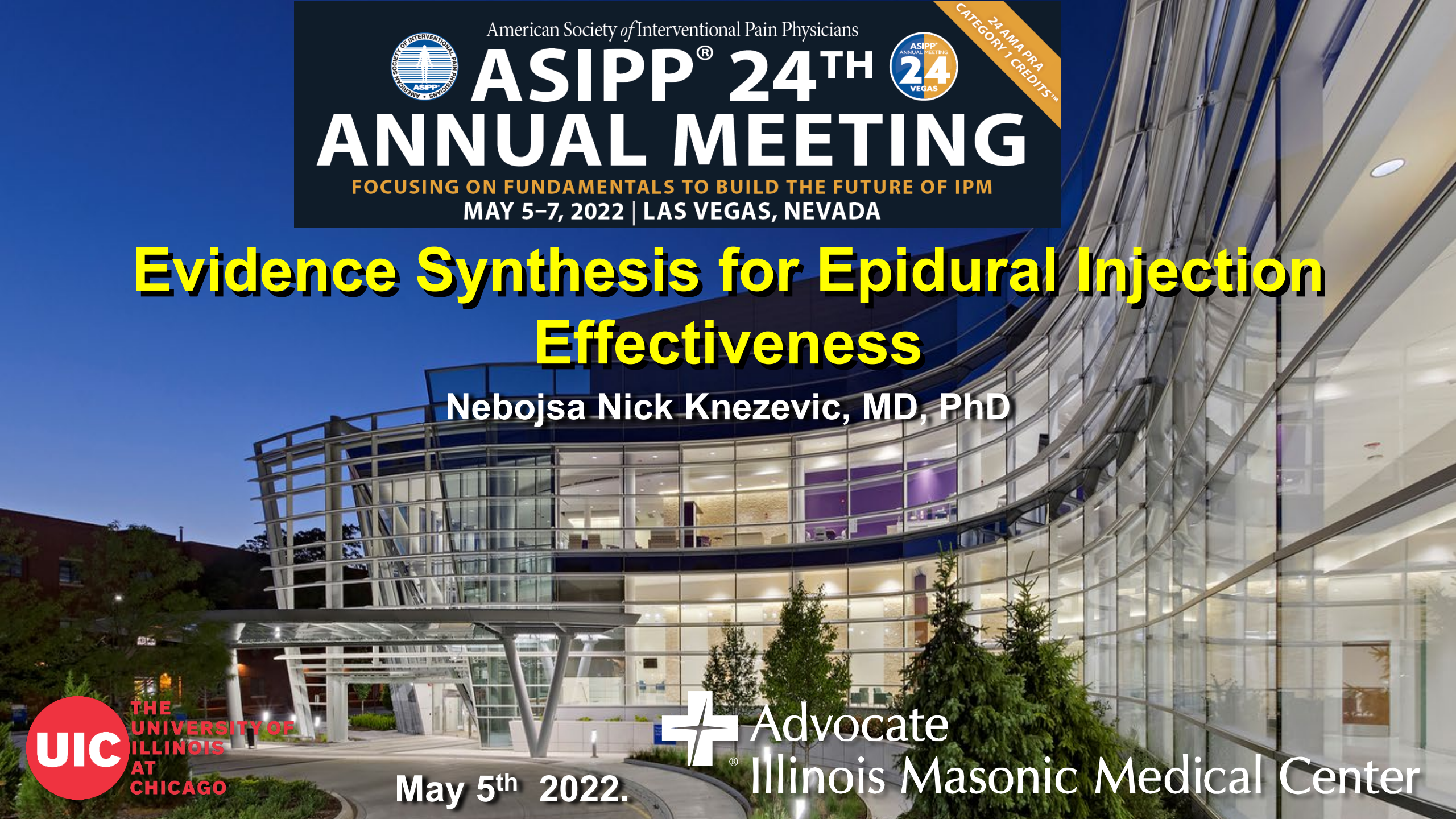
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FOCUSING ON FUNDAMENTALS TO BUILD THE FUTURE OF IPM
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Evidence Synthesis for Epidural Injection Effectiveness
Nebojsa Nick Knezevic, MD, PhD
THE UNIVERSITY OF ILLINOIS AT CHICAGO
May 5th 2022.
Advocate Illinois Masonic Medical Center

Disclaimer

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- President of the Illinois Society of Interventional Pain Physicians
- Section Editor – Pain Physician & Pain Practice
- Assistant Editor – Anesthesia & Analgesia; Editorial Board of Pain Medicine Case Reports

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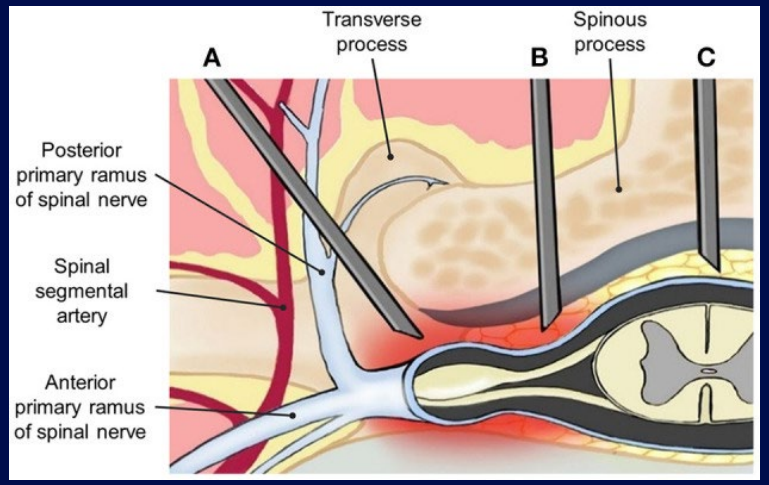
A Comparative Systematic Review and Meta-Analysis of 3 Routes of Administration of Epidural Injections in Lumbar Disc Herniation

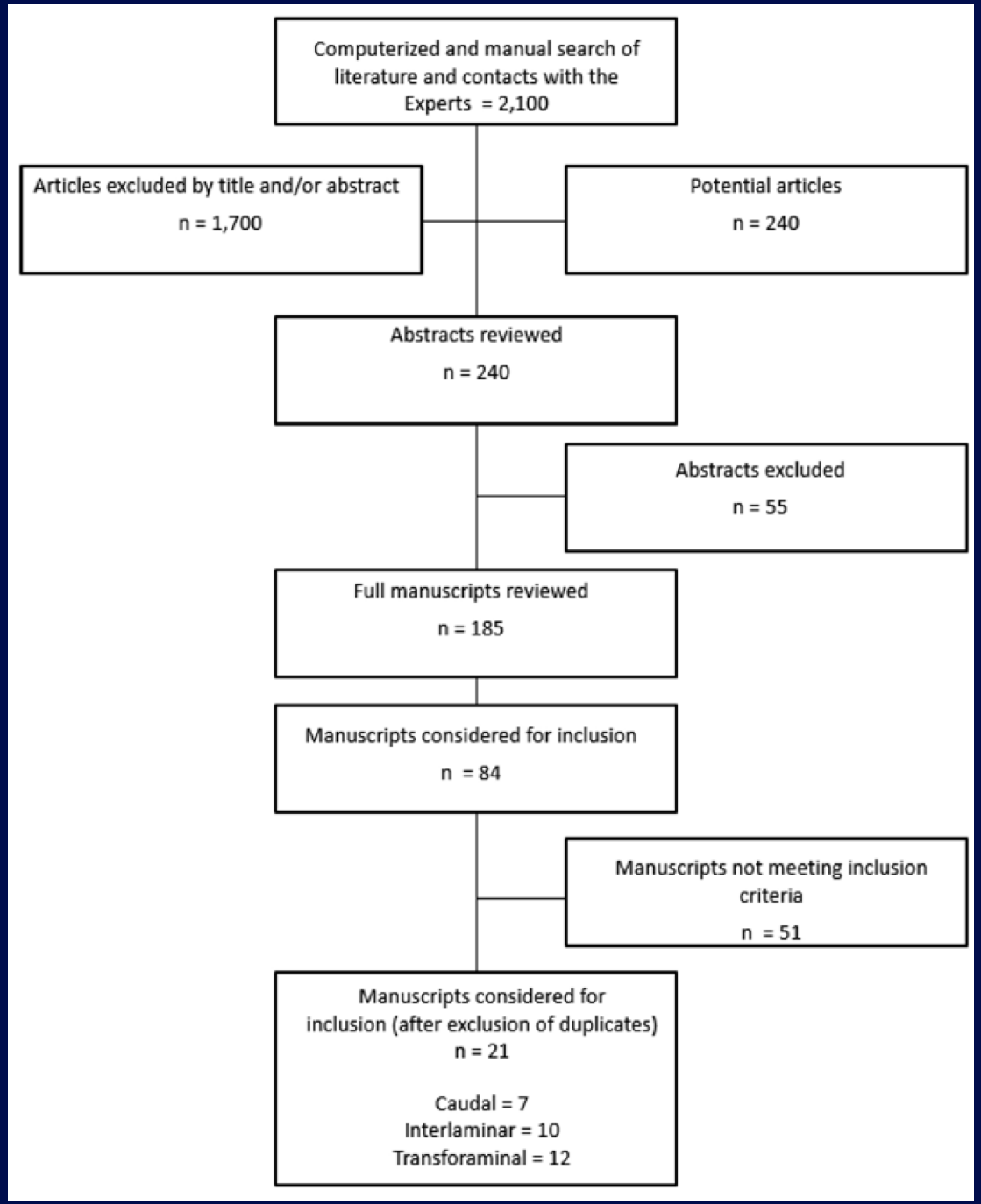
Laxmaiah Manchikanti, MD[1], Emilija Knezevic[2], Nebojsa Nick Knezevic, MD, PhD[3], Bramha Prasad Vangala, MBBS[4], Mahendra R. Sanapati, MD[1], Srinivasa Thota, MD[1], Salahadin Abdi, MD, PhD[5], Alaa Abd-Elsayed, MD[6], Alan D. Kaye, MD, PhD[7], and Joshua A. Hirsch, MD[8]

