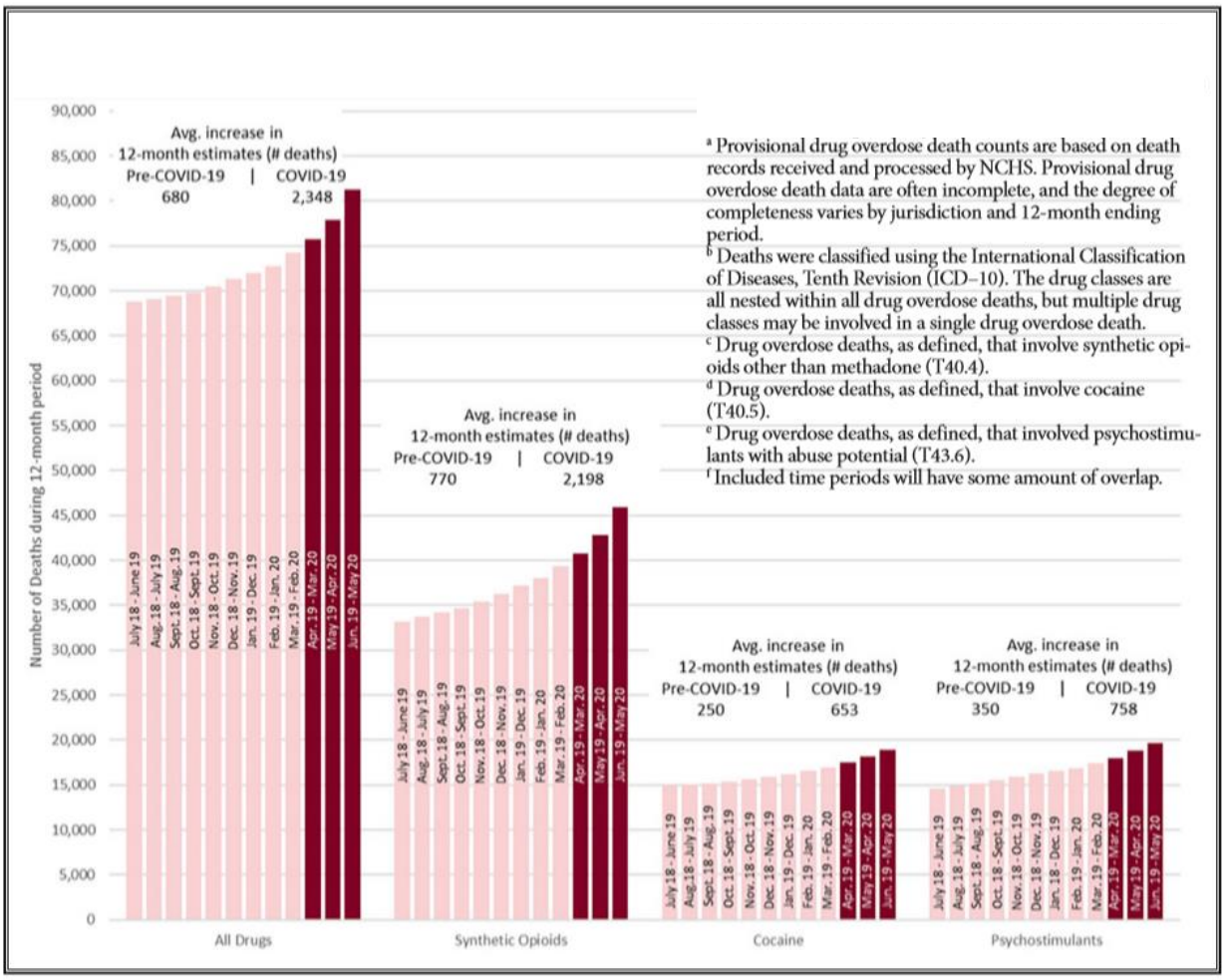
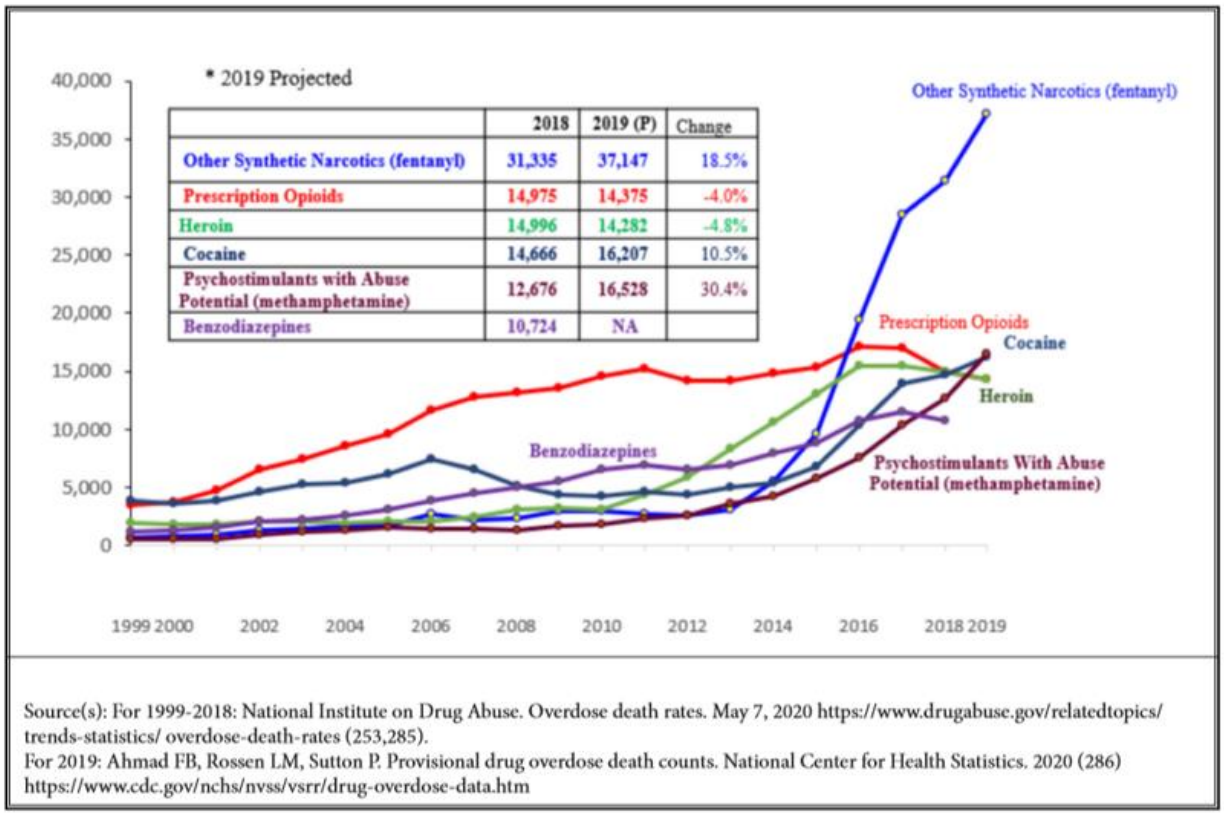


