major adverse events	24 mos.		Risk of bias Imprecision	C-ADR 24.4%, ACDF 32.4% RD -7.9% (95% CI -18.5%, 2.6%) **Conclusion: Serious adverse events were less common with C-ADR**	⊕⊕◯◯ **LOW**
Device-related adverse events	24 mos.		Risk of bias Imprecision	C-ADR 16.0%, ACDF 34.3% RD -18.3% (95% CI -28.6%, -8.0%) **Conclusion: Device-related adverse events were less common with C-ADR**	⊕⊕◯◯ **LOW**

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KQ2: Safety C-ADR vs. ACDF (Mixed Levels) - RCTs
Secondary Surgery and Adverse Events

Outcome	Follow-up	RCTs	Reasons for Downgrading	Conclusion*	Quality
Secondary surgery at the index level	24-36 mos.	2 RCTs (Skepphol m 2015, Cheng 2011) N=234	Risk of bias Imprecision	**24 mos. (N=151):** C-ADR 6.2%, ACDF 1.4% RD 4.7% (95% CI -1.2%, 10.7%) **36 mos. (N=83):** C-ADR 0%, ACDF 0% **Conclusion: No statistical difference**	⊕⊕◯◯ LOW
Serious, major AE			Risk of bias Imprecision	**Conclusion: None reported by either trial.**	⊕⊕◯◯ LOW
Device-related adverse events			Risk of bias Imprecision	**Conclusion**: No summary was reported. Device-related complications occurred similarly between groups, and in relatively few patients (0-2.4% of the C-ADR group; 0% in the ACDF group) across both trials. Exception: dysphagia, was less common in the C-ADR group than in the ACDF group (Skeppholm: 11.8% vs. 19.9% through 24 months, p=0.31; Cheng 2011: 2.4% vs. 16.7% through 36 months, p<0.01),	⊕⊕◯◯ LOW

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KQ3: Differential Efficacy or Safety of C-ADR

No studies were identified which stratified on patient characteristics or evaluated effect modification.

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KQ4: Cost-effectiveness of C-ADR (1-level)

QHES	Radcliff 2016 (91/100)	Qureshi 2013 (73/100)	McAnany 2014 (87/100)	Lewis 2014 (62/100)
Population	DDD; (ProDisc-C) IDE trial (N=209)	DDD, radiculopathy (hypothetical)	Acute disc herniation, myelopathy (hypothetical)	DDD, radiculopathy (hypothetical)
ICER	Incremental NMB*: $20,679 (95% CI $6053, $35,377)	C-ADR dominates (ICER = $-2,394) [60 months	C-ADR dominates (ICER = $-557,849) at 60 months	NR 60 months
Author's Conclusion	Over 7 years, C-ADR more effective, less costly than ACDF	C-ADR and ACDF cost-effective; C-ADR was generally more so.	Both C-ADR and ACDF are cost-effective with WTP threshold of $50,000.	ACD more effective, less costly than C-ADR or ACDF; unclear if C-ADR more cost-effective than ACDF.

U.S. based CUAs suggest that 1-level C-ADR may be more effective and less costly at WTP = $50,000

Study limitations: Time horizon (60 months), limited sensitivity analyses around assumptions, complexity of determining utilities and modeling health states

KQ4: Cost-effectiveness of C-ADR (2-level) Mobi-C IDE Trial (N = 330)

	Ament 2014	Ament 2016
Perspective	Base case: societal Sensitivity analysis: payer	Societal (includes direct + indirect costs) Healthcare (includes direct costs only)
Time horizon	Base case: 24 months Sensitivity analysis: 12-120 months	60 months Sensitivity analysis: 24 & 96 months
BASE CASE		
ICER (Δ$/ΔQALY)	$24,594	Societal: $-165,103* Healthcare: $8,518*
Author's Conclusion	C-ADR appears to be highly cost-effective when compared to ACDF for 2-level DDD.	C-ADR cost effective than two-year study. Authors reason that the greater QALYs and reduced cost as well as more realistic return to work data are the driving factors.

CUA (U.S.) suggest 2-level C-ADR is cost-effective vs. ACDF at all time frames evaluated; ICER < $50,000 (payer)

Limitations: Follow-up data for short time frame (60 months), complete costing data and hospital LOS not well captured

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Summary: Cervical-ADR

Key Question	Summary: C –ADR vs. ADCF
KQ1: Efficacy	**MODERATE evidence that C-ADR is** • **Superior to ACDF:** Clinical Success (to 60 months, 1-level; 24 months 2-level) and NDI success (2-level, 24 months, 1 RCT) • **Slightly better than ACDF:** Neurological Success (to 60 months), NDI Success (24 months) • **Comparable to ACDF:** Scores for arm pain, neck pain (to 60 months, 1-level) **LOW evidence that C-ADR is** • **Superior to ACDF:** Clinical Success, (to 84 months, 1-level) • **Slightly better than ACDF:** NDI scores **(**84 months, 1-level) • **Comparable to ACDF:** NDI success (1-level, 48-84 months); pain scores, NDI scores, arm pain success, neck pain success (all time frames, 1- , 2-levels and mixed)

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Summary: Cervical-ADR

Key Question	Summary: C-ADR vs. ACDF
KQ2: Safety	**MODERATE evidence that** • Secondary surgery and device-related AEs are less common with C-ADR at 24 months (1-level) **LOW evidence that** • Secondary surgery, less common with C-ADR 48-84 months (1-level), at 24 months for 2-level • Device-related AEs, less common following 1-level C-ADR at 48-84 months, 2-level at 24 months • Serious AEs, less common with C-ADR at 24 months for 1 or 2-level • C-ADR and ACDF are comparable with regard to: Serious AEs (1-level, 24-84 months, single RCTs); • C-ADR and ACDF are comparable in 2 studies of mixed 1 or 2-level: secondary surgery, device-related complications (except dysphagia); no serious adverse events reported in either trial
KQ 3:	No evidence on differential efficacy or safety
KQ 4: Cost-effectiveness	**1-level C-ADR (4 CUA studies), 2-level C-ADR (2 studies, same population)** C-ADR appears to be cost-effective at WTP threshold of $50,000

Lumbar Disc Arthroplasty (L-ADR)- Overview

L-ADR vs. Multidisciplinary Rehabilitation (1 RCT)

L-ADR vs. Fusion (all other studies)

- 60 month follow-up to same index RCTs as 2009 report of 1-level ADR vs. fusion
- 2 new RCTs of multiple-level L-ADR vs. fusion
- Efficacy findings are similar to 2009 report: LOW evidence that L-ADR is comparable to fusion for overall clinical success, ODI success, neurological success (single-level, 2-level studies) and pain success or pain relief at 24 months (all levels) and 60 months in studies of single-level and 1 or 2 level intervention.

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KQ1: Evidence Base for Lumbar-ADR

Key Question	Original 2008 Report	Update
L-ADR vs. Fusion (1-level)		
KQ1: Efficacy	2 RCTs, 5 comparative observational, 7 case series	2 index RCTs, (4 additional publications)
KQ2: Safety	2 RCTs 22 case series	2 index RCTs, 5 additional publications; 2 comparative observational studies
KQ3 and KQ4	0 studies	0 studies
L-ADR vs. Fusion (2-level)		
KQ1: Efficacy **KQ2: Safety**	0 studies 0 studies	1 RCT
KQ3: and 4	0 studies	0 studies
L-ADR vs. Fusion (1- or 2-level, or levels not specified)		
KQ1: Efficacy & Effectiveness	0 studies	1 index RCT, (2 additional publications) 1 comparative observational
KQ2: Safety	0 studies	1 index RCT,1 additional publication) 3 comparative observational studies
KQ3: Differential Effects	0 studies	0 studies
KQ4: Cost-effectiveness	0 studies	2 studies
L-ADR vs. Multidisciplinary Rehabilitation		
KQ1: Efficacy	0 studies	1 RCT

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Lumbar Disc Arthroplasty (L-ADR)

CMS NCD: L-ADR is not covered for Medicare beneficiaries over 60; years of age; there is no NCD for beneficiaries age ≤ 60 years.