Pain Physician 2021; 24:425-440

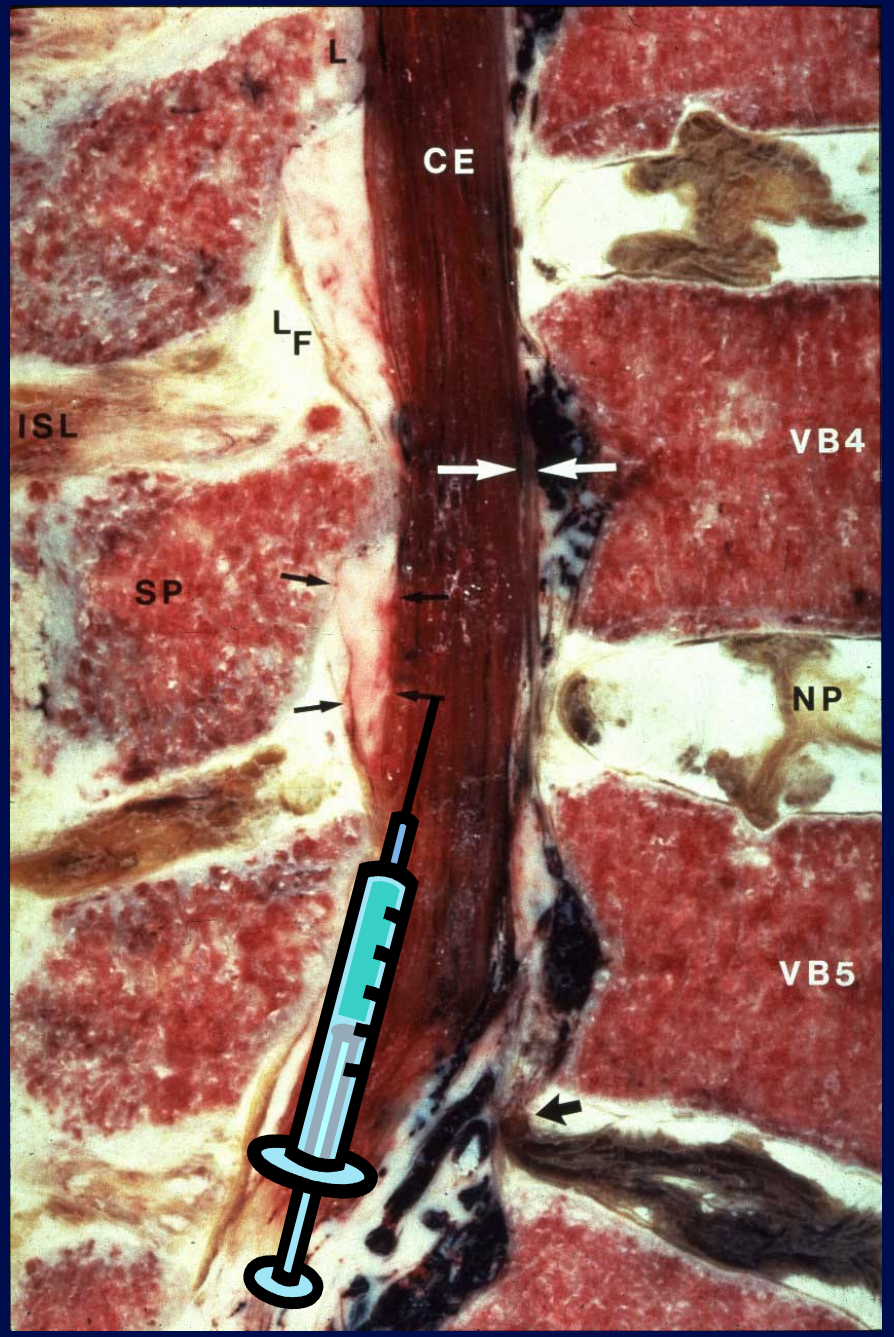
- Objectives: To assess the efficacy of 3 routes of administration of epidural injections for lumbar disc herniation, including 21 RCTs



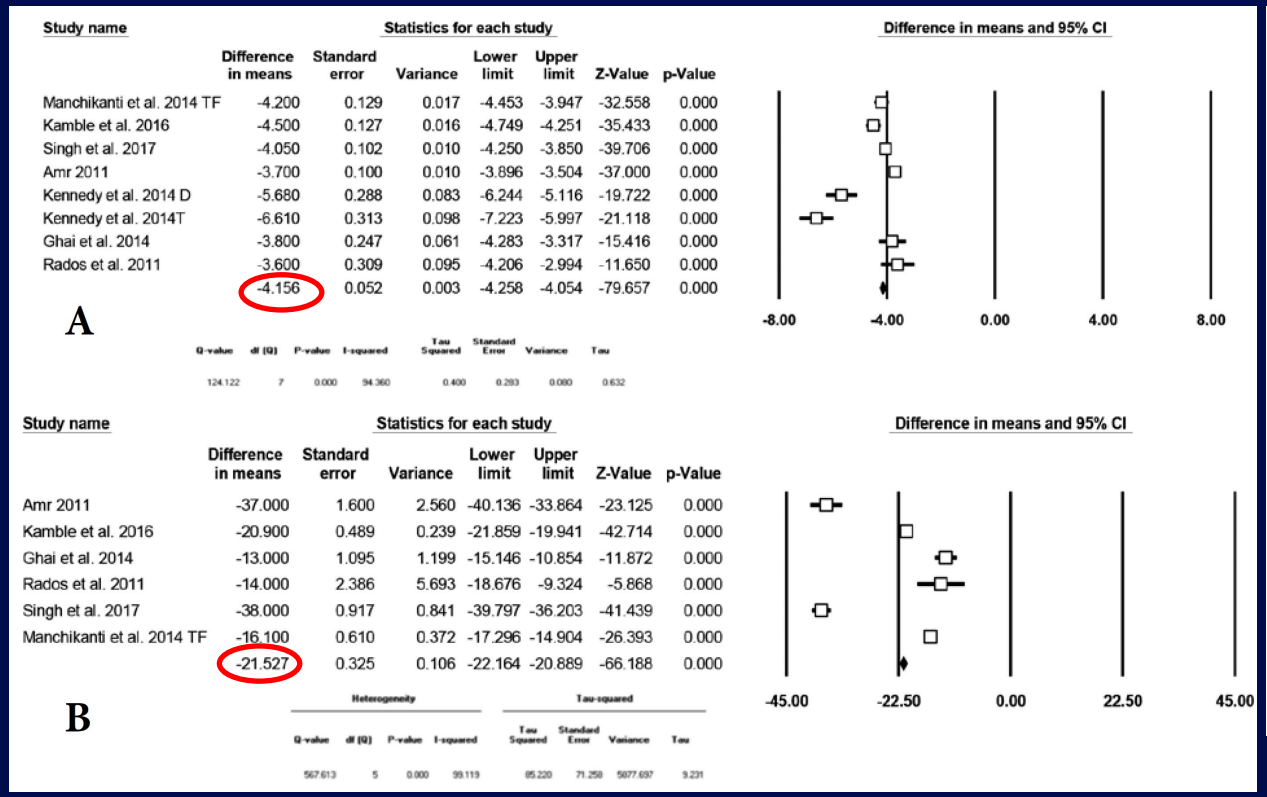
Knezevic NN, Paredes S, Cantillo S, Hamid A and Candido KD (2021) Parasagittal Approach of Epidural Steroid Injection as a Treatment for Chronic Low Back Pain: A Systematic Review and Meta-Analysis. Front. Pain Res. 2:676730.



Sagittal
TFESI



Pain Physician 2021; 24:425-440



Single-arm meta-analyses testing the effects of transforaminal epidural steroid injections on pain and functionality at 6 and 12 months.