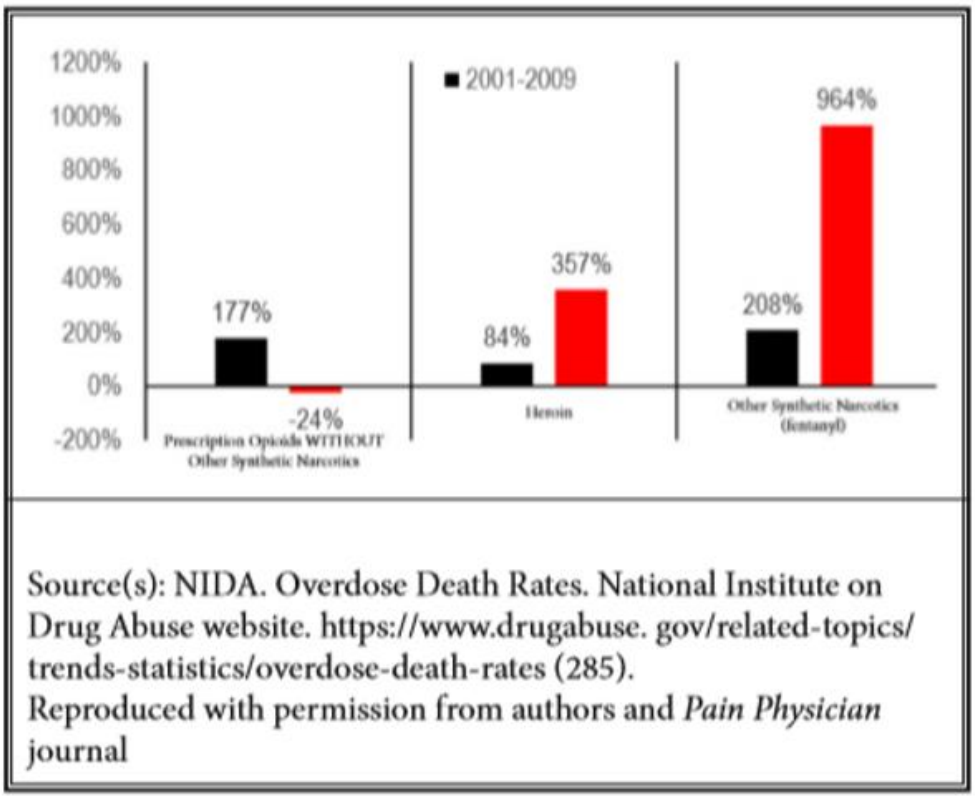
Fig. 1. *Twelve-month provisional[a] drug overdose death counts for all drugs[b], synthetic opioids[c], cocaine[d], and psychostimulants[e], for 50 states, the District of Columbia, and New York City: 12-months ending in June 2019 to 12-months ending in May 2020[f].*