Guidelines (Section 2.4):

- **APS (2009):** For patients with non-radicular low back pain, panel recommends that clinicians consider offering the intervention (no difference between ADR and fusion through 2 years); insufficient evidence to adequately evaluate long-term benefits and harms (no recommendation for or against).
- **Colorado Department of Labor (2014):** L-ADR is recommended for patients with LBP
- **ACEOM (2011):** Does not recommend L-ADR for chronic, non-specific LBP, radicular syndromes (e.g. sciatica) or spinal stenosis

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KQ 1: Outcomes efficacy/effectiveness – L-ADR

1. Overall clinical success (FDA), a composite:
   - ODI improvement (≥15 points from baseline)
   - No device failure (revision, reoperation, removal)
   - No neurological deterioration compared with preoperative status
   - Blumenthal et al. added no major complication, Zigler, et al added any improvement in SF-36 and radiographic success (studies vs. fusion)

1. ODI Success (≥15 points from baseline)
2. Neurological success (no deterioration from baseline)
3. Pain reduction compared with baseline

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Results: L-ADR vs. Multidisciplinary Rehab

KQ1: L-ADR vs. Multidisciplinary Rehab

1 moderately high RoB Trial (N = 139) with 24 month follow-up

Outcome	L-ADR % (n/N)	Rehab % (n/N)	RD (95% CI)	p-value
ODI Success (≥15 point improvement)	70% (51/73)‡	47% (31/66)‡	22.9% (6.9, 38.9)	0.0063
	L-ADR mean ± SD	**Rehab mean ± SD**	**MD (95% CI) (author ITT)**	**p-value**
VAS Pain (0-100 [worst])	35.4 ± 29.1 (n=86)	49.7 ± 28.4 (n=86)	-14.3 (-23.0, -5.6)	0.001

LOW evidence:

- L-ADR may be superior to MDR regarding ODI Success (completer)
- Pain was slightly less following L-ADR; unclear if adjusted for worse baseline scores in the MDR group (8.7 pt. difference); wide CIs; clinical significance unclear

KQ1: L-ADR vs. Multidisciplinary Rehab

1 moderately high RoB Trial (N = 139) with 24 month follow-up

Other outcomes (Appendix I Tables 16-18); SoE not performed

	Mean ±SD		Δ from baseline† (95% CI)			
ITT Analysis*	ADR (n=86)	Rehab (n=86)	ADR	Control	MD (95% CI)†	p-value
ODI score	21.2 ± 17.1	30.0 ± 16.0	−20.8 (−25.2, −16.4)	−12.4 (−16.3, −8.5)	−8.4 (−13.2, −3.6)	0.001
SF-36 PCS	43.3 ± 11.7	37.7 ± 10.1	NR	NR	5.8 (2.5, 9.1)	0.001
SF-36 MCS	50.7 ± 11.6	48.6 ± 12.8	NR	NR	1.0 (−2.4, 4.4)	0.50
EQ-5D	0.69 ± 0.33	0.63 ± 0.28	NR	NR	0.06 (−0.05, 0.18)	0.26

*Author's ITT analysis based on last observation carried forward; clinical significance of MD unclear;

Scales: ODI, 0-100 (worst); SF-36 0-100 (best); EQ-5D, -0.59 – 1.0 (best)

Completer analysis	F/U	ADR % (n/N)	Rehab % (n/N)	RD (95% CI)	p-value
Work status (working; includes part time sick leave)†	0 mos.	28% (24/86)‡	26% (22/86)‡	2.3% (-10.9, 15.6)	0.7312
	24 mos.	31% (21/68)§	23% (15/65)§	7.8% (-7.2, 22.8)	0.3130
Medication usage (daily use)	0 mos.	27% (23/86)‡	20% (17/86)‡	7.0% (-5.6 19.6)	0.2802
	24 mos.	22% (16/73)§	18% (14/78)§	4.0% (-8.8, 16.7)	0.5426

KQ2: Safety L-ADR vs. Multidisciplinary Rehab (L-ADR related only)

Outcome	Follow-up	RCTs	Reasons for Downgrading	Conclusion*	Quality
Secondary Surgery at Index Level	24 mos.	1 RCT Hellum N=77	Risk of Bias Imprecision	L-ADR: 6.5% (5/77)	⊕⊕◯◯ LOW
Major complication resulting in impairment‡				L-ADR: 7.8% (6/77)	⊕⊕◯◯ LOW
Any complication§				L- ADR: 33.8% (26/77)	⊕⊕◯◯ LOW

Safety events were only defined with respect to L-ADR. Authors do not provide information on events in the rehabilitation group.

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KQ4: Cost-effectiveness of L-ADR

L-ADR vs. Multidisciplinary Rehabilitation: One high-quality CUA from Norway

	L-ADR vs. Rehabilitation
	Johnsen 2014 (Norway)
Perspective	Societal
Funding	Norwegian Back Pain Association; Authors report relevant financial activities related to consultancy, payment for lectures and grants.
Model	Bootstrapping; Based on Hellum RCT; Net Monetary Benefit (NMB)
Outcomes	Hellum RCT;EQ-5D, SF-6D used for comparison
Results:	
ICER	**EQ-5D: €39,748 /QALY ($49,132 USD/QALY)** **SF-6D: €128,238/QALY ($158,514 USD/QALY)**
Author's Conclusion	**L-ADR is cost-effective vs. MDR when QALY's measured with EQ-5D (for willingness to pay >$49,132); CE probability of 90%** **L-ADR not cost effective based on SF-6D; 40% probability of being cost-effective**
LIMITATIONS	**Short time horizon (24 months); failure to describe/evaluate impact of adverse events for L-ADR in particular (e.g. reoperation); Applicability to U.S. healthcare system unclear**

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Results: L-ADR vs. Fusion

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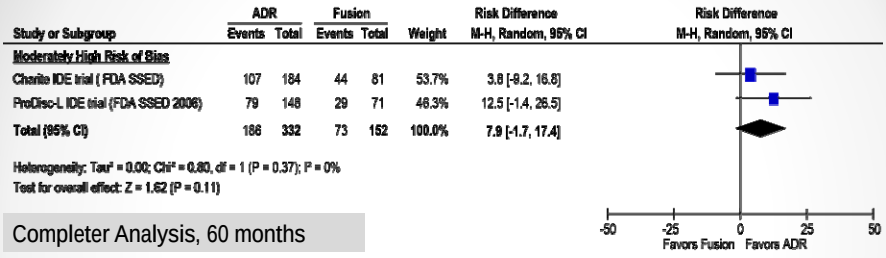
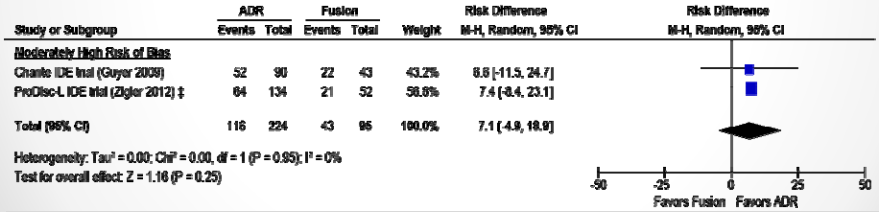
Overall Clinical Success: Single-level L-ADR vs. Fusion

Completer Analysis, 24 months



Completer Analysis, 60 months

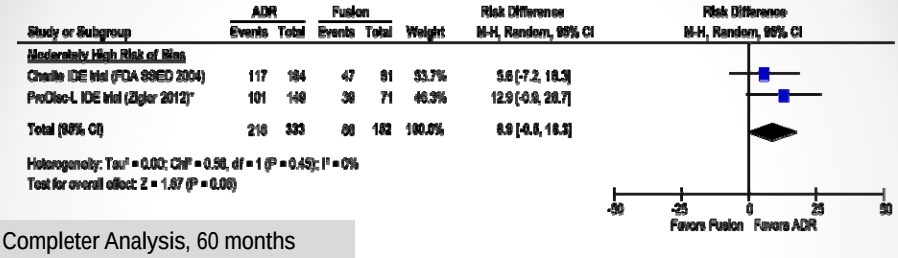


LOW quality evidence: L-ADR is comparable to fusion at 24 and 60 months

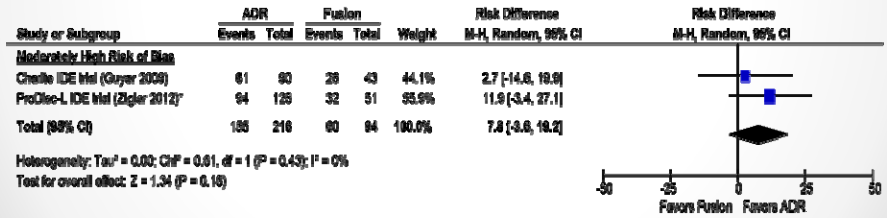
65

ODI Success(≥ 15 point improvement): Single-level L-ADR vs. Fusion

Completer Analysis, 24 months



Completer Analysis, 60 months



LOW quality evidence: L-ADR is comparable to fusion for ODI Success ate24 and 60 months