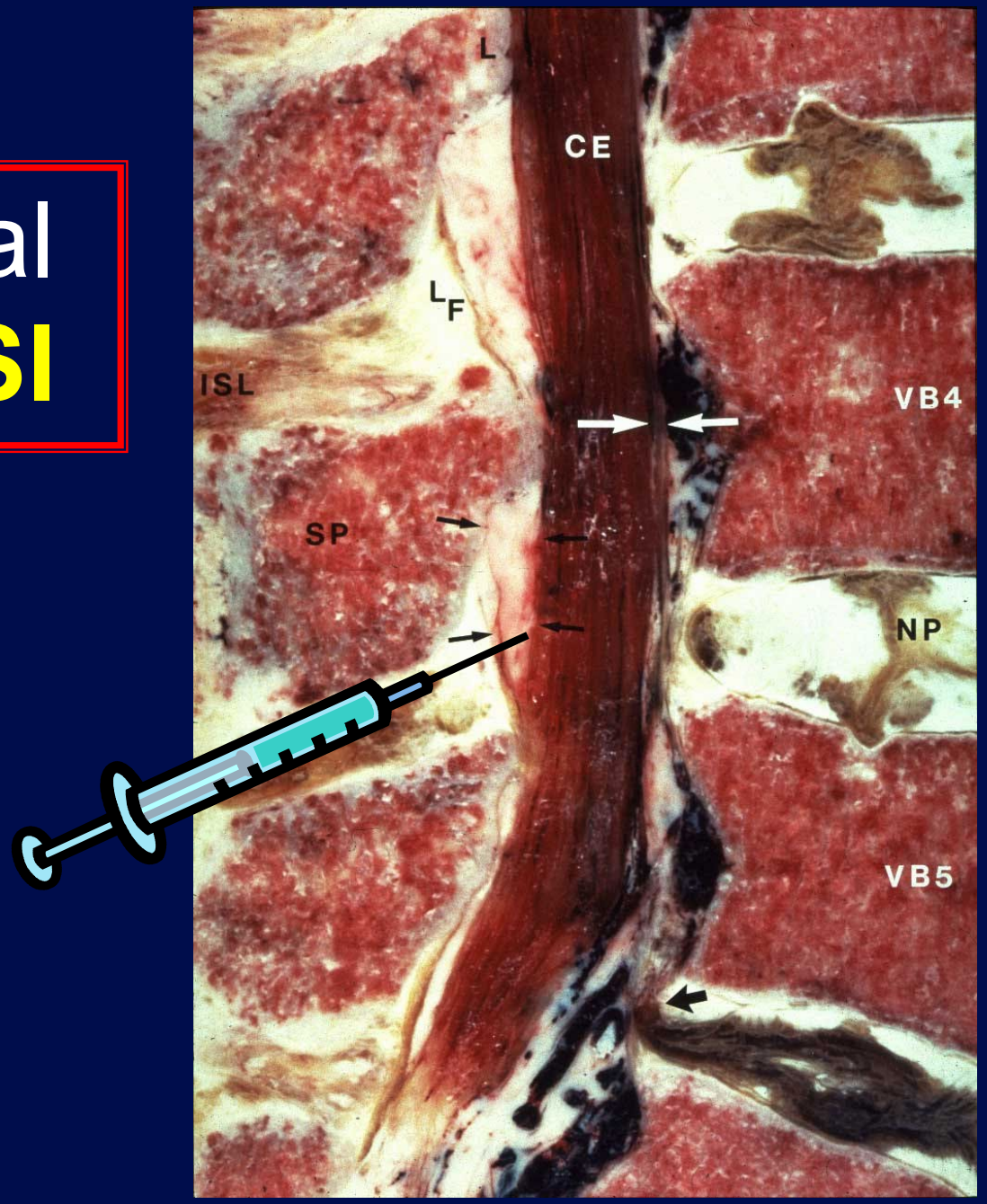
A. Change in pain level at 6 months

B. Change in functionality level at 6 months

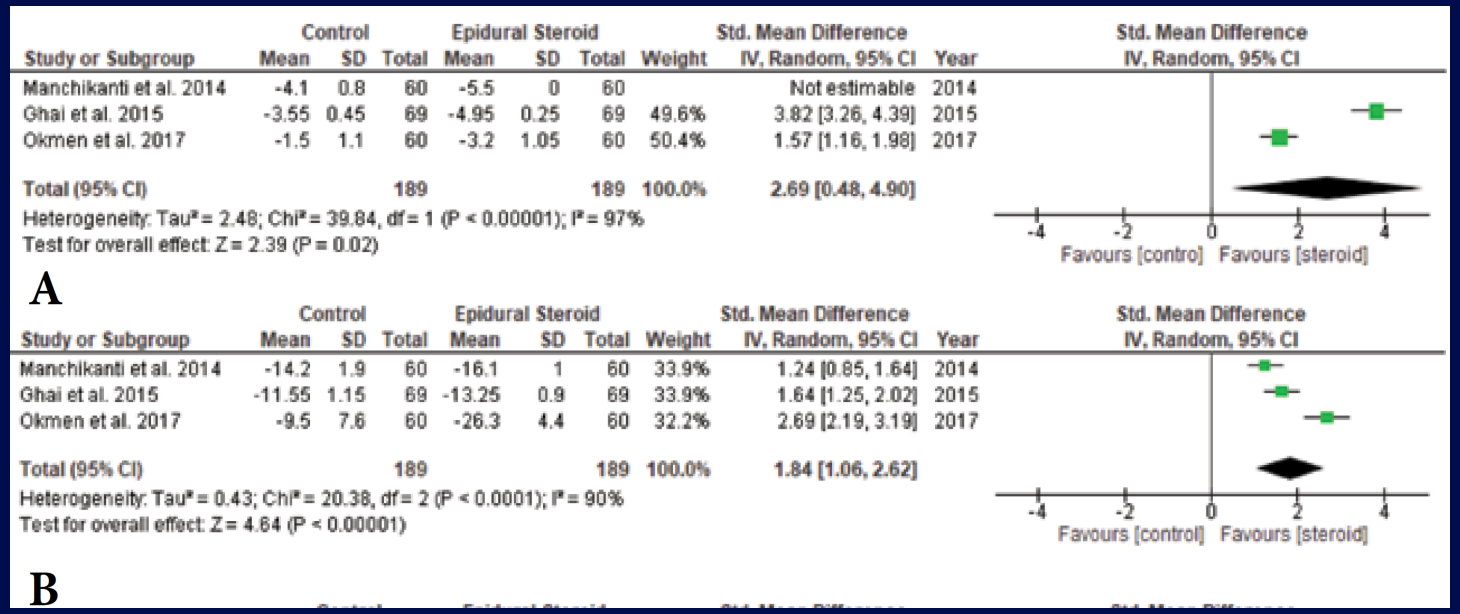
C. Change in pain level at 12 months

D. Change in functionality level at 12 months

Sagittal
IL LESI



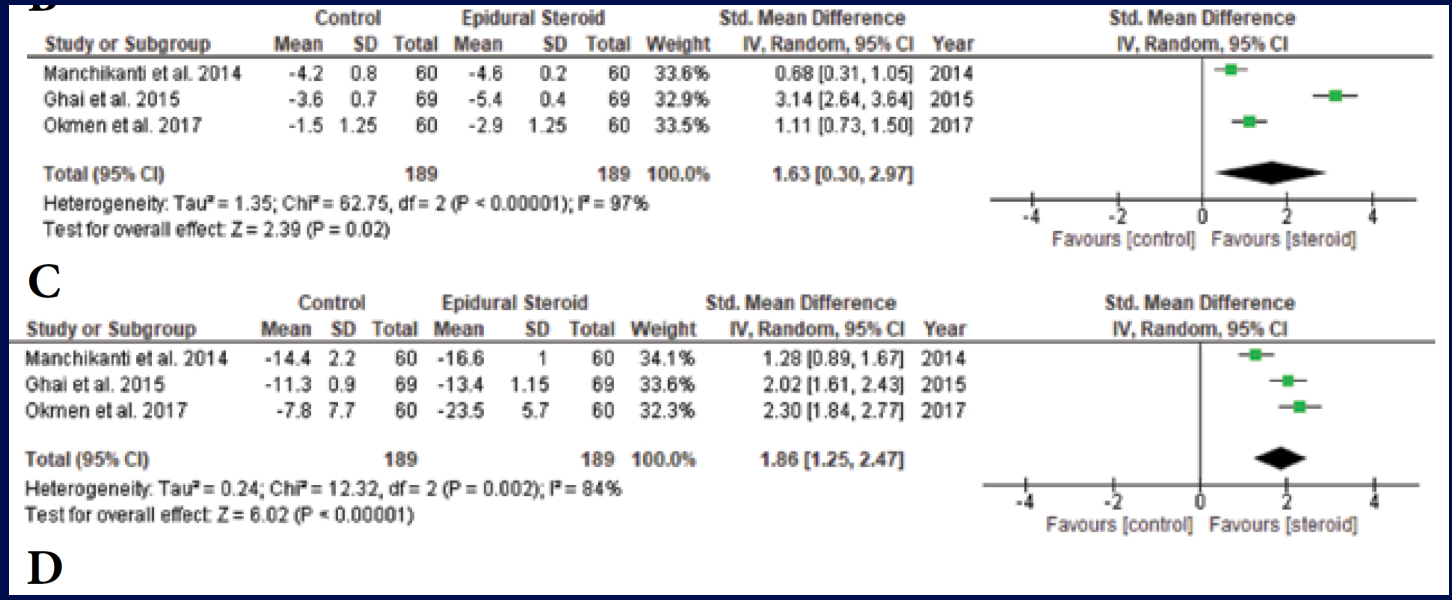
Pain Physician 2021; 24:425-440



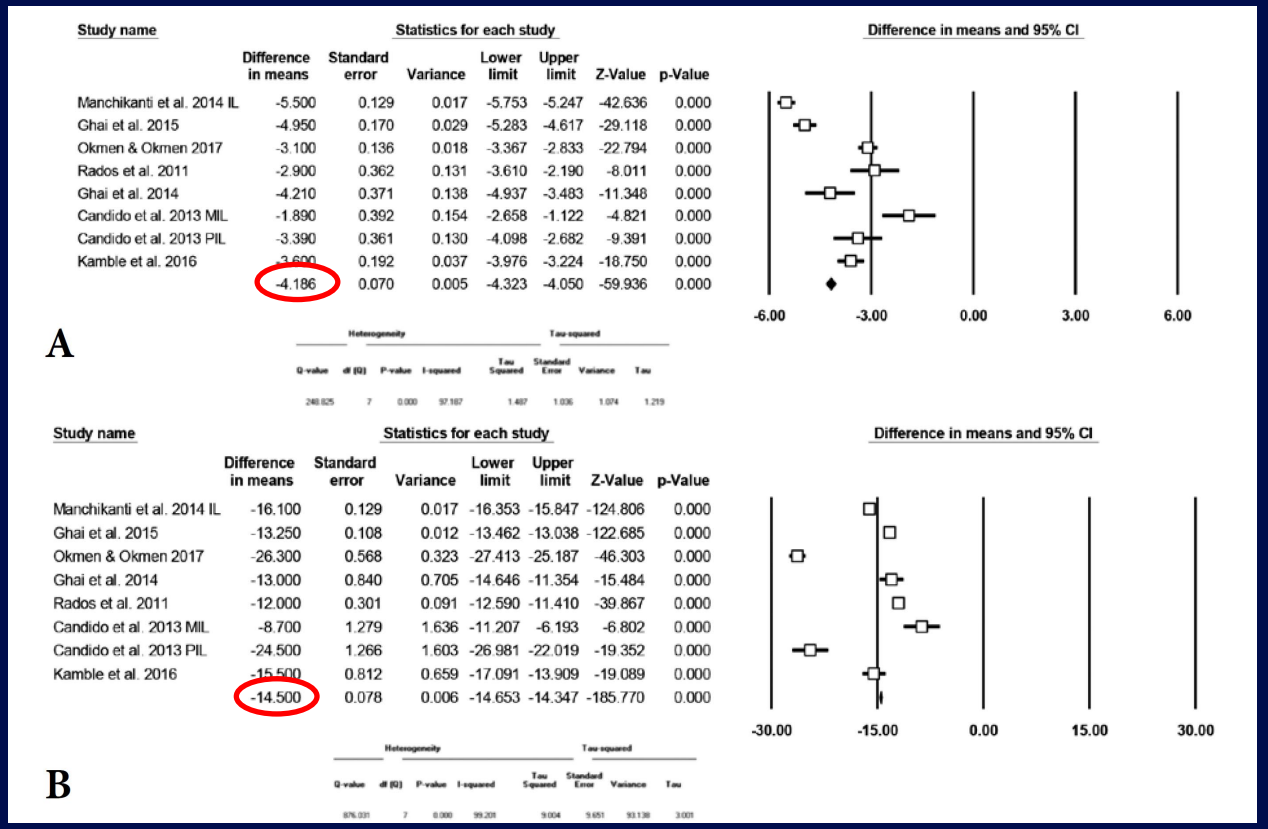
378 pts.