	2018	2019 (P)	Change
Other Synthetic Narcotics (fentanyl)	31,335	37,147	18.5%
Prescription Opioids	14,975	14,375	-4.0%
Heroin	14,996	14,282	-4.8%
Cocaine	14,666	16,207	10.5%
Psychostimulants with Abuse Potential (methamphetamine)	12,676	16,528	30.4%
Benzodiazepines	10,724	NA	

Source(s): For 1999-2018: National Institute on Drug Abuse. Overdose death rates. May 7, 2020 https://www.drugabuse.gov/relatedtopics/trends-statistics/ overdose-death-rates (253,285).
For 2019: Ahmad FB, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2020 (286) https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

Fig. 2. *Number of opioid overdose deaths by category, 1999 to 2019.*



Source(s): NIDA. Overdose Death Rates. National Institute on Drug Abuse website. https://www.drugabuse. gov/related-topics/trends-statistics/overdose-death-rates (285).
Reproduced with permission from authors and *Pain Physician* journal

Fig. 3. *Quantification of opioid deaths.*

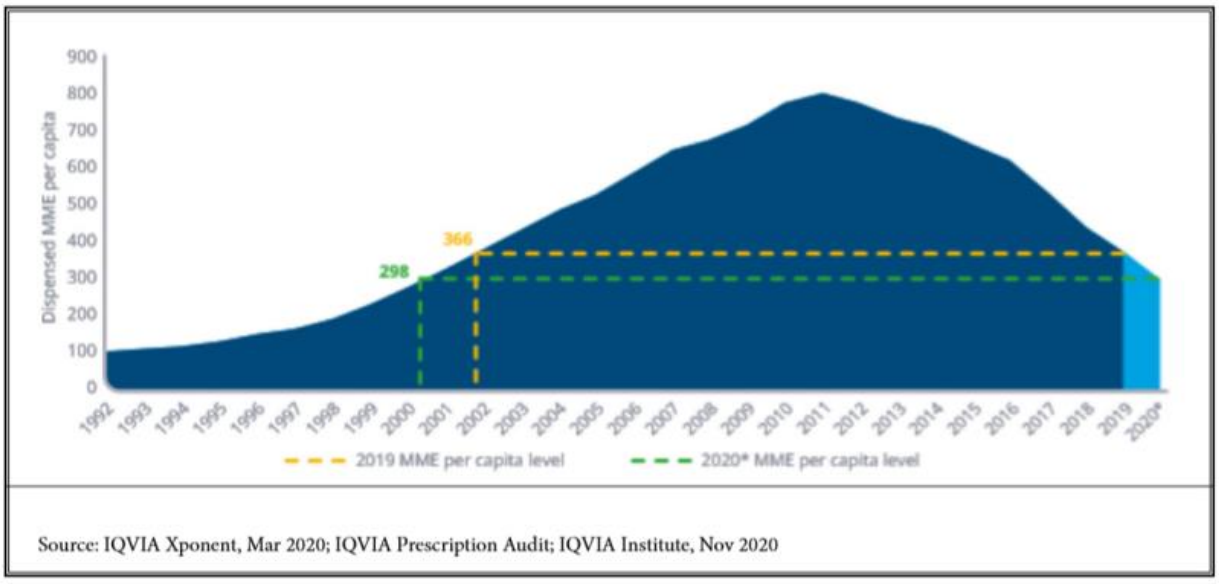


Fig. 4. *Prescription opioid use in morphine milligram equivalents (MME) per capita, 1992-2020*.*