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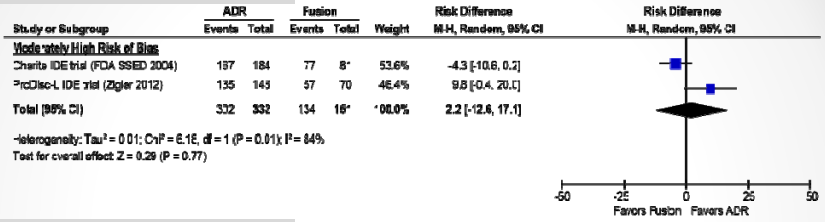
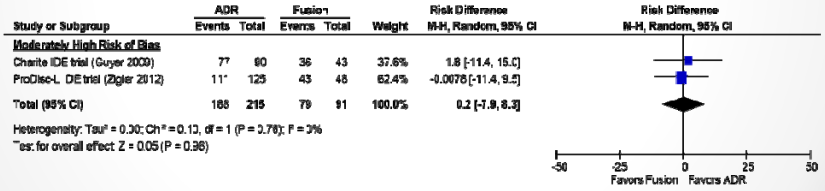
KQ1: Neurological Success: Single-level L-ADR vs. Fusion

Completer Analysis, 24 months



Completer Analysis, 60 months



INSUFFICIENT evidence at 24 months, LOW evidence at 60 months that L-ADR is comparable to fusion

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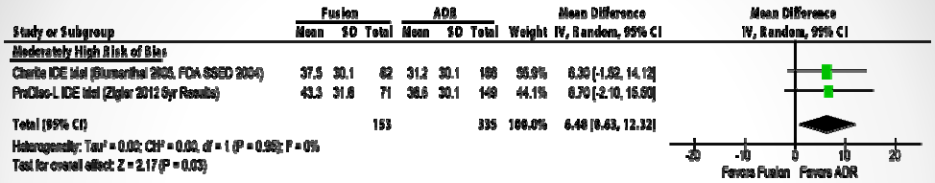
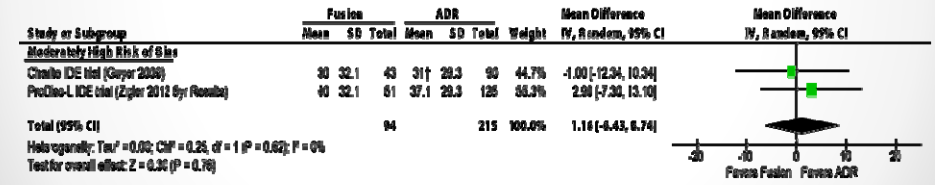
KQ1: VAS Pain (0-100[worst]): Single-level L-ADR vs. Fusion

Completer Analysis, 24 months



Completer Analysis, 60 months



LOW evidence: VAS Pain L-ADR is comparable to fusion for pain relief at 24 and 60 months

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KQ1: 2-Level L-ADR vs. Fusion

Completer Analysis at 24 months; 1 moderately high RoB Trial

Outcome	L-ADR % (n/N)	Fusion % (n/N)	RD (95% CI)	p-value
Overall Clinical Success	58.8% (87/148)	47.8% (32/67)	11.0% (-3.3, 25.4)	0.13
Neurological Success	89.2% (132/148)	80.6% (50/62)	8.5% (-2.5, 19.6)	0.10
	mean ± SD (n)	**mean ± SD (n)**	**MD (95% CI)**	**p-value**
ODI (0-100 [worst])	30.3 ± 24.3 (n=148)	38.7 ± 24.1 (n=67)	-8.4 (-15.4, -1.4)	0.02
VAS Pain (0-100 [worst])	31.9 ± 30.5 (n=143)	38.4 ± 29.8 (n=60)	-6.5 (-15.7, 2.7)	0.16

LOW evidence:

2-level L-ADR is as good as fusion for achieving clinical or neurological success and pain relief;

It may be slightly be better than fusion for disability improvement but ODI change may not be clinically meaningful

KQ1: 1 or 2-Level L-ADR vs. Fusion

Completer Analyses; 1 moderately high RoB Trial (N = 152)

Outcome	F/U (Mos)	L-ADR % (n/N)	Fusion % (n/N)	RD (95% CI)	p-value
Overall Clinical Success (Global Pain)	24 mos.	70.0% (56/80)	63.9% (46/72)	6.1% (-8.9, 21.1)	0.42
	60 mos.	72.5% (58/80)	67.6% (48/71)	4.9% (-9.7, 19.5)	0.51
ODI success (≥ 25% improvement)	24 mos.	64%(51/80)	55% (40/72)	8.2% (-7.4, 23.8)	0.31
	60 mos.	77.5% (62/80)	64.8% (46/71)	12.7% (-1.7, 27.1)	0.09

LOW evidence:

L-ADR is as good as fusion for achieving clinical success (totally pain free OR much better) and ODI success at 24 and 60 months

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KQ1: 1 or 2-Level L-ADR vs. Fusion

Completer Analyses; 1 moderately high RoB Trial (N = 152)

Outcome	F/U (Mos)	L-ADR mean ± SD (n)	Fusion mean ± SD (n)	MD (95% CI)	p-value
VAS back pain (0-100 [worst])	24 mos.	25.4 ± 29.8 (n=80)	29.2 ± 24.6 (n=72)	-3.8 (-12.6, 5.0)	0.40
	60 mos.	22.7 ± 29.2 (n=80)	30.5 ± 26.9 (n=71)	-7.8 (-16.9, 1.3)	0.09
VAS leg pain (0-100 [worst])	24 mos.	16.4 ± 24.5 (n=80)	20.7 ± 24.3 (n=72)	-4.3 (-12.1, 3.5)	0.28
	60 mos.	14.0 ± 23.1 (n=80)	20.3 ± 24.7 (n=71)	-6.3 (-14.0, 1.4)	0.11

LOW evidence:

L-ADR is as good as fusion at relieving back and leg pain at 24 and 60 months

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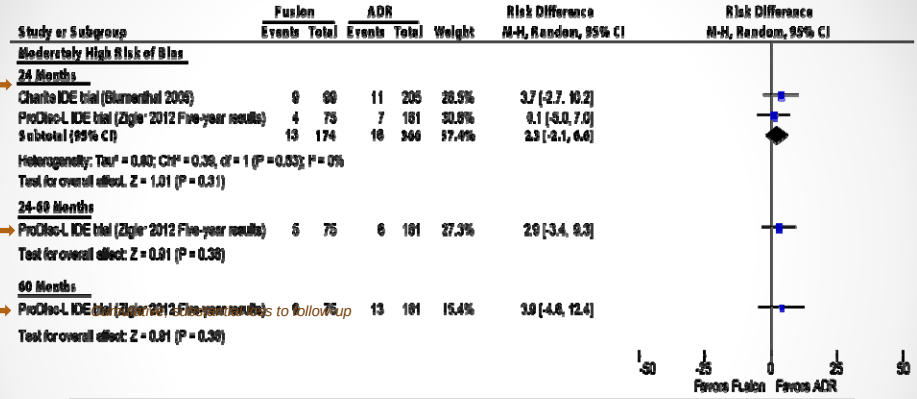
KQ2: Safety L-ADR vs. Fusion (1 level) - RCTs Subsequent Surgery* at Index Level



LOW evidence: L-ADR is comparable to fusion, all time frames;