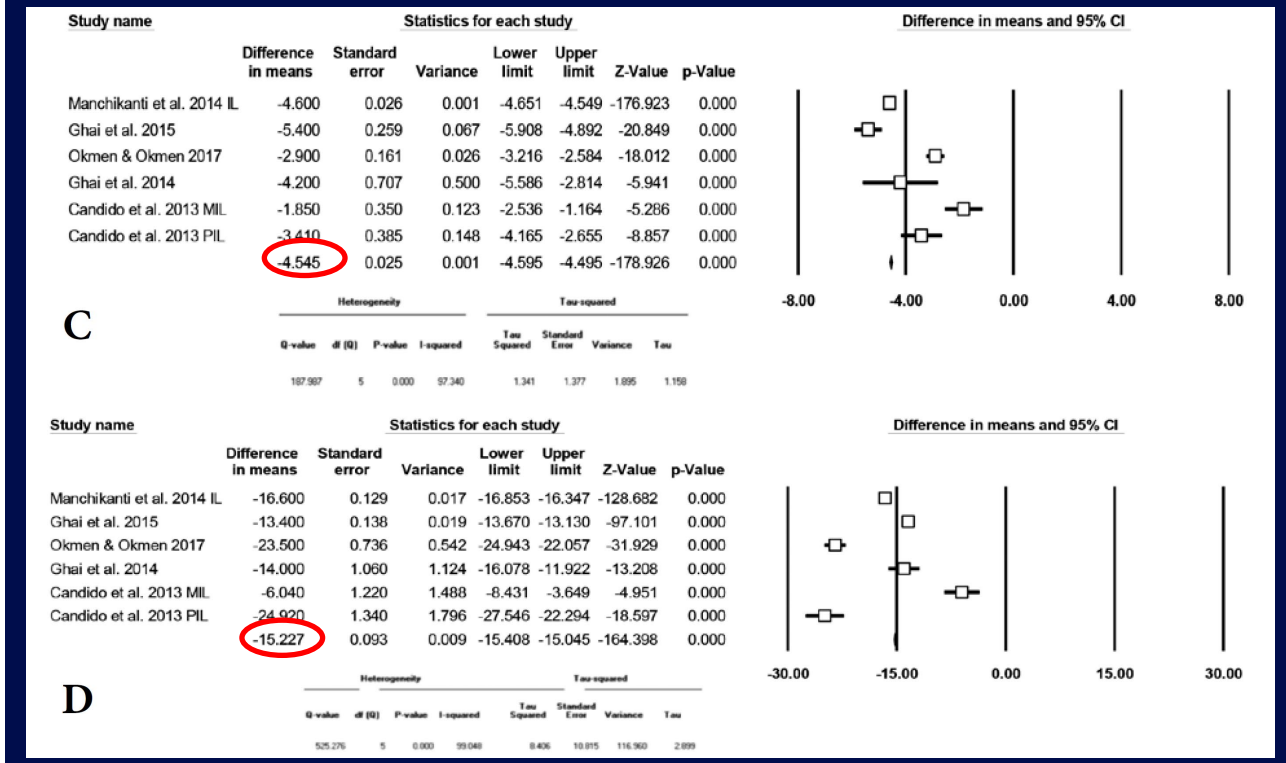
Dual-arm meta-analyses testing the effects of interlaminar epidural steroid injections on pain and functionality at 6 and 12 months.

A. Change in pain level at 6 months
B. Change in functionality at 6 months
C. Change in pain at 12 months
D. Change in functionality at 12 months



Pain Physician 2021; 24:425-440





Single-arm meta-analysis testing the effects of interlaminar epidural steroid injections on pain and functionality at 6 and 12 months.

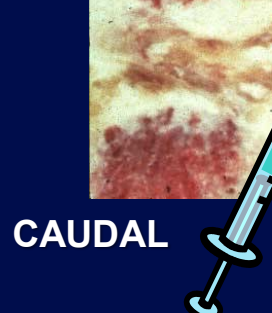
A. Change in pain level at 6 months

B. Change in functionality level at 6 months

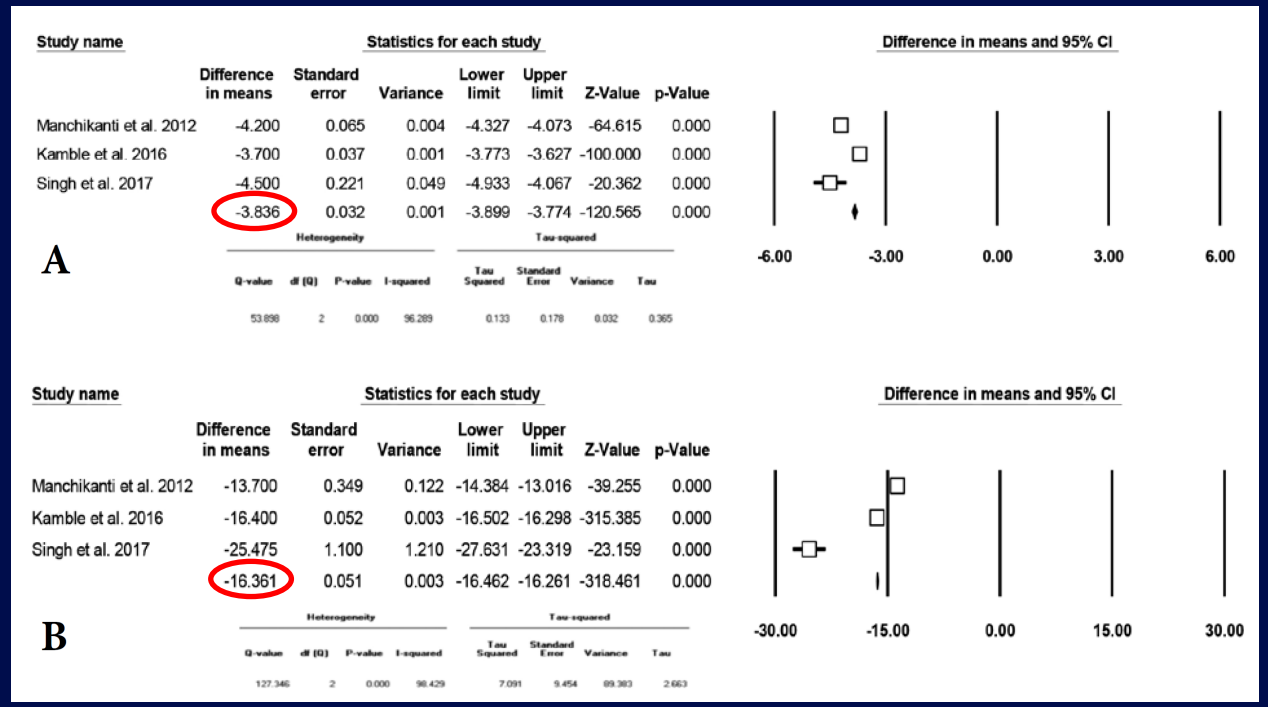
C. Change in pain level at 12 months

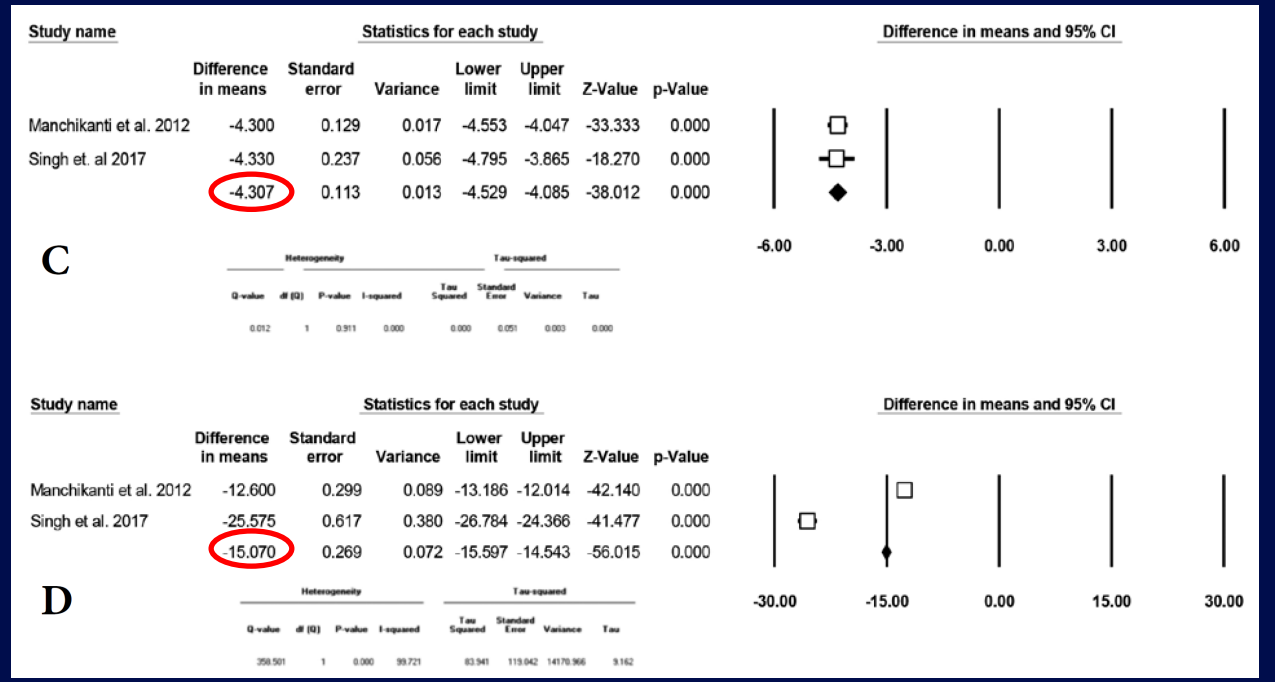
D. Change in functionality level at 12 months

Sagittal
CAUDAL



Pain Physician 2021; 24:425-440





Single-arm meta-analysis testing the effects of caudal epidural steroid injections on pain and functionality at 6 and 12 months.