Table 1. *National drug overdose (od) deaths, 2000-2018.*

	2000	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019 (R)	2019 (P)
Total Overdose Deaths	17,415	38,329	41,340	41,502	43,982	47,055	52,404	63,632	70,237	67,367	71,364	71,987
Any Opioid[1] (T40.0-T40.4, T40.6)	8,407	21,088	22,784	23,164	25,050	28,647	33,091	42,249	47,600	46,802	50,343	50,806
Prescription Opioids[2] (T40.2-T40.3)	3,785	14,583	15,140	14,240	14,145	14,838	15,281	17,087	17,029	14,975	14,252	14,375
Prescription Opioids AND Other Synthetic Narcotics	167	939	889	861	1,015	1,489	2,263	4,055	5,444	5,417	NA	NA
Prescription Opioids WITHOUT Other Synthetic Narcotics	3,618	13,644	14,251	13,379	13,130	13,349	13,018	13,032	11,585	9,558	NA	NA
Other Synthetic Narcotics (fentanyl)[3] (T40.4), other than methadone	782	3,007	2,666	2,628	3,105	5,544	9,580	19,413	28,466	31,335	36,733	37,147
Heroin[4] (T40.1)	1,842	3,036	4,397	5,925	8,257	10,574	12,989	15,469	15,482	14,996	14,157	14,282
Cocaine[5] (T40.5)	3,544	4,183	4,681	4,404	4,944	5,415	6,784	10,375	13,942	14,666	16,071	16,207
Psychostimulants With Abuse Potential (methamphetamine)[6] (T43.6)	578	1,854	2,266	2,635	3,627	4,298	5,716	7,542	10,333	12,676	16,356	16,528
Benzodiazepines[7] (T42.4)	1,298	6,497	6,872	6,524	6,973	7,945	8,791	10,684	11,537	10,724	NA	NA

R – Reported; P – Predicted values
Source for 2000 to 2018: https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates
For 2019: https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm (data based on 12/6/2020)

Table 2. *Characteristics of fluoroscopic randomized trials of caudal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comments
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≥ 6 mos	Long Term > 6 mos.	≥ 12 mos.	24 mos.	
Manchikanti et al, 2012 (765) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 12/13 IPM-QRB = 44/48	Total = 120 Lidocaine = 60 Lidocaine with steroids = 60 Lidocaine vs lidocaine mixed with steroid Number of injections = 1 to 5	NRS, ODI, employment status, opioid intake Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 62% vs. LA with steroid 72% Responsive: LA 77% vs LA with steroid 80%	Overall: LA 72% vs LA with steroid 73% Responsive: LA 87% vs LA with steroid 86%	Overall: LA 67% vs LA with steroid 72% Responsive: LA 85% vs LA with steroid 84%	Overall: LA 60% vs LA with steroid 65% Responsive: LA 77% vs LA with steroid 76%	Lidocaine & lidocaine with steroid effective	Lidocaine & lidocaine with steroid effective	Lidocaine & lidocaine with steroid effective	Lidocaine & lidocaine with steroid effective	• Positive double-blind randomized trial with superiority of steroids with average pain relief for steroids. Overall improvement with local anesthetic alone or with steroids was similar. • Nonresponsive patients were also similar with 13 and 10 in local anesthetic only and with steroids group. • Over a period of 2 years, on average, a total of 5-6 injections were provided.
Manchikanti et al, 2012 (767) RA, AC, F Central spinal stenosis Quality Scores: Cochrane = 12/13 IPM-QRB = 44/48	Total = 100 Lidocaine = 50 Lidocaine + steroid = 50 Lidocaine 0.5% vs. lidocaine mixed with steroid. Average number of injections = 5 to 6 for 2 years	NRS, ODI, employment status, opioid intake Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 58% vs LA with steroid 48% Responsive: LA 78% vs. LA with steroid 65%	Overall: LA 54% vs LA with steroid 50% Responsive: LA 73% vs. LA with steroid 68%	Overall: LA 44% vs LA with steroid 46% Responsive: LA 54% vs. LA with steroid 62%	Overall: LA 38% vs LA with steroid 44% Responsive: LA 51% vs LA with steroid 57%	Both treatments effective	Both treatments effective	Both treatments effective	Both treatments effective	• Double-blind design in a practical setting. • Similar results with local anesthetic or with local anesthetic and steroids. • Nonresponsive patients: local anesthetic = 13, steroids = 13. • A total of 5-6 injections on average were provided over a period of 2 years; compared to all patients with significant improvement of 38% in local anesthetic group, 44% in steroid group.