*Surgeries included revision, reoperation, device/hardware removal, supplemental fixation, hemi-laminectomy and discectomy with decompression

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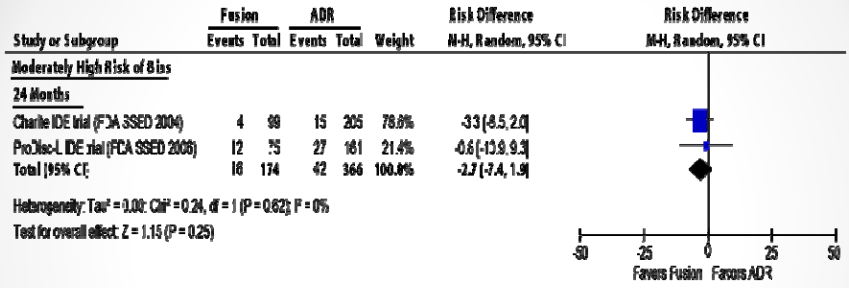
KQ2: Safety L-ADR vs. Fusion (1 level)- RCTs
Device-related Adverse Events*



LOW evidence: L-ADR is comparable to fusion at 24 months ;

*Defined as adverse events considered by the investigators to be device-related, including back and lower extremities pain, nerve root injury, implant displacement, and subsidence; calculations exclude secondary surgery at the index level.

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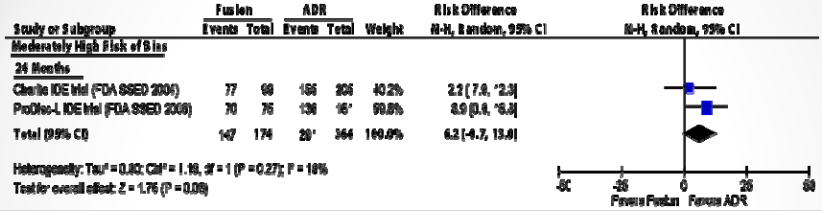
KQ2: Safety L-ADR vs. Fusion (1 level)- RCTs

All adverse events/complications*



LOW evidence: Any AE

24 months (2 RCTs) : L-ADR is comparable to fusion

60 months (1RCT): L-ADR 5.1/patient, fusion 5.4/patient, p= 0.507

*Any/all complications regardless of relationship to treatment.

INSUFFICIENT Evidence: Major or Serious AEs including Death

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KQ2: Safety L-ADR vs. Fusion (2 level) –1 RCT, 24 months

Outcome	RCTs (N)	Reasons for Downgrading	Conclusion	Quality
Secondary surgical procedure at index level(s)†	1 RCT (Delamarter) N=237	Risk of Bias[1] (-1) Imprecision[3] (-1)	L-ADR 2.4%, fusion 8.3% RD -5.9% (95% CI -12.7%, 0.09%) Conclusion: Additional surgery was less common with L-ADR	⊕⊕◯◯ LOW
Major surgery-related complications‡		Risk of Bias[1] (-1) Imprecision[4] (-1)	L-ADR 0.7%, fusion 4.9% RD -6.7% (95% CI -14.0%, 0.6%) Conclusion: Major surgery-related complications were less common with L-ADR; however no statistical difference*	⊕⊕◯◯ LOW
Device related complications (Subsidence or migration)§		Risk of Bias[1] (-1) Imprecision[3] (-2)	L-ADR 2.4%, Fusion 1.4% RD 1.0% (-2.5%, 4.6%) Conclusion: No statistical difference between groups.*	⊕◯◯◯ INSUFFICIENT

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KQ2: Safety L-ADR vs. Fusion (1- or 2- level)

Outcome	Follow-up	RCTs	Reasons for Downgrading	Conclusion	Quality
Any Secondary Surgical Procedure at Index Level†	24 mos. 60 mos.	1 RCT (Berg, Skold) N=152 N=151	Risk of Bias Imprecision	**24 months**: L-ADR 10.0%, fusion 30.6% RD -20.6% (-33.1%, -8.1%) **60 months:** L-ADR 17.5%, fusion 36.6% RD -19.1% (-33.1%, -5.2%) **Conclusion**: L-ADR was associated with significantly fewer secondary surgeries; the majority were device related	⊕⊕◯◯ LOW
Device-related reoperation†	24 and 60 mos.		Risk of Bias Imprecision	**24 months**: L-ADR 5.0%, fusion 27.8% RD -22.8% (95% CI -34.2%, -11.4%) **60 months:** L-ADR 11.3%, fusion 28.2% RD -16.9% (95% CI -29.5%, -4.4%) **Conclusion**: L-ADR was associated fewer device-related surgeries; these are the only device-related adverse events reported	⊕⊕◯◯ LOW

KQ2: Safety L-ADR vs. Fusion (1- or 2- level)

Outcome	Follow-up	RCTs	Reasons for Downgrading	Conclusion	Quality
Total major complications	60 mos.	1 RCT (Berg, Skold) N= 151	Risk of Bias Imprecision	L-ADR 2.5%, fusion 8.3% RD -5.8% (95% CI -13.1%, 1.4%) **Conclusion**: Fewer major complications following L-ADR; *statistical significance was not reached*, possibly due to sample size. All events occurred within 24 months	⊕⊕◯◯ LOW
Any (total) complication	60 mos.		Risk of Bias Imprecision	L-ADR 17.5%, fusion 20.8% RD -3.3% (95% CI -15.9%, 9.2%) **Conclusion:** L-ADR comparable to fusion with regard to frequency of any complications through 24 months. All events occurred within 24 months	⊕⊕◯◯ LOW

KQ3: Differential Efficacy or Safety of L-ADR

No studies were identified which stratified on patient characteristics or evaluated effect modification.

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KQ4: Cost-effectiveness of L-ADR

L-ADR vs. Fusion (1 or 2-level): Two moderate- to high-quality CUAs results were mixed, U.S. applicability unclear

	L-ADR vs. Fusion	
	Fritzell 2011 (Sweden) 1 or 2 levels	**Parkinson 2013 (Australia) Levels not specified**
Perspective	Societal and Healthcare	Healthcare
Funding	Industry	Australian Dept. of Health
Model	Bootstrapping; Net Monetary Benefit (NMB)	Markov Model
Outcomes:	Berg 2009 RCT, Swedish Spine Register	Berg 2009 RCT, FDA IDE trials
Results:		
ICER	**$252,519 (no-difference in EQ-5D).** • **No significant societal cost difference** • **Based on net benefit approach, L-ADR could not be demonstrated to be cost effective vs. fusion.**	**Depends on efficacy outcome** • **Cost/QALY gained (EQ-5D): No difference QALYs** • **Cost/ODI Success (≥25% improvement): $73,662 (L-ADR less costly, less effective)** • **Cost/overall success (FDA definition): L-ADR dominates-less costly, more effective vs. fusion** • **Cost/narcotic discontinuation: L-ADR dominates (less costly, more effective)**
Author's Conclusion	**Inconclusive; fusion is more costly from a healthcare perspective when reoperation included.**	**ADR is potentially cost saving compared with lumbar fusion, depending on the outcome.**
LIMITATION:	**Short time horizon (24 months), adverse events don't seem to be well represented, limited sensitivity analysis description; outcomes data sources poorly specified**	

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Summary L-ADR (Lumbar arthroplasty)

Key Question	Summary
KQ1: Efficacy	**1 or 2 level L-ADR vs. Multidisciplinary Rehabilitation** (1 RCT) **LOW evidence that L-ADR may be superior to multidisciplinary rehabilitation** with regard to ODI Success. Pain was less following L-ADR; it is unclear if results are adjusted for baseline differences or clinically meaningful. **L-ADR vs. Fusion** (2 RCTs of 1-level, 1 RCT of 2-level, 1 RCT of 1 or 2 level) **LOW evidence that L-ADR is comparable to fusion** with regard to overall clinical success, ODI success, neurological success (single-level, 2-level studies) and pain success or pain relief at 24 months for all levels and at 60 months in studies of single-level and 1 or 2 level intervention. **For non-inferiority trials the assumption is that reference treatment must have an established efficacy** or that it is in widespread use. The efficacy lumbar fusion for degenerative disc disease remains uncertain, especially compared with non-operative care.