A. Change in pain level at 6 months
B. Change in functionality level at 6 months
C. Change in pain level at 12 months
D. Change in functionality level at 12 months

A Comparative Systematic Review and Meta-Analysis of 3 Routes of Administration of Epidural Injections in Lumbar Disc Herniation

Laxmaiah Manchikanti, MD[1], Emilija Knezevic[2], Nebojsa Nick Knezevic, MD, PhD[3], Bramha Prasad Vangala, MBBS[4], Mahendra R. Sanapati, MD[1], Srinivasa Thota, MD[1], Salahadin Abdi, MD, PhD[5], Alaa Abd-Elsayed, MD[6], Alan D. Kaye, MD, PhD[7], and Joshua A. Hirsch, MD[8]

Pain Physician 2021; 24:425-440

Conclusions

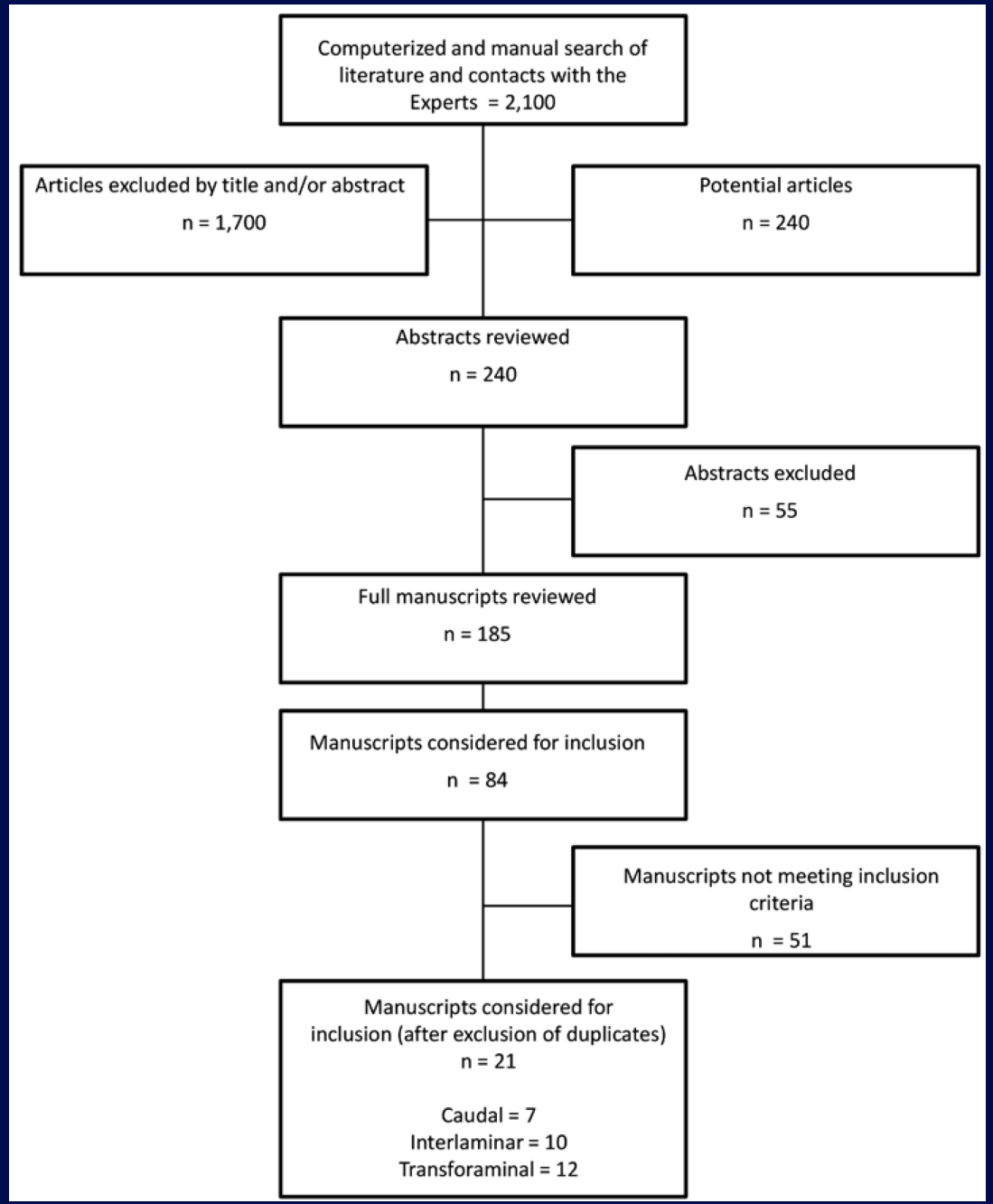
- Epidural injections with local anesthetic and steroids showed **Level I** evidence for transforaminal and interlaminar approaches, whereas with *local anesthetic alone* **Level II** evidence was demonstrated
- Caudal epidural injections showed **Level II** evidence with local anesthetic with steroids or local anesthetic alone

Epidural Injections for Lumbar Radiculopathy or Sciatica: A Comparative Systematic Review and Meta-Analysis of Cochrane Review

Laxmaiah Manchikanti, MD[1], Emilija Knezevic[2], Nebojsa Nick Knezevic, MD, PhD[3], Mahendra R. Sanapati, MD[1], Srinivasa Thota, MD[1], Alaa Abd-Elsayed, MD[4], and Joshua A. Hirsch, MD[5]

Pain Physician 2021; 24:E539-E554

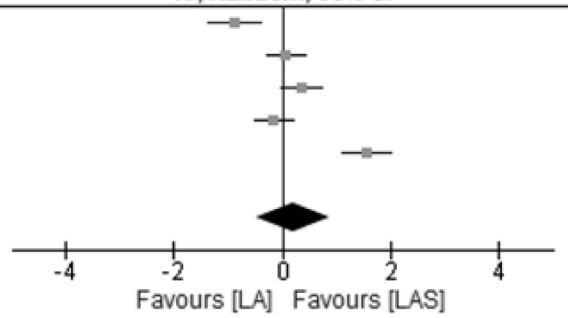
- Objectives: To assess the efficacy of 3 categories of epidural injections for lumbar radiculopathy or sciatica performed utilizing saline with steroids, local anesthetic alone, or steroids with local anesthetic, including 21 RCTs



2A

Study or Subgroup	LA Mean	LA SD	LA Total	LAS Mean	LAS SD	LAS Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ghai et al. 2015	-5	1.6	34	-3.5	1.75	35	19.3%	-0.88 [-1.38, -0.39]
Manchikanti et al. 2012	-4.2	1.35	60	-4.3	1.3	60	20.3%	0.07 [-0.28, 0.43]
Manchikanti et al. 2014 IL	-4.1	1.2	60	-4.5	1	60	20.3%	0.36 [-0.00, 0.72]
Manchikanti et al. 2014 TF	-4.3	1.2	60	-4.1	1.3	60	20.3%	-0.16 [-0.52, 0.20]
Ökmen & Ökmen 2017	-1.5	1.1	50	-3.2	1.05	48	19.7%	1.57 [1.11, 2.02]
Total (95% CI)			**264**			**263**	**100.0%**	**0.19 [-0.49, 0.87]**

Heterogeneity: Tau² = 0.56; Chi² = 58.13, df = 4 (P < 0.00001); I² = 93%
Test for overall effect: Z = 0.56 (P = 0.58)



2B

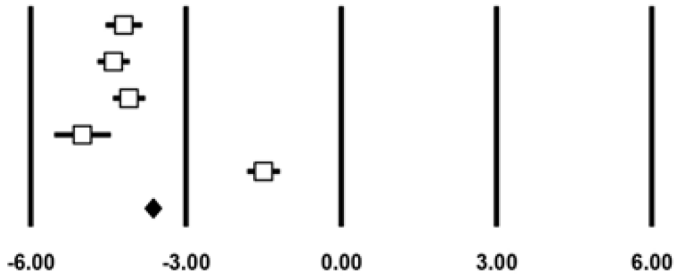
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2012	-4.200	0.174	0.030	-4.541	-3.859	-24.138	0.000
Manchikanti et al. 2014 TF	-4.400	0.155	0.024	-4.704	-4.096	-28.405	0.000
Manchikanti et al. 2014 IL	-4.100	0.155	0.024	-4.404	-3.796	-26.452	0.000
Ghai et al. 2015	-5.000	0.274	0.075	-5.537	-4.463	-18.248	0.000
Ökmen & Ökmen 2017	-1.500	0.156	0.024	-1.806	-1.194	-9.615	0.000
	-3.637	0.077	0.006	-3.787	-3.487	-47.525	0.000

Heterogeneity

Q-value	df (Q)	P-value	I-squared
256.055	4	0.000	98.438

Tau-squared

Tau Squared	Standard Error	Variance	Tau
1.894	1.427	2.036	1.376



2C

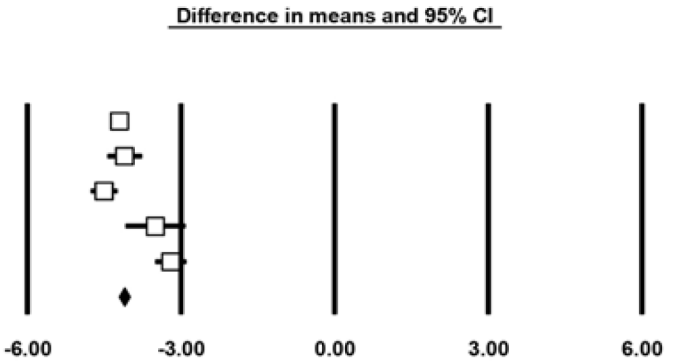
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2012	-4.200	0.065	0.004	-4.327	-4.073	-64.615	0.000
Manchikanti et al. 2014 TF	-4.100	0.168	0.028	-4.429	-3.771	-24.405	0.000
Manchikanti et al. 2014 IL	-4.500	0.129	0.017	-4.753	-4.247	-34.884	0.000
Ghai et al. 2015	-3.500	0.295	0.087	-4.078	-2.922	-11.864	0.000
Ökmen & Ökmen 2017	-3.200	0.152	0.023	-3.498	-2.902	-21.053	0.000
	-4.105	0.051	0.003	-4.204	-4.005	-80.749	0.000

Heterogeneity

Q-value	df (Q)	P-value	I-squared
51.168	4	0.000	92.183

Tau-squared

Tau Squared	Standard Error	Variance	Tau
0.210	0.193	0.037	0.458



Pain Physician 2021; 24:E539-E554

527 pts.

Change in pain level using NRS from baseline at 6 months.

A) Change in pain level at 6 months (local anesthetic vs. local anesthetic with steroid).

B) Change in pain level at 6 months (local anesthetic).

C) Change in pain level at 6 months (local anesthetic with steroid).

Pain Physician 2021; 24:E539-E554

527 pts.

Change in **functionality** level using ODI from baseline at **6 months**.

A) Change in functionality level at 6 months (**local anesthetic** vs. **local anesthetic with steroids**).

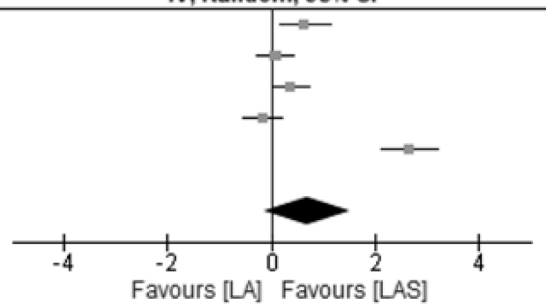
B) Change in functionality level at 6 months (**local anesthetic**).

C) Change in functionality level at 6 months (**local anesthetic with steroid**).