Table 2 (con't). *Characteristics of fluoroscopic randomized trials of caudal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comments
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≥ 6 mos	Long Term > 6 mos.	Long Term ≥ 12 mos.	Long Term 24 mos.	
Manchikanti et al, 2012 (762) RA, AC, F Axial or discogenic Quality Scores: Cochrane = 12/13 IPM-QRB = 44/48	Total = 120 Lidocaine = 60 Lidocaine with steroids = 60 Lidocaine vs. lidocaine mixed with steroid Average number of injections = 5 to 6 for 2 years	NRS pain scale, ODI, employment status, opioid intake Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 60% vs LA with steroid 72% Responsive: LA 87% vs LA with steroid 88%	Overall: LA 62% vs LA with steroid 72% Responsive: LA 89% vs. LA with steroid 93%	Overall: LA 56% vs LA with steroid 68% Responsive: LA 84% vs. LA with steroid 85%	Overall: LA 54% vs LA with steroid 60% Responsive: LA 84% vs LA with steroid 73%	P	P	P	P	• Positive randomized double-blind trial with similar results with local anesthetic or with local anesthetic and steroids. • There was an inordinately high proportion of patients failing to respond initially in both groups, 23 in local anesthetic group, and 19 in steroid group. • On average, a total of 5-6 injections were provided over a period of 2 years.
Manchikanti et al, 2012 (766) RA, AC, F Post-surgery syndrome Quality Scores: Cochrane = 12/13 IPM-QRB = 44/48	Total = 140 Lidocaine = 70 Lidocaine + steroid = 70 Lidocaine vs. lidocaine mixed with non-particulate betamethasone Average number of injections = 5 to 6 for 2 years	NRS, ODI, employment status, opioid intake Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 56% vs LA with steroid 54% Responsive: LA 76% vs. LA with steroid 67%	Overall: LA 56% vs LA with steroid 61% Responsive: LA 74% vs. LA with steroid 78%	Overall: LA 53% vs LA with steroid 59% Responsive: LA 70% vs. LA with steroid 75%	Overall: LA 47% vs LA with steroid 58% Responsive: LA 62% vs LA with steroid 69%	P	P	P	P	• Positive results with local anesthetics with or without steroids. • Similar results with local anesthetic or with local anesthetic and steroids. • Nonresponsive patients: local anesthetic = 17, steroids = 15. • On average, 5-6 injections were provided over a period of 2 years; compared to all patients with significant improvement of 47% in local anesthetic group, 58% in steroid group.

Table 2 (con't). *Characteristics of fluoroscopic randomized trials of caudal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comments
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≥ 6 mos	Long Term > 6 mos.	≥ 12 mos.	24 mos.	
Ackerman & Ahmad, 2007 (783) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Methylprednisolone + saline Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	N/A	N/A	Effective in all arms	Effective in all arms	N/A	N/A	Positive mid-term results in a relatively small trial.
Dashfield et al, 2005 (784) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 33/48	Total = 60 Caudal = 30 Endoscopy =30 Lidocaine with triamcinolone Number of injections = 1	Pain relief, SF-MPQ, HADS scores	SI	SI	N/A	N/A	Lidocaine with triamcinolone effective	Lidocaine with triamcinolone effective	N/A	N/A	Positive mid-term results in a relatively small trial.
Murakibhavi & Khemka, 2011 (786) RA, NTC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 27/48	Group A = 50 control conservative management Group B = 52 caudal epidural with lidocaine and methylprednisolone Total = 102 patients Conservative management or caudal epidural steroid injections	VAS, ODI, BDI, NPI	Group A = 32% Group B = 92%	Group A = 24% Group B = 86%	N/A	N/A	Steroids effective	Steroids effective	N/A	N/A	Positive short-term results, with methylprednisolone and lidocaine.
Kamble et al, 2016 (770) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	N/A	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	N/A	N/A	All 3 techniques were effective	N/A	N/A	N/A	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.

Table 2 (con't). *Characteristics of fluoroscopic randomized trials of caudal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comments
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≥ 6 mos	Long Term > 6 mos.	≥ 12 mos.	24 mos.	
Pandey, 2016 (769) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	N/A	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	N/A	P	P	P	N/A	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.
Singh et al, 2017 (779) RA, AC, F Single level prolapsed lumbar intervertebral disc Quality Scores: Cochrane = 8/13 IPM-QRB = 30/48	Number of patients = 80 Caudal with steroids group = 40 2 mL of methylprednisolone, 80 mg along with lignocaine 2% diluted in 20 mL of normal saline 3 caudal epidural injections were given at an interval of 3 weeks irrespective of previous epidural injection effect SRNB = 40 A single injection of 2 mL of methylprednisolone, 80 mg, mixed with 5 mL of lignocaine 2%	VAS, ODI & significant pain relief of 50%	VAS Caudal vs. SNRB = 61.5% vs. 55.5% ODI decreased caudal vs. SNRB = 64.6% vs. 52.8%	VAS Caudal vs. SNRB= 59.6% vs. 52.9% ODI decreased caudal vs. SNRB = 65.1% vs. 48.6%	VAS Caudal vs. SNRB= 58.2% vs. 46.8% ODI decreased caudal vs. SNRB = 65.4% vs. 46.7%	N/A	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Positive short-term and long-term relief in both caudal and SNRB; however, relief in the caudal group was superior. However, this study suffered with multiple limitations of 3 caudal epidural injections compared to one SNRB and high volumes of injections, which are clinically inappropriate in both caudal and SNRB groups.

Source: Manchikanti L, et al. Assessment of methodologic quality of randomized trials of interventional techniques: Development of an interventional pain management specific instrument. *Pain Physician* 2014; 17:E263-E290 (153).