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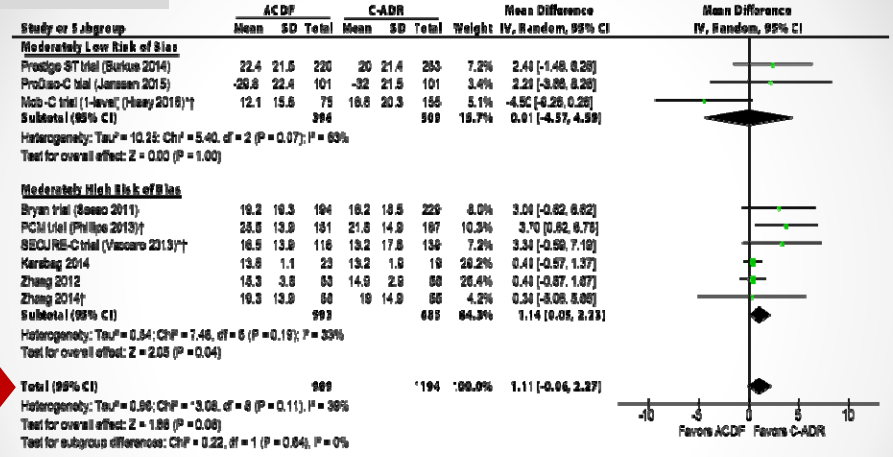
Summary L-ADR (Lumbar arthroplasty)

Key Question	Summary
KQ2: Safety	**L-ADR vs. Multidisciplinary Rehabilitation (1 RCT)** Only ADR-related complications reported. **L-ADR vs. Fusion** **Single-Level (2 RCTs)** **LOW evidence that L-ADR is comparable to fusion** for subsequent surgeries at the index level, device-related adverse events and any adverse event. **INSUFFICIENT evidence** that L-ADR and fusion are comparable regarding major/serious adverse events including death, in part due to sample sizes. **2-Level (1 RCT) and 1 or 2-level (1 RCT)** **LOW evidence**: **Secondary surgeries were significantly less common with L-ADR**. Major surgery-related complications or major complications (general) were less common but statistical significance was not reached. **INSUFFICENT evidence** for comparability regarding device-related complications; sample sizes were small
KQ3:	No evidence on differential efficacy or safety
KQ4: Cost-effectiveness	**L-ADR vs. Multidisciplinary Rehabilitation (1 CUA study)** Cost-effectiveness of L-ADR vs. rehab is unclear **1 or 2-level L-ADR vs. Fusion (2 CUA studies)** Cost-effectiveness of L-ADR vs. fusion is unclear

Appendix slides: C-ADR

NDI SCORES (1-100 [worst]), C-ADR vs. ACDF (1-Level)

24 months

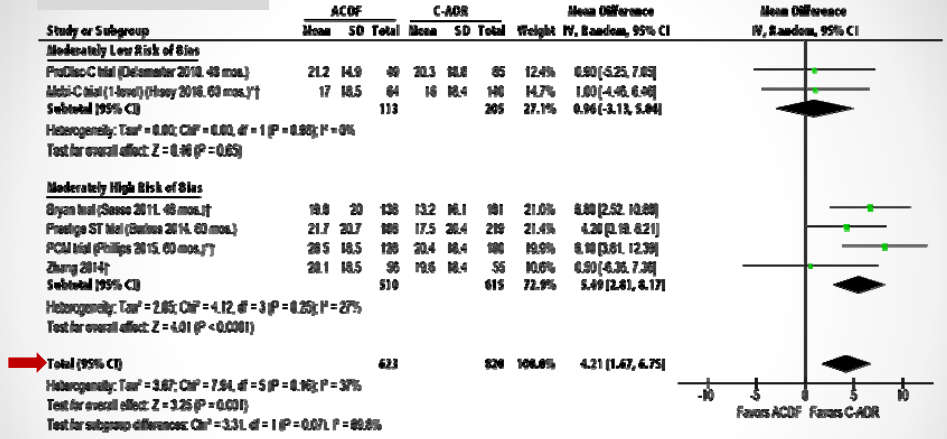


MODERATE evidence:

C-ADR may be comparable to ACDF with regard to NDI scores; WMD 1.11 (95% CI -0.06, 2.27) at 24 months

NDI SCORES (0-100[worst]), C-ADR vs. ACDF (1-Level)

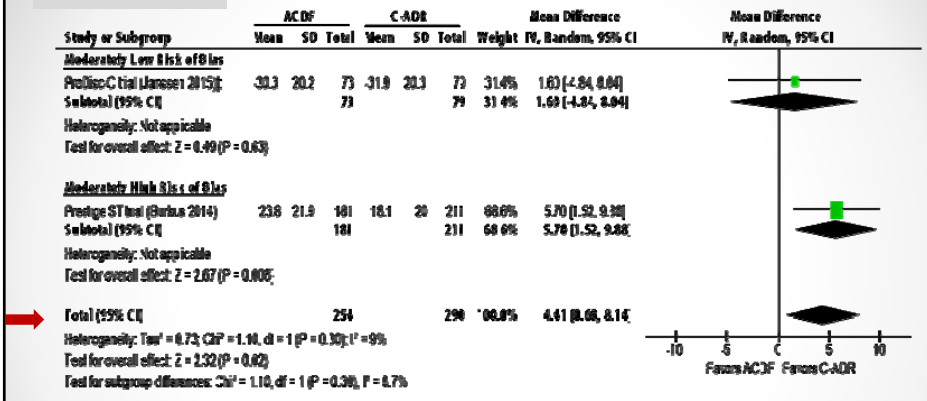
48-60 months



MODERATE evidence: NDI scores were slightly better following C-ADR vs. ACDF however the difference is likely not clinically meaningful; WMD 4.21 (95% CI 1.67, 6.75). 4 moderately high ROB trials contribute subtantially to pooled estimate

NDI SCORES (0-100[worst]), C-ADR vs. ACDF (1-Level)

84 months



LOW evidence: NDI scores were slightly better following C-ADR vs. ACDF; difference is likely not clinically meaningful; WMD 4.41 (95% CI 0.68, 8.1). One moderately high ROB trial contributes subtantially to pooled estimate

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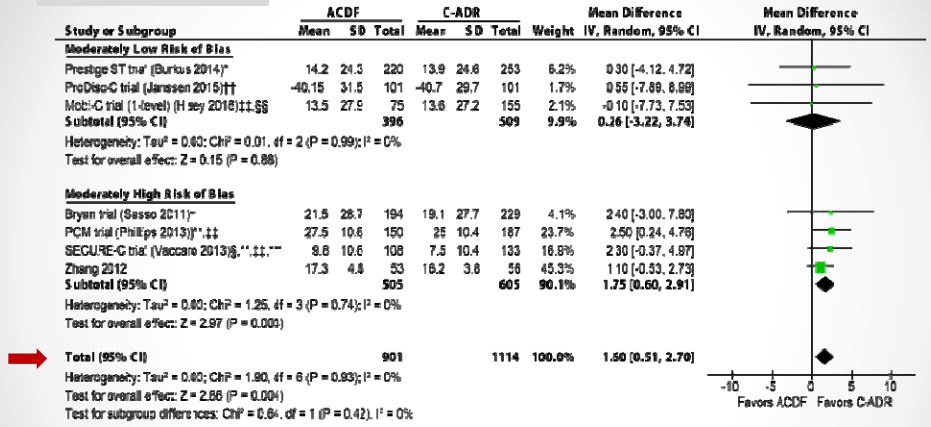
Arm Pain VAS/NRS Scores C-ADR vs. ACDF (1-Level)