3A

Study or Subgroup	LA Mean	LA SD	LA Total	LAS Mean	LAS SD	LAS Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ghai et al. 2015	-13	6.75	34	-17	5.5	35	19.7%	0.64 [0.16, 1.13]
Manchikanti et al. 2012	-13.7	5.95	60	-14.2	5.9	60	20.3%	0.08 [-0.27, 0.44]
Manchikanti et al. 2014 IL	-14.2	5.65	60	-16.1	4.7	60	20.3%	0.36 [0.00, 0.72]
Manchikanti et al. 2014 TF	-14.7	5.75	60	-13.7	5.95	60	20.3%	-0.17 [-0.53, 0.19]
Okmen & Okmen 2017	-9.5	7.6	50	-26.3	4.4	48	19.3%	2.67 [2.12, 3.22]
Total (95% CI)			**264**			**263**	**100.0%**	**0.70 [-0.11, 1.51]**

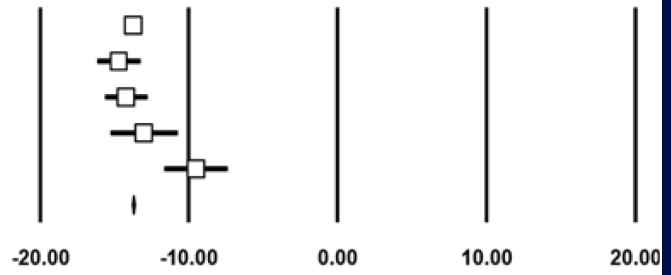
Heterogeneity: Tau² = 0.81; Chi² = 78.94, df = 4 (P < 0.00001); I² = 95%
Test for overall effect: Z = 1.68 (P = 0.09)



3B

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2012	-13.700	0.045	0.002	-13.788	-13.612	-304.444	0.000
Manchikanti et al. 2014 TF	-14.700	0.742	0.551	-16.154	-13.246	-19.811	0.000
Manchikanti et al. 2014 IL	-14.200	0.729	0.531	-15.629	-12.771	-19.479	0.000
Ghai et al. 2015	-13.000	1.150	1.323	-15.254	-10.746	-11.304	0.000
Ökmen & Ökmen 2017	-9.500	1.070	1.145	-11.597	-7.403	-8.879	0.000
	-13.697	0.045	0.002	-13.785	-13.609	-306.018	0.000

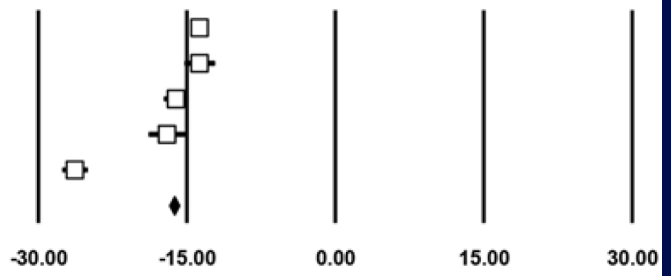
Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
10.061	4	0.001	77.852	1.329	1.487	2.210	1.153



3C

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2012	-13.700	0.349	0.122	-14.384	-13.016	-39.255	0.000
Manchikanti et al. 2014 TF	-13.700	0.768	0.590	-15.205	-12.195	-17.839	0.000
Manchikanti et al. 2014 IL	-16.100	0.607	0.368	-17.290	-14.910	-26.524	0.000
Ghai et al. 2015	-17.000	0.929	0.863	-18.821	-15.179	-18.299	0.000
Ökmen & Ökmen 2017	-26.300	0.635	0.403	-27.545	-25.055	-41.417	0.000
	-16.258	0.248	0.062	-16.744	-15.772	-65.554	0.000

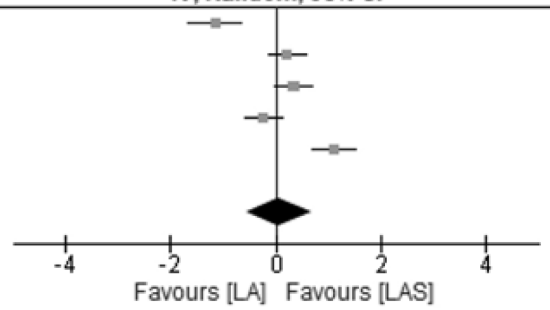
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
315.609	4	0.000	98.733	28.273	22.985	528.301	5.317



4A

Study or Subgroup	LA Mean	LA SD	LA Total	LAS Mean	LAS SD	LAS Total	Weight	Std. Mean Difference IV, Random, 95% CI
Ghai et al. 2015	-5.5	1.5	34	-3.5	1.9	35	19.1%	-1.15 [-1.67, -0.64]
Manchikanti et al. 2012	-4	1.35	60	-4.3	1.4	60	20.4%	0.22 [-0.14, 0.58]
Manchikanti et al. 2014 IL	-4.2	1.2	60	-4.6	1.1	60	20.4%	0.35 [-0.02, 0.71]
Manchikanti et al. 2014 TF	-4.4	1.25	60	-4.1	1.25	60	20.4%	-0.24 [-0.60, 0.12]
Okmen & Okmen 2017	-1.5	1.25	50	-2.9	1.25	48	19.8%	1.11 [0.68, 1.54]
Total (95% CI)			**264**			**263**	**100.0%**	**0.07 [-0.56, 0.69]**

Heterogeneity: Tau² = 0.47; Chi² = 50.10, df = 4 (P < 0.00001); I² = 92%
Test for overall effect: Z = 0.21 (P = 0.84)

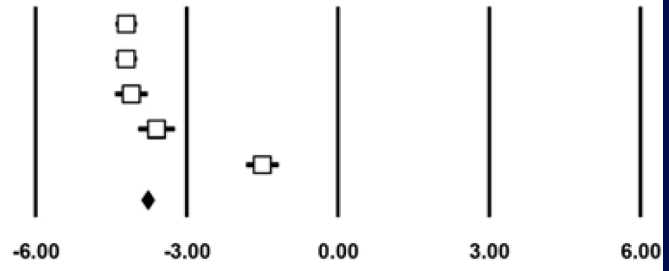


4B

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2012	-4.200	0.103	0.011	-4.402	-3.998	-40.777	0.000
Manchikanti et al. 2014 IL	-4.200	0.103	0.011	-4.402	-3.998	-40.777	0.000
Manchikanti et al. 2014 TF	-4.100	0.161	0.026	-4.416	-3.784	-25.466	0.000
Ghai et al. 2015	-3.600	0.181	0.033	-3.955	-3.245	-19.890	0.000
Ökmen & Ökmen 2017	-1.500	0.161	0.026	-1.816	-1.184	-9.317	0.000
	-3.773	0.058	0.003	-3.887	-3.660	-64.943	0.000

Statistics for each study

Difference in means and 95% CI



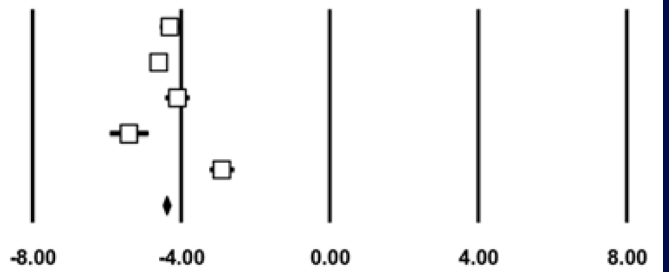
Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
238.729	4	0.000	98.324	1.053	0.822	0.676	1.026

4C

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2012	-4.300	0.129	0.017	-4.553	-4.047	-33.333	0.000
Manchikanti et al. 2014 IL	-4.600	0.060	0.004	-4.718	-4.482	-76.667	0.000
Manchikanti et al. 2014 TF	-4.100	0.161	0.026	-4.416	-3.784	-25.466	0.000
Ghai et al. 2015	-5.400	0.259	0.067	-5.908	-4.892	-20.849	0.000
Ökmen & Ökmen 2017	-2.900	0.161	0.026	-3.216	-2.584	-18.012	0.000
	-4.388	0.048	0.002	-4.483	-4.294	-90.993	0.000

Statistics for each study

Difference in means and 95% CI



Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
116.836	4	0.000	96.576	0.481	0.428	0.184	0.693

Pain Physician 2021; 24:E539-E554

527 pts.

Change in pain level using NRS from baseline at 12 months.

A) Change in pain level at 12 months (local anesthetic vs. local anesthetic with steroid).

B) Change in pain level at 12 months (local anesthetic).

C) Change in pain level at 12 months (local anesthetic with steroid).

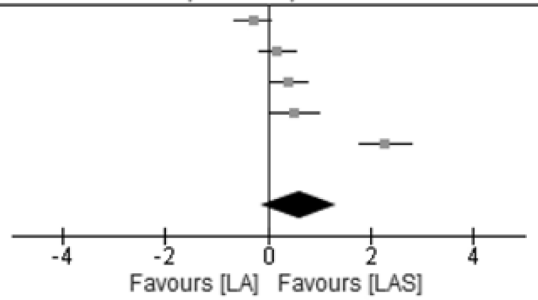
Pain Physician 2021; 24:E539-E554

527 pts.

5A

Study or Subgroup	LA Mean	LA SD	LA Total	LAS Mean	LAS SD	LAS Total	Weight	Std. Mean Difference IV, Random, 95% CI
Manchikanti et al. 2014 TF	-15.2	5.85	60	-13.5	5.95	60	20.3%	-0.29 [-0.65, 0.07]
Manchikanti et al. 2012	-13.7	6.17	60	-14.8	5.9	60	20.3%	0.18 [-0.18, 0.54]
Manchikanti et al. 2014 IL	-14.4	5.8	60	-16.6	4.7	60	20.3%	0.41 [0.05, 0.78]
Ghai et al. 2015	-13.5	6.75	34	-17	7	35	19.6%	0.50 [0.02, 0.98]
Okmen & Okmen 2017	-7.8	7.7	50	-23.5	5.7	48	19.4%	2.29 [1.78, 2.81]
Total (95% CI)			**264**			**263**	**100.0%**	**0.61 [-0.14, 1.35]**

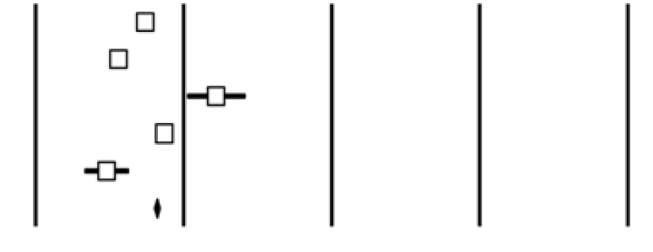
Heterogeneity: Tau² = 0.68; Chi² = 67.61, df = 4 (P < 0.00001); I² = 94%
Test for overall effect: Z = 1.59 (P = 0.11)