RA = Randomized; AC = Active Control; F = Fluoroscopy; NRS = Numeric Rating Scale; ODI = Oswestry Disability Index; IPM-QRB = Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment; LA = local anesthetic; BDI = Beck Depression Inventory; SF-MPQ = Short-Form McGill Pain Questionnaire; HADS = Hospital Anxiety and Depression Scale; NTC = No treatment control; VAS = Visual Analog Scale; NPI = Numerical Pain Intensity; JOA – Japanese Orthopaedic Association; SNRB – selective nerve root block; SI = significant improvement; NA = Not Applicable; P = Positive; N = negative

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Table 3. *Characteristics of fluoroscopic randomized controlled trials of lumbar interlaminar epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Manchikanti et al, 2014 (797) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 11/13 IPM-QRB = 44/48	Total = 120 Local anesthetic = 60 Local anesthetic and steroids = 60 Xylocaine or Xylocaine with non-particulate Celestone Average number of injections = 5 to 6 for 2 years	NRS, ODI, employment status, opioid intake, significant improvement 50% or greater of NRS scores and ODI scores Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: Lidocaine 72% vs. lidocaine with steroid 82% Responsive: Lidocaine 86% vs. lidocaine with steroid 83%	Overall: Lidocaine 63% vs. lidocaine with steroid 85% Responsive: Lidocaine 76% vs. lidocaine with steroid 86%	Overall: Lidocaine 67% vs. lidocaine with steroid 85% Responsive: Lidocaine 80% vs. lidocaine with steroid 86%	Overall: Lidocaine 60% vs lidocaine with steroid 70% Responsive: Lidocaine 72% vs. lidocaine with steroid 71%	Both treatments are effective	Both treatments are effective	Both treatments are effective	Both treatments are effective	• Positive randomized trial with long-term follow-up. • Overall, similar results with local anesthetic or with local anesthetic and steroids with significant improvement. • Steroids were superior at 6 months with pain relief and 12 months with functional status • A significantly higher proportion of patients non-responsive to the first 2 injections in the local anesthetic group 10 vs one. • On average, a total of 5-6 injections were provided over a period of 2 years.
Ghai et al, 2015 (804) RA, DB, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 39/48	Total = 69 Lidocaine = 34 Lidocaine + methylprednisolone = 35 Local anesthetic group: 8 mL of 0.5% lidocaine Lidocaine + methylprednisolone: 6 ml of 0.5% lidocaine mixed with 80 mg (2 mL) of methylprednisolone acetate Average procedures: 2	NRS and functional disability using Modified Oswestry Disability Questionnaire Follow-up: 1 year	Lidocaine: 50% Lidocaine with methylprednisolone: 86%,	Lidocaine: 56% Lidocaine with methylprednisolone: 86%	Lidocaine: 59% Lidocaine with methylprednisolone: 89%	N/A	Both arms effective. Steroids superior	Both arms effective. Steroids superior	Both arms effective. Steroids superior	N/A	This active control trial with a long-term follow-up comparing lidocaine alone with lidocaine with methylprednisolone showed similar results after 3 months, even though quality of relief was superior in the local anesthetic with steroid group.

Table 3 (con't). *Characteristics of fluoroscopic randomized controlled trials of lumbar interlaminar epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Manchikanti et al 2015 (799) RA, AC, F Central spinal stenosis Quality Scores: Cochrane = 11/13 IPM-QRB = 43/48	Total = 120 Local anesthetics = 60 Local anesthetics and steroids = 60 Lidocaine alone or with Celestone Average number of injections = 5 to 6 for 2 years	NRS, ODI, employment status, opioid intake Responsive was defined as those patients responding with at least 3 weeks of improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 83% vs LA with steroid 77% Responsive: LA 90% vs LA with steroid 86%	Overall: LA 72% vs LA with steroid 75% Responsive: LA 78% vs LA with steroid 83%	Overall: LA 77% vs LA with steroid 67% Responsive: LA 84% vs LA with steroid 71%	Overall: LA 72% vs LA with steroid 73% Responsive: LA 84% vs LA with steroid 85%	Both treatments effective	Both treatments effective	Both treatments effective	Both treatments effective	• Positive results in a large active control trial. • Both local anesthetic alone or with steroids were effective with no significant difference between the groups. • On average, a total of 5-6 injections were administered over a period of 2 years.
Ökmen & Ökmen 2017 (817) RA, AC, F Disc herniation Quality Scores: Cochrane = 12/13 IPM-QRB = 40/48	Total = 120 Epidural bupivacaine 0.25%, 10 mL = 60 Epidural bupivacaine 0.25%, 10 mL + 40 mg of methylprednisolone = 60 Procedures administered at L4-5 under fluoroscopic guidance Number of injections = 1-2	VAS, ODI Follow-up: 1 to 12 months	Significantly better results in epidural bupivacaine and steroid group Both groups showed significant improvement from baseline, more significant in the steroid group than bupivacaine alone group.	Significantly better results in epidural bupivacaine and steroid group Both groups showed significant improvement from baseline, more significant in the steroid group than bupivacaine alone group.	Significantly better results in epidural bupivacaine and steroid group Both groups showed significant improvement from baseline, more significant in the steroid group than	N/A	Bupivacaine steroids superior	Bupivacaine steroids superior	Bupivacaine steroids superior	N/A	• Positive results for both epidural bupivacaine and epidural bupivacaine with steroids. • Significant improvement in epidural bupivacaine and steroid group from baseline with pain and function, as well as ODI compared to bupivacaine.
Friedly et al, 2014 (278,818) RA, AC, F Central and foraminal spinal stenosis Quality Scores: Cochrane = 8/13 IPM-QRB = 30/48	Total = 400 Lidocaine Group: Interlaminar = 139 Transforaminal = 61 Glucocorticoids plus Lidocaine Group: Interlaminar = 143 Transforaminal = 57 Lidocaine alone or glucocorticoid plus lidocaine Variable doses	NRS, RMDQ	Significant improvement. At 3 weeks and 6 weeks RMDQ scores were significantly less in glucocorticoid-lidocaine group compared to lidocaine group. Leg pain was also significantly less in the steroid group compared to lidocaine alone group.	No significant differences or improvement in observational study	No significant differences or improvement in observational study	N/A	Both treatments effective with superiority of steroid with lidocaine	None	None	N/A	Large trial with flawed design and assessment with positive results at 3 months. Even though based on flawed analysis it shows negative results. Multiple flaws include not only the design and analysis of the data, but patient selection, technical considerations, and inherent bias. Follow-up observational study has not provided additional information.