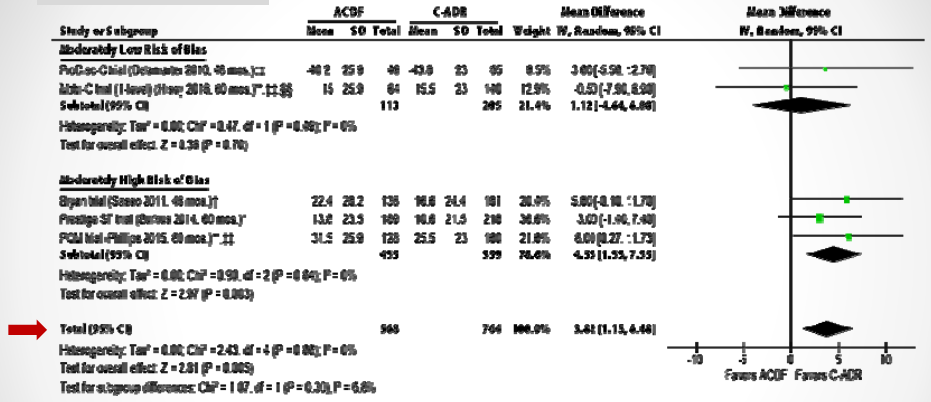
24 months



MODERATE Evidence: At 24 months arm pain VAS scores were slightly better with C-ADR vs. ACDF but not clinically meaningful. WMD 1.60 (95% CI 0.51, 2.70). 2 additional trials, reached similar conclusions but were not included in the pooled analysis

Arm Pain VAS/NRS Scores C-ADR vs. ACDF (1-Level)

48-60 months



MODERATE Evidence: At 48-60 months, arm pain VAS scores may be slightly better with C-ADR versus ACDF; difference between groups is probably not clinically meaningful. WMD 3.82 (95% CI 1.15, 6.48)

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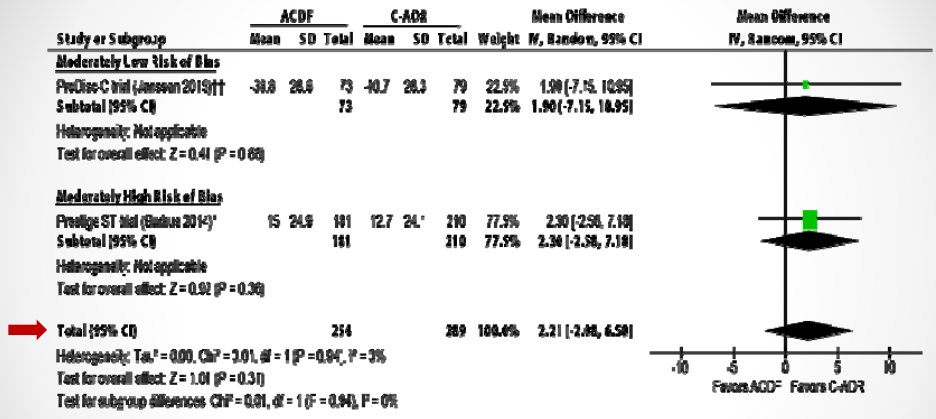
Arm Pain VAS/NRS Scores C-ADR vs. ACDF (1-Level)

84 months



LOW evidence: At 84 months, C-ADR and ACDF appear to be comparable; no significant difference between groups. WMD 2.21 (95% CI -2.08, 6.50)

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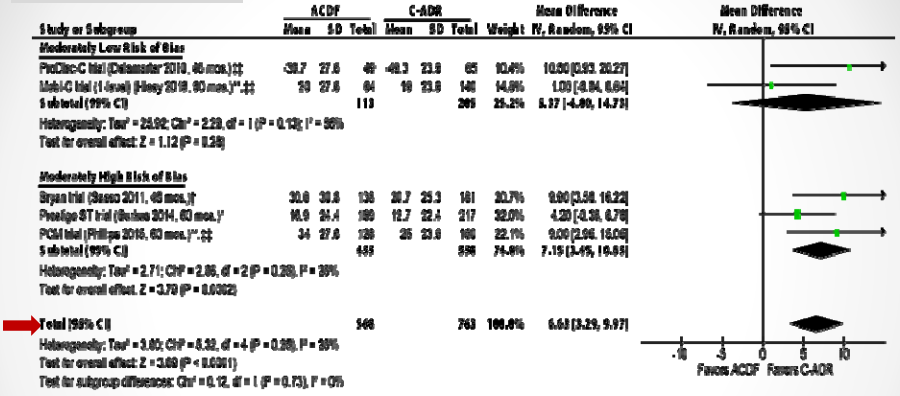
Neck Pain VAS/NRS Scores C-ADR vs. ACDF (1-Level)

48-60 months



MODERATE Evidence: C-ADR is comparable to or slightly better than ACDF. Similar findings to 24 months; The difference between groups is most likely not clinically meaningful ; WMD 6.63 (95% CI 3.29, 9.97)

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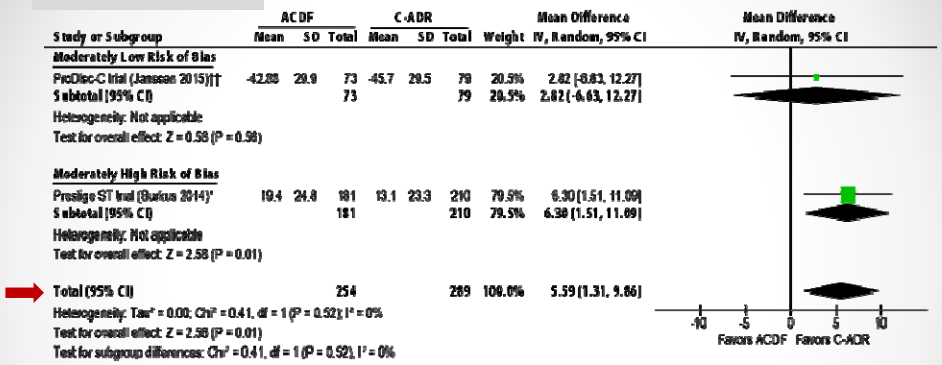
Neck Pain VAS/NRS Scores C-ADR vs. ACDF (1-Level)

84 months



LOW Evidence: C-ADR is comparable to or slightly better than ACDF; difference between groups is probably not clinically meaningful on 100 point scale, WMD 5.59 (95% CI 1.31, 9.86);

Moderately high ROB trial contributes subtantially to pooled estimate

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Appendix slides: L-ADR

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KQ2: Safety L-ADR vs. Fusion (1-level)

Outcome	F/U	Study	L-ADR* % (n/N)	Fusion* % (n/N)	RD (95% CI)† RR (95% CI)†	p-value	Quality
Major adverse events‡	24 mos.	Charite IDE trial	1.0% (2/205)	1.0% (1/99)	0.03% (-2.4, 2.4) 1.0 (0.9, 10.5)	0.98	⊕◯◯◯ INSUFFICIENT
		ProDisc-L IDE trial	0% (0/161)	0% (0/75)	0% (NC) NC	NS	
	60 mos.	Charite IDE (Guyer)	0% (0/90)	0% (0/43)	0% (NC) NC	NS	⊕◯◯◯ INSUFFICIENT
Severe, life-threatening	60 mos.	ProDisc-L IDE trial	0.58/pt (n=161)	0.38/pt (n=75)	NR	0.036	⊕◯◯◯ INSUFFICIENT
Death (treatment)	24 mos.	Charite IDE trial	0.5% (1/205)	0% (0/99)	0.5% (NC) NC	0.49	⊕◯◯◯ INSUFFICIENT
		ProDisc IDE trial	0% (0/161)	0% (0/75)	0% (NC)	NS	
Death (unrelated)	60 mos.	ProDisc-L IDE trial	2.5% (4/161)	1.3% (1/75)	1.2% (-2.4, 4.7) 1.9 (0.2, 16.4)	0.57	⊕◯◯◯ INSUFFICIENT

*Small sample size may preclude detection of rare events or difference between groups

spectrumresearch

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Washington State Health Care Authority
Health Technology Assessment

FINAL key questions and background

Artificial disc replacement – re-review

Background

Back and neck pain due to degenerative disc disease (DDD) is the leading cause of pain and disability in adults in the United States, and as such, a large proportion of health care expenditures is used for the evaluation and treatment of this condition. Because aging is the primary risk factor for development of DDD, as the US population ages, the incidence of DDD is expected to increase.

Initially, treatment of symptomatic DDD typically consists of nonsurgical approaches, such as physical therapy, epidural steroid injections, and medications. However, an estimated 10% to 20% of people with lumbar DDD and up to 30% with cervical DDD are unresponsive to nonsurgical treatment. In addition, cervical DDD may lead to radiculopathy and/or myelopathy; 25% of people with cervical radiculopathy and 50% to 70% of those with cervical myelopathy do not respond to nonsurgical treatment.