5B

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2012	-12.600	0.287	0.082	-13.163	-12.037	-43.902	0.000
Manchikanti et al. 2014 IL	-14.400	0.284	0.081	-14.957	-13.843	-50.704	0.000
Ökmen & Ökmen 2017	-7.800	0.994	0.988	-9.748	-5.852	-7.847	0.000
Ghai et al. 2015	-11.300	0.108	0.012	-11.512	-11.088	-104.630	0.000
Manchikanti et al. 2014 TF	-15.200	0.755	0.570	-16.680	-13.720	-20.132	0.000
	-11.809	0.094	0.009	-11.993	-11.624	-125.551	0.000

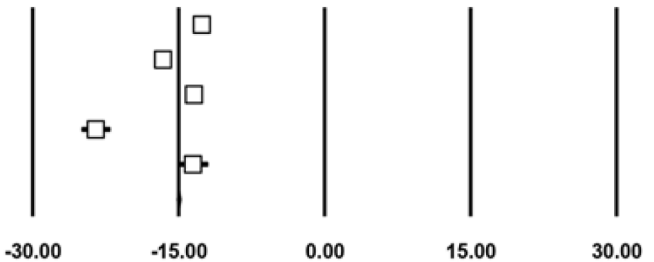
Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
149.481	4	0.000	97.324	3.210	3.255	10.598	1.792



5C

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2012	-12.600	0.299	0.089	-13.186	-12.014	-42.140	0.000
Manchikanti et al. 2014 IL	-16.600	0.129	0.017	-16.853	-16.347	-128.682	0.000
Ghai et al. 2015	-13.400	0.138	0.019	-13.670	-13.130	-97.101	0.000
Ökmen & Ökmen 2017	-23.500	0.736	0.542	-24.943	-22.057	-31.929	0.000
Manchikanti et al. 2014 TF	-13.500	0.768	0.590	-15.005	-11.995	-17.578	0.000
	-14.988	0.089	0.008	-15.161	-14.814	-169.122	0.000

Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
489.864	4	0.000	99.183	6.369	6.910	47.753	2.524



Change in **functionality** level using ODI from baseline at **12 months**.

A) Change in functionality level at 12 months (**local anesthetic** vs. **local anesthetic with steroids**).

B) Change in functionality level at 12 months (**local anesthetic**).

C) Change in functionality level at 12 months (**local anesthetic with steroid**).

Epidural Injections for Lumbar Radiculopathy or Sciatica: A Comparative Systematic Review and Meta-Analysis of Cochrane Review

Laxmaiah Manchikanti, MD[1], Emilija Knezevic[2], Nebojsa Nick Knezevic, MD, PhD[3], Mahendra R. Sanapati, MD[1], Srinivasa Thota, MD[1], Alaa Abd-Elsayed, MD[4], and Joshua A. Hirsch, MD[5]

Pain Physician 2021; 24:E539-E554

Conclusions

- Epidural injections with or without steroids for radiculopathy showed significant effectiveness with **Level I** or strong evidence for local anesthetic with steroids
- and **Level II to I** or moderate to strong evidence with local anesthetic alone

Epidural Interventions in the Management of Chronic Spinal Pain: American Society of Interventional Pain Physicians (ASIPP) Comprehensive Evidence-Based Guidelines

Laxmaiah Manchikanti, MD, Nebojsa Nick Knezevic, MD, PhD, Annu Navani, MD, Paul J. Christo, MD, Gerard Limerick, MD, PhD, Aaron K. Calodney, MD, Jay Grider, DO, PhD, Michael E. Harned, MD, Lynn Cintron, MD, Christopher G. Gharibo, MD, Shalini Shah, MD, Devi E. Nampiaparampil, MD, Kenneth D Candido, MD, Amol Soin, MD, Alan D. Kaye, MD, PhD, Radomir Kosanovic, MD, Trevor R. Magee, BS, Douglas P. Beall, MD, Sairam Atluri, MD, Myank Gupta, MD, Standiford Helm II, MD, Bradley W. Wargo, DO, Sudhir Diwan, MD, Steve M. Aydin, DO, Mark V. Boswell, MD, PhD, Bill W. Haney, MD, Sheri L. Albers, DO, Richard Latchaw, MD, Alaa Abd-Elsayed, MD, MPH, Ann Conn, MD, Hans Hansen, MD, Thomas T. Simopoulos, MD, John R. Swicegood, MD, David A. Bryce, MD, Vijay Singh, MD, Salahadin Abdi, MD, Sanjay Bakshi, MD, Ricardo M. Buenaventura, MD, Joseph A. Cabaret, MD, Jessica Jameson, MD, Sunny Jha, MD, Adam M. Kaye, PharmD, Ramarao Pasupuleti, MD, Kartic Rajput, MD, PhD, Mahendra Sanapati, MD, Nalini Sehgal, MD, Andrea M. Trescot, MD, Gabor B. Racz, MD, Sanjeeva Gupta, MD, Manohar Lal Sharma, MBBS, Vahid Grami, MD, Allan T. Parr, MD, Emilija Knezevic, Sukdeb Datta, MD, Kunj G. Patel, MD, Deborah H. Tracy, MD, Harold J. Cordner, MD, Lee T. Snook, MD, Ramsin M. Benyamin, MD, and Joshua A. Hirsch, MD

Pain Physician 2021; 24:S27-S208

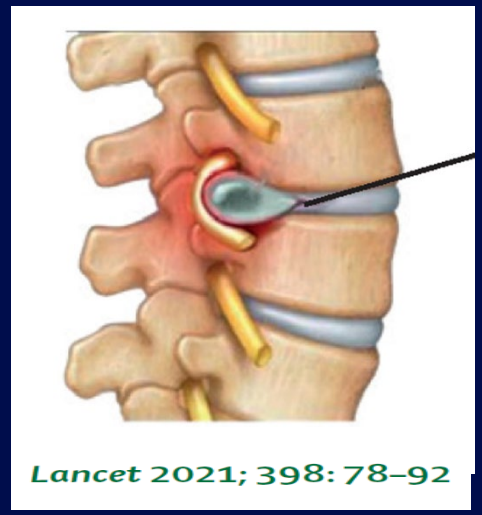
- **Objective**: To provide **evidence-based guidance** in performing **therapeutic epidural procedures**, including caudal, interlaminar in lumbar, cervical, and thoracic spinal regions, transforaminal in lumbar spine.

- Evidence synthesis includes **47 systematic reviews** and **43 RCTs** covering all epidural interventions

Pain Physician 2021; 24:S27-S208

Evidence Recommendations for Disc Herniation

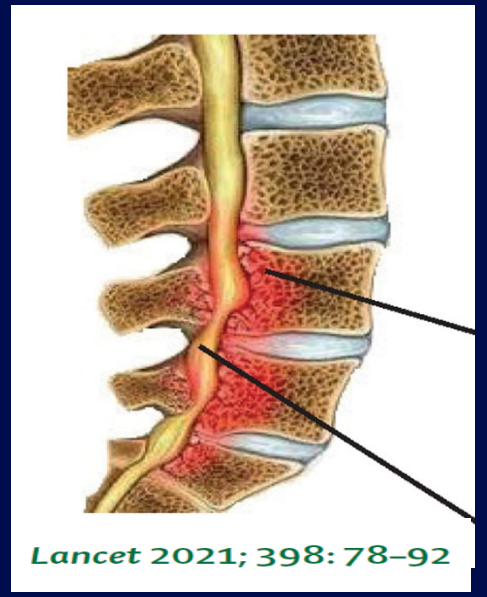
- Based on relevant, high-quality fluoroscopically guided epidural injections, with or without steroids, and results of previous systematic reviews, the **evidence is Level I** for
  - ✓ caudal epidural injections
  - ✓ lumbar interlaminar epidural injections
  - ✓ lumbar transforaminal epidural injections
  - ✓ and cervical interlaminar epidural injections **with strong recommendation** for long-term effectiveness



- For thoracic disc herniation, based on one relevant, high-quality RCT of thoracic epidural with fluoroscopic guidance, with or without steroids, the evidence is **Level II with moderate to strong recommendation** for long-term effectiveness

Evidence Recommendations for Spinal Stenosis

- The evidence based on one high-quality RCT in each category the evidence is
- ✓ **Level III to II** for fluoroscopically guided caudal epidural injections **with moderate to strong recommendation**
- ✓ **Level II** for fluoroscopically guided lumbar and cervical interlaminar epidural injections **with moderate to strong recommendation** for long-term effectiveness



Lancet 2021; 398: 78–92

- The evidence for lumbar transforaminal epidural injections is **Level IV to III with moderate recommendation** with fluoroscopically guided lumbar transforaminal epidural injections for long-term improvement

Pain Physician 2021; 24:S27-S208

Evidence Recommendations for Axial Discogenic Pain

- The evidence for axial discogenic pain without facet joint pain or sacroiliac joint pain in the lumbar and cervical spine with fluoroscopically guided caudal, lumbar and cervical interlaminar epidural injections, based on one relevant high quality RCT in each category is **Level II with moderate to strong recommendation** for long-term improvement, with or without steroids.

Evidence Recommendations for Post-surgery Syndrome

- The evidence for lumbar and cervical post-surgery syndrome based on one relevant, high-quality RCT with fluoroscopic guidance for caudal and cervical interlaminar epidural injections, with or without steroids, is **Level II with moderate to strong recommendation** for long-term improvement.