Table 3 (con't). *Characteristics of fluoroscopic randomized controlled trials of lumbar interlaminar epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Manchikanti et al, 2013 (801) RA, AC, F Axial or discogenic Quality Scores: Cochrane = 11/13 IPM-QRB = 44/48	Total = 120 Local anesthetics = 60 Local anesthetics and steroids = 60 Lidocaine alone or with Celestone Average number of injections = 5 to 6 for 2 years	NRS, ODI, employment status, opioid intake Responsive was defined as those patients responding with at least 3 weeks of improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 83% vs LA with steroid 77% Responsive: LA 90% vs LA with steroid 86%	Overall: LA 72% vs LA with steroid 75% Responsive: LA 78% vs LA with steroid 83%	Overall: LA 77% vs LA with steroid 67% Responsive: LA 84% vs LA with steroid 71%	Overall: LA 72% vs LA with steroid 67% Responsive: LA 78% vs LA with steroid 70%	P	P	P	P	• Positive results in a large active control trial. • Both local anesthetic alone or with steroids were effective with no significant difference between the groups. • On average, a total of 5-6 injections were administered over a period of 2 years.
Ackerman & Ahmad, 2007 (783) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Methylprednisolone + saline Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	N/A	N/A	Effective in all arms	Effective in all arms	N/A	N/A	• Positive mid-term results in a relatively small trial. • Shows effectiveness of steroids with all approaches with superiority of transforaminal
Rados et al, 2011 (821) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 9/13 IPM-QRB = 30/48	Total = 64 IL = 32 TF = 32 Lidocaine with methylprednisolone Number of injections = 1 to 3	VAS, ODI, 50% pain relief Follow-up: 6 months	N/A	Interlaminar lidocaine with methylprednisolone = 53% Transforaminal lidocaine with methylprednisolone = 63%	N/A	N/A	Effective with both approaches	N/A	N/A	N/A	• Positive results with short follow-up period in comparison of 2 approaches with lidocaine with methylprednisolone
Ghai et al, 2014 (617) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 42/48	Total = 62 Parasagittal interlaminar = 32 Transforaminal = 30 2 mL of methylprednisolone (80 mg) mixed with 2 mL of normal saline for both PIL and transforaminal groups Number of epidural steroid injections: Transforaminal group: 60 PIL group: 58 Average procedures: 2	Visual analog scale, Oswestry Disability questionnaire, significant improvement, greater than 50% pain relief from baseline, Patient Global Impression	PIL group: 78% Transforaminal group: 77%	PIL group: 75% Transforaminal group: 77%	PIL group: 69% Transforaminal group: 77%	N/A	Effectiveness in both arms	Effectiveness in both arms	Effectiveness in both arms	N/A	This is relatively small active control trial with a long-term follow-up assessing the role of parasagittal interlaminar epidural injections and transforaminal epidural injections showing equal improvement with steroids without local anesthetic.