Surgery may be considered when nonoperative treatments for at least six months fail to relieve symptoms attributed to spinal DDD or to prevent progression of nerve damage in the case of radiculopathy or myelopathy. Historically, lumbar or cervical fusion (also called arthrodesis) has been offered as a surgical option with the goal of removing the disc and fusing the vertebrae, thereby limiting the motion at the symptomatic segment. Spinal fusion is thought by some to promote the degeneration of the vertebrae above or below the fusion site (adjacent segment disease); however, many uncertainties remain regarding the extent to which this occurs. Guidelines recommend consideration of intensive multidisciplinary rehabilitation and appropriate patient selection as an integral part of decisionmaking particularly for lumbar fusion. For cervical DDD resulting in radiculopathy or myelopathy, the current surgical standard is anterior cervical discectomy and spinal fusion (ACDF), the goal of which is nerve decompression and restoration of spinal alignment and stability.

A surgical alternative to fusion is artificial disc replacement (ADR). Disc prostheses were developed to mimic the decompressive and supportive properties of intervertebral discs as well as to preserve motion at the index level, thereby improving pain and function as well as decreasing stresses on adjacent segment structures and theoretically the risk of adjacent segment disease. Lumbar ADR (L-ADR) is currently indicated in patients with single-level DDD who have failed at least six months of nonoperative care, while cervical ADR (C-ADR) is indicated in patients with radiculopathy or myelopathy secondary to one- or two-level DDD that has not responded to six weeks of nonsurgical treatment.

A Health Technology Assessment titled: *Artificial Disc Replacement*, was published on September 19, 2008 by the Health Care Authority.; the resulting Findings and Coverage Decision were released on October 17, 2008 and adopted on March 20, 2009. Based on a signal update report (1/25/2016), new randomized controlled trials for lumbar and cervical ADR have been published subsequent to the 2008 report. In addition, longer-term follow-up of patients is now available for some of these trials, and at least one device has subsequently received FDA approval for two-level placement.

Policy context

This technology was originally reviewed September 2008 and was selected for re-review based on new literature identified which may invalidate aspects of the previous report.

Objectives

The primary aim of this assessment is to update the 2008 report based on systematic review and synthesis of subsequently published evidence on the efficacy, safety, and cost-effectiveness of artificial disc replacement (ADR) in the cervical and lumbar spine.

Scope

Population:
Lumbar: Patients undergoing primary L-ADR for DDD without neurological compromise and who have not had prior spine surgery at the instrumented level.

Cervical: Patients undergoing primary C-ADR for DDD resulting in radiculopathy or myelopathy and who have not had prior surgery at the instrumented level.

Intervention: L-ADR or C-ADR with commercially available device (defined as FDA-approved devices or unapproved devices in Phase III trials with ≥ 1 year of follow-up data in a peer-reviewed journal)

Comparators: Non-operative treatment, spinal fusion, other spine surgery. Comparator interventions that employ a device not FDA-approved for use in the US will be excluded.

Outcomes:
Studies must report on at least one of the following:

- Physical function/disability (overall clinical success, ODI [L-ADR] or NDI [C-ADR]).
- Pain/pain reduction.
- Device failure (reoperation at the index level, to include revision, reoperation or removal).
- Complications (e.g., migration, subsidence, neurologic injury as well as infection, vascular damage, heterotopic ossification others).

The following secondary outcomes are reported if presented with studies meeting the above criteria:

- Quality of life (SF-36).
- Incidence of adjacent segment disease.

Non-clinical outcomes such as range of motion and alignment are excluded from the scope.

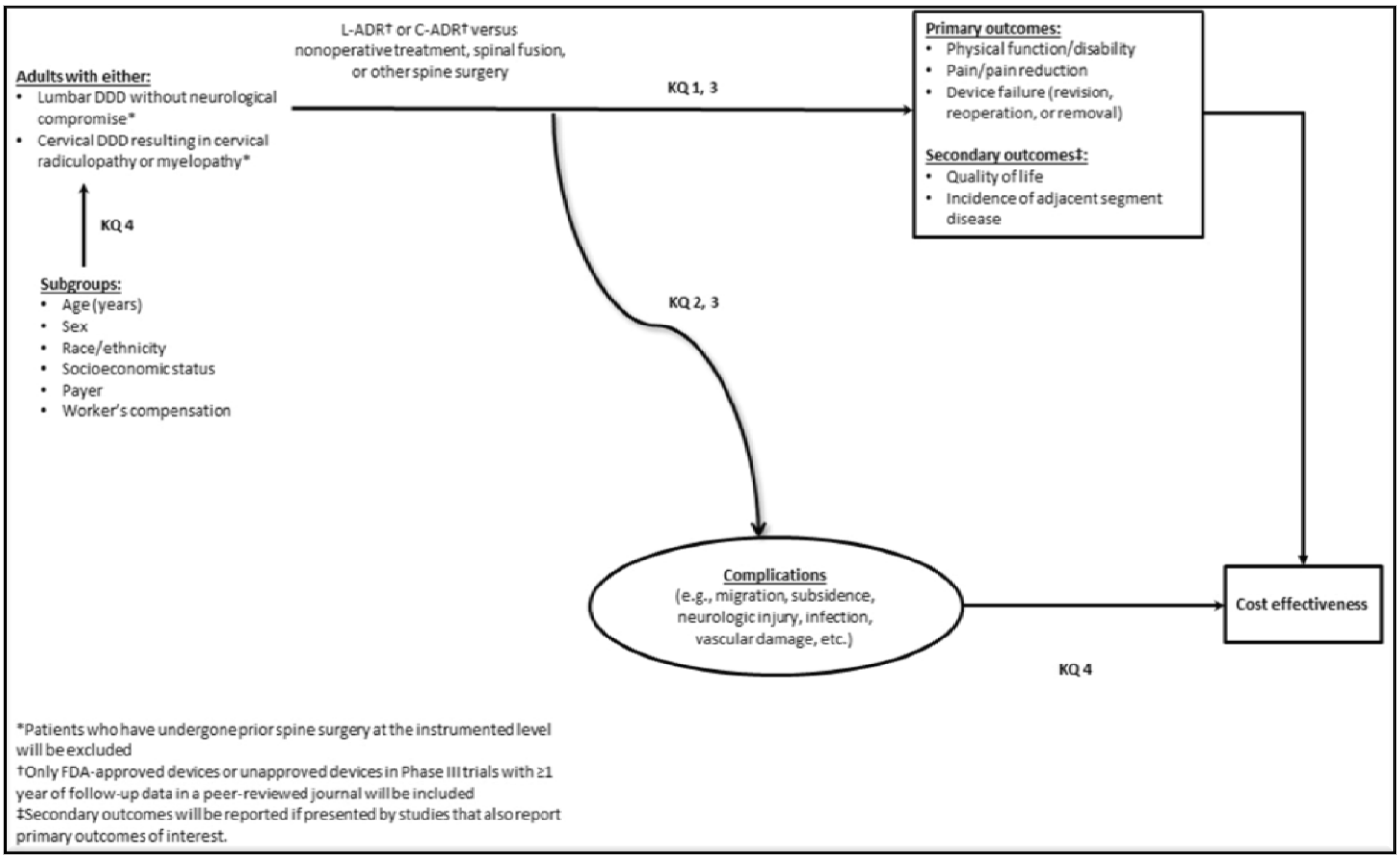
Key questions

1. What is the evidence of efficacy and effectiveness of ADR compared with comparative therapies (including non-operative therapy; spinal fusion; other surgery)?
2. What is the evidence related to the ADR safety profile? (including device failure, reoperation)
3. What is the evidence of differential efficacy or safety issues amongst special populations (including but not limited to the elderly and workers compensation populations)?
4. What are the cost implications and cost effectiveness for ADR?