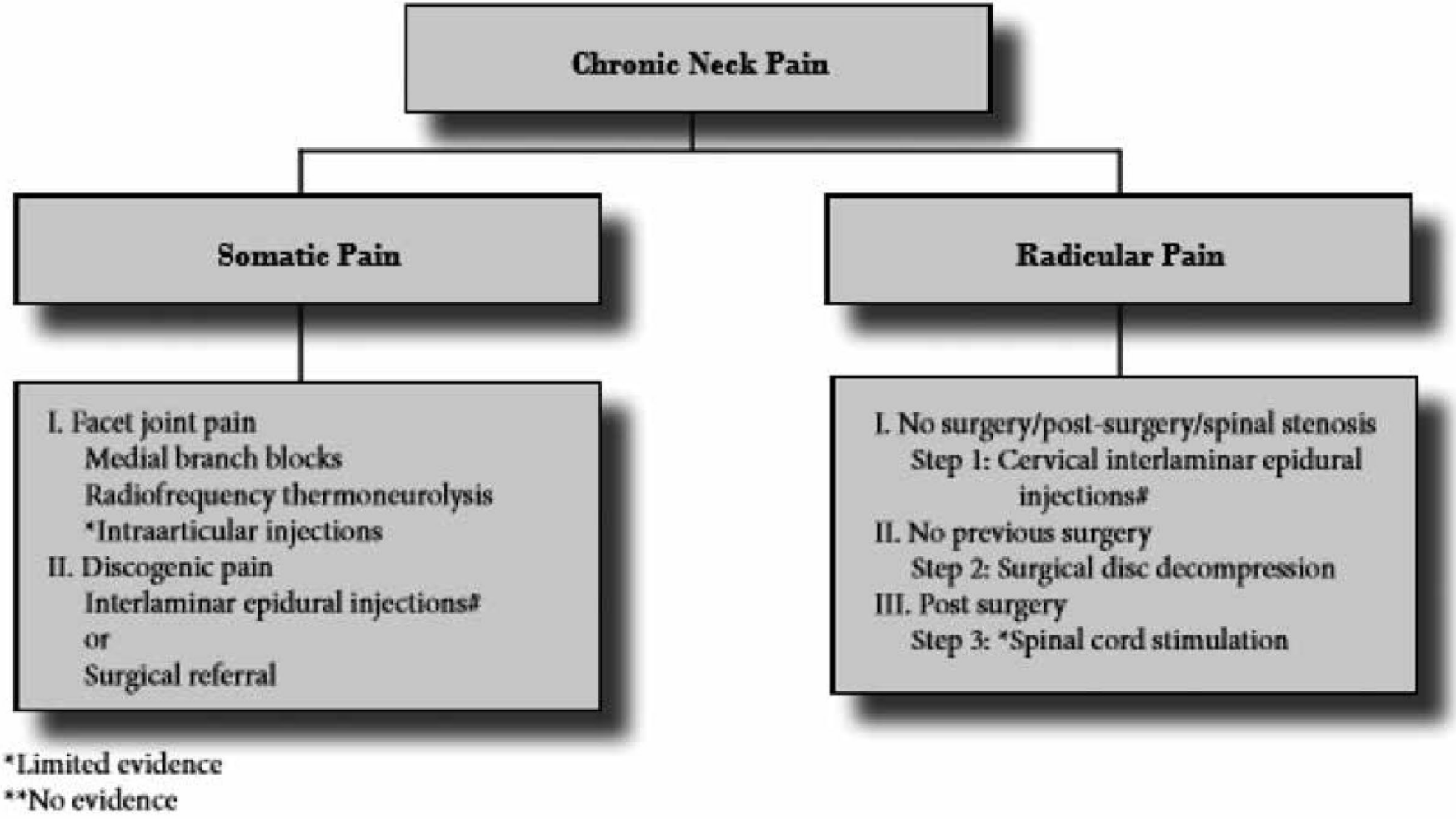


Fig. 29. *A suggested algorithm for therapeutic interventional techniques in management of chronic low back pain.*

Pain Physician 2021; 24:S27-S208

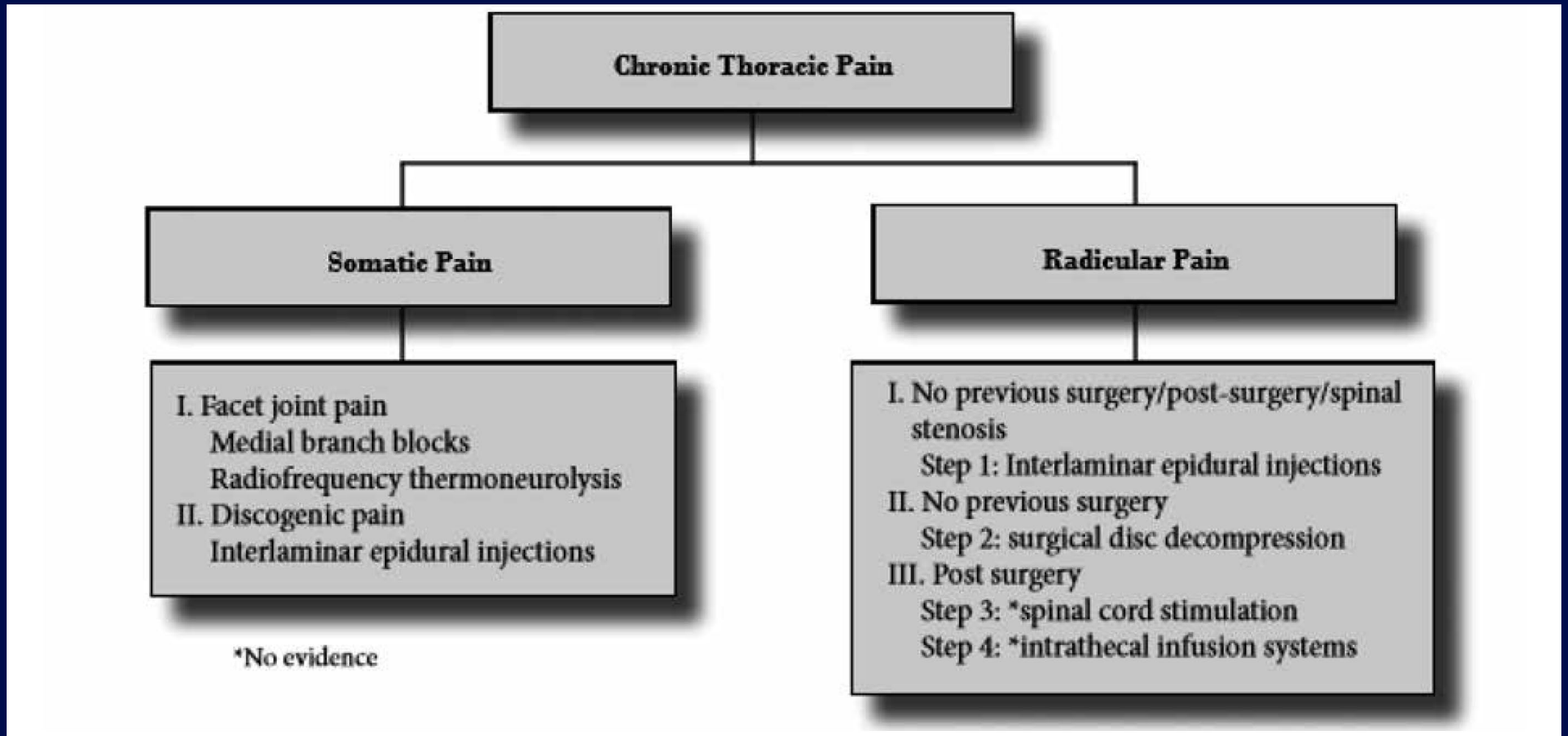


Fig. 30. *A suggested algorithm for therapeutic interventional techniques in the management of chronic thoracic pain.*

Pain Physician 2021; 24:S27-S208

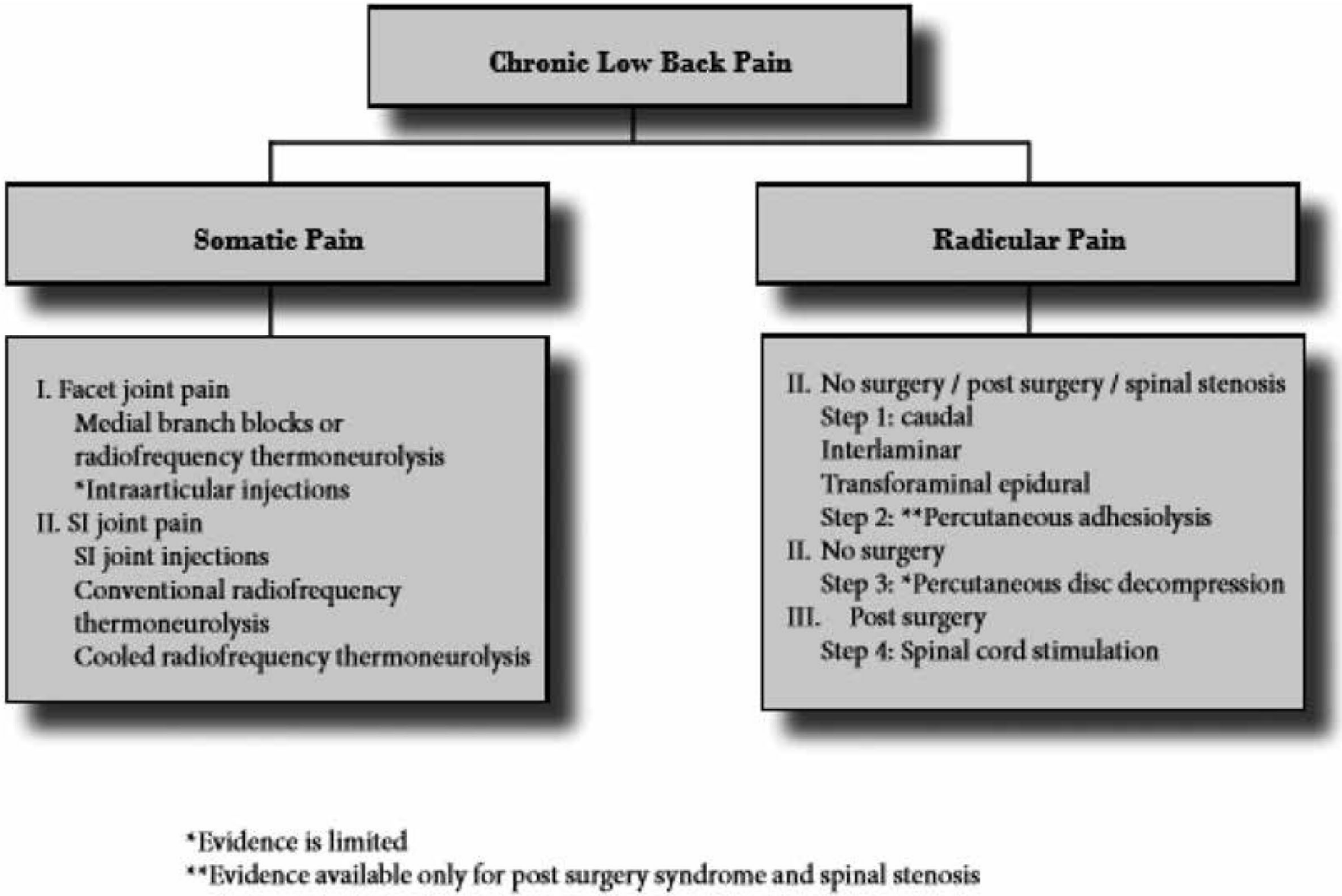


Fig. 28. *A suggested algorithm for therapeutic interventional techniques in management of chronic low back pain.*


dr.nick.knez
Thank you!!!