Study design

This report will focus on evidence that evaluates efficacy and effectiveness and has the least potential for bias. For Key Question 1, only randomized controlled trials (RCTs) and comparative studies with concurrent controls will be considered (N≥50 for lumbar ADR; N≥100 for cervical ADR). For Key Question 2, adverse events or harms reported in the RCTs and nonrandomized studies included for Key Question 1 will be included; in addition, summaries of case series with the evaluation of safety as a primary study objective may be considered and very briefly summarized to provide additional context. High quality systematic reviews will be appraised and incorporated if feasible. RCTs and comparative cohort studies with concurrent controls and low risk of bias published subsequent to such reviews and will be evaluated based on the PICO inclusion/exclusion criteria. As this report serves to update the 2008 assessment, only comparative studies published subsequent to that review will be included and described; results will be described based on the context of previous findings. For Key Question 3, RCTs which stratify on patient or other characteristics and formally evaluate statistical interaction (effect modification) will be sought. For Key Question 4 only full, formal economic studies (i.e., cost-effectiveness, cost-utility, cost-minimization, and cost-benefit studies) will be considered.

Analytic framework



HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on three questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are evidence-based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective[1] as expressed by the following standards[2]:

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms[3]:

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.

[1] Based on Legislative mandate: See RCW 70.14.100(2).

[2] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

[3] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

Using evidence as the basis for a coverage decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. Availability of Evidence:

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. Sufficiency of the Evidence:

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence[4] using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- The amount of evidence (sparse to many number of evidence or events or individuals studied);
- Consistency of evidence (results vary or largely similar);
- Recency (timeliness of information);
- Directness of evidence (link between technology and outcome);
- Relevance of evidence (applicability to agency program and clients);
- Bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. Factors for Consideration - Importance

At the end of discussion a vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

[4] Based on GRADE recommendation: http://www.gradeworkinggroup.org/FAQ/index.htm

- Risk of event occurring;
- The degree of harm associated with risk;
- The number of risks; the burden of the condition;
- Burden untreated or treated with alternatives;
- The importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- The degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- Value variation based on patient preference.

Clinical Committee Findings and Decisions

Efficacy Considerations

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value?
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy?
  - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices?

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
  - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
  - Adverse effect on health that can result in lasting harm or can be life-threatening?
- Other morbidity concerns?
- Short term or direct complication versus long term complications?
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives?
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?

Next Step: Cover or No Cover

If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions

If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?
    - Refer to evidence identification document and discussion.
    - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
    - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
    - What are the known conditions/criteria and evidence state
    - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Clinical Committee Evidence Votes

First Voting Question

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there? (Applies to the population in the PICO for this review)

Safety Outcomes	Importance of Outcome	Safety Evidence / Confidence in Evidence
Revision/secondary surgery		
Device-related adverse events		
Serious/major adverse events		

Efficacy – Effectiveness Outcomes	Importance of Outcome	Efficacy / Effectiveness Evidence
Clinical success		
Neck Disability Index		
Neurological success		
Pain reduction		
Function/Disability		

Cost Outcomes	Importance of Outcome	Cost Evidence
Cost-utility		
Cost-effectiveness		
Direct cost		

Special Population / Considerations Outcomes	Importance of Outcome	Special Populations/ Considerations Evidence

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

For Safety: Is there sufficient evidence that the technology is safe for the indications considered?

Unproven (no)	Less (yes)	Equivalent (yes)	More in some (yes)	More in all

For Efficacy/Effectiveness: Is there sufficient evidence that the technology has a meaningful impact on patients and patient care?

Unproven (no)	Less (yes)	Equivalent (yes)	More in some (yes)	More in all

For Cost Outcomes/Cost-Effectiveness: Is there sufficient evidence that the technology is cost-effective for the indications considered?

Unproven (no)	Less (yes)	Equivalent (yes)	More in some (yes)	More in all

Discussion

Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second Vote

Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____Not Covered _____ Covered Unconditionally _____ Covered Under Certain Conditions

Discussion Item

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Next Step: Proposed Findings and Decision and Public Comment

At the next public meeting the committee will review the proposed findings and decision and consider any public comments as appropriate prior to a vote for final adoption of the determination.

1) Based on public comment was evidence overlooked in the process that should be considered?

2) Does the proposed findings and decision document clearly convey the intended coverage determination based on review and consideration of the evidence?

Next Step: Final Determination

Following review of the proposed findings and decision document and public comments:

Final Vote

Does the committee approve the Findings and Decisions document with any changes noted in discussion?

If yes, the process is concluded.

If no, or an unclear (i.e., tie) outcome Chair will lead discussion to determine next steps.

Medicare Coverage and Guidelines

[From page 99 of the Final Evidence Report]

Lumbar Artificial Disc Replacement (L-ADR)

- **Centers for Medicare and Medicaid Services National Coverage Decisions:** CMS has determined that L-ADR is not covered for Medicare beneficiaries over 60 years of age.

Cervical Artificial Disc Replacement (C-ADR)

- **Centers for Medicare and Medicaid Services National Coverage Decisions:** CMS does not have a NCD for C-ADR.

Guidelines

[From pages 70-71 of Final Evidence Report]

Table 2. Summary of Clinical Guidelines

Guideline	Evidence Base	Recommendation	Rating/ Strength of Recommendation
Lumbar			
American Pain Society *Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: an evidence-based clinical practice guideline from the American Pain Society (2009)*[32]	1 SR of 161 RCTs	For patients with non-radicular low back pain, L-ADR for single-level degenerative disc diseases is recommended through 2 years.	B/Fair*
State of Colorado Department of Labor and Employment, Division of Workers' Compensation *Low back pain medical treatment guidelines (2014)*[36]	L-ADR: NR	In patients with low back pain: • There is some evidence that L-ADR has a slight advantage over multidisciplinary intensive treatment for 60 hours over 5 weeks. • There is strong evidence that L-ADR is not inferior to fusion at 24 months for relief of back pain, reduction of disability, and provision of patient satisfaction. • There is good evidence that the Charites disc is not inferior to allograft fusion with the BAK cage for single-level disease and some evidence that the ProDisc is non-inferior to circumferential fusions with iliac crest autograft for single-level disease. • There is some evidence that a two-level lumbar disc replacement is not inferior to circumferential fusion in patients with 2-level DDD 24 months after surgery. • There is good evidence from a comparison of ProDisc-L versus circumferential fusion that arthroplasty is not inferior to fusion and for preservation of motion over fusions. • There is some evidence from a five-year follow-up of ProDisc-L versus circumferential fusion that arthroplasty reduces the risk of adjacent disease.	NR

Guideline	Evidence Base	Recommendation	Rating/ Strength of Recommendation
American College of Occupational and Environmental Medicine (ACOEM)† *Low back disorders (2011)*[2]	NR	For low back disorders, ACOEM **does not recommend:** • ADR for chronic non-specific LBP; • ADR for radicular pain syndromes, including sciatica; or • ADR for spinal stenosis.	 I‡ I‡ I‡
Cervical			
North American Spine Society (NASS) *Diagnosis and Treatment of Cervical Radiculopathy from Degenerative Disorders (2010)*[155]	2 RCTs	ACDF and C-ADR are suggested to be comparable treatments, resulting in similarly successful short term outcomes, for single level degenerative cervical radiculopathy. However, more long term follow-up and additional independent, masked, prospective RCTs are needed to further validate these results.	B§
State of Colorado Department of Labor and Employment, Division of Workers' Compensation *Cervical spine injury medical treatment guidelines (2014)*[35]	C-ADR: 2 SRs	For cervical spine injury patients with single-level radiculopathy or myelopathy: • There is strong evidence that C-ADR produces 2 year success rates at least equal to those of ACDF with allograft interbody fusion and an anterior plate. • There is some evidence that C-ADR requires fewer revision operations than ACDF after the first two years of treatment, and that C-ADR slightly decreases neck pain at 5 years compared to ACDF. • There is good evidence that arthroplasty produces greater segmental range of motion after 1-2 years than fusion, but the clinical significance is unknown.	NR
American College of Occupational and Environmental Medicine (ACOEM)‡ *Cervical and thoracic spine disorders (2011)*[1]	NR	For cervical and thoracic spine disorders, ACOEM **does not recommend:** • ADR for chronic cervicothoracic pain; or • ADR for chronic non-specific cervical pain. For cervical and thoracic spine disorders, ACOEM **does recommend:** • ADR for subacute or chronic radiculopathy; and • ADR for myelopathy.	 I‡ I‡ B‡ B‡