Table 3 (con't). *Characteristics of fluoroscopic randomized controlled trials of lumbar interlaminar epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Candido et al, 2013 (616) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 37/48	106 patients Midline interlaminar = 53 Parasagittal interlaminar = 53 120 mg methylprednisolone with 2 mL of 0.5% lidocaine Number of Injections: Not available	Pain relief, disability, NRS, ODI, use of optoid medication Follow-up: 12 months	ODI Midline = 36% Parasagittal = 51% Pain: Midline = 29% Parasagittal = 50%	ODI Midline = 21% Parasagittal = 55% Pain: Midline = 29% Parasagittal = 53%	ODI Midline = 15% Parasagittal = 56% Pain: Midline = 28% Parasagittal = 55%	N/A	Parasagittal superior	Parasagittal superior	Parasagittal superior	N/A	• The authors showed significant evidence that parasagittal approach with injection of local anesthetic and steroids was superior to midline approach of interlaminar epidural injections. • This study shows combination of methylprednisolone with lidocaine was superior administered with a parasagittal approach compared to midline approach.
Amr, 2011 (823) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 12/13 IPM-QRB = 38/48	Total = 200 Local anesthetic + steroid = 100 Local anesthetic + steroid + ketamine = 100 Triamcinolone plus preservative free ketamine and 0.9% saline Number of injections = 1	Pain scores, Oswestry low back pain disability questionnaire	Significant improvement in ketamine group	Significant improvement in ketamine group	Significant improvement in ketamine group	N/A	Effective with addition of ketamine to bupivacaine and triamcinolone	Effective with addition of ketamine to bupivacaine and triamcinolone	Effective with addition of ketamine to bupivacaine and triamcinolone	N/A	• Positive randomized trial for ketamine with long-term follow-up with ketamine with local anesthetic and steroid.
Kamble et al, 2016 (770) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	N/A	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	N/A	N/A	All 3 techniques were effective	N/A	N/A	N/A	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.

Table 3 (con't). *Characteristics of fluoroscopic randomized controlled trials of lumbar interlaminar epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Pandey, 2016 (769) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	N/A	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	N/A	P	P	P	N/A	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.

RA = Randomized; AC = Active Control; F = Fluoroscopy; DB = Double-Blind; P = Positive; N = Negative; NA = Not Applicable; LA = local anesthetic; NRS = Numeric Rating Scale; ODI = Oswestry Disability Index; VAS = Visual Analog Scale; PIL = Parasagittal Interlaminar; RMDQ = Roland Morris Disability Questionnaire; JOA = Japanese Orthopaedic Association; IPM-QRB = Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment

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Table 4. *Characteristics of fluoroscopic randomized controlled trials of lumbar transforaminal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Karppinen et al, 2001 (856) RA, PC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 13/13 IPM-QRB = 34/48	Total=160 Methylprednisolone-bupivacaine = 80 Saline = 80 Sodium chloride solution, or methylprednisolone (40 mg) and bupivacaine (5 mg) Number of injections = 1	VAS, ODI, Nottingham Health Profile, cost, physical examination Follow-up: 12 months with only initial procedures	A significant treatment effect in favor of saline treatment for back pain.	The treatment effects in both leg pain and back pain favored the saline treatment.	There were no treatment effects in favor of either treatment.	N/A	Lack of effectiveness of steroid with bupivacaine	Lack of effectiveness of steroid with bupivacaine	Lack of effectiveness of steroid with bupivacaine	N/A	• An ineffective or inappropriate placebo design, without applicable results. • Overall saline appears to have been superior at 3 months and 6 months, but no significant difference at one year between both groups. • Leg pain decreased on average by 65% in both groups. • Surgery was avoided in the majority of the patients with 18 patients in the steroid group and 15 in the saline group undergoing surgery.
Manchikanti et al, 2014 (860) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 11/13 IPM-QRB = 44/48	Total = 120 Lidocaine = 60 Lidocaine with steroids = 60 Lidocaine vs lidocaine mixed with steroid with infraneural approach Average number of injections = 5 to 6 for 2 years	NRS pain scale, ODI, employment status, opioid intake Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 75% vs LA with steroid 67% Responsive: LA 90% vs LA with steroid 82%	Overall: LA 73% vs LA with steroid 67% Responsive LA 88% vs LA with steroid 87%	Overall: LA 75% vs LA with steroid 57% Responsive LA 92% vs LA with steroid 73%	Overall: LA 65% vs LA with steroid 57% Responsive LA 80% vs LA with steroid 73%	Effectiveness in both groups. Lidocaine alone or with steroids effective.	Effectiveness in both groups. Lidocaine alone or with steroids effective.	Effectiveness in both groups. Lidocaine alone or with steroids effective.	Effectiveness in both groups. Lidocaine alone or with steroids effective.	• Similar results with local anesthetic or with local anesthetic and steroids. • Nonresponsive patients: local anesthetic = 11, steroids = 15. • Local anesthetics were somewhat superior, though not statistically significant. • On average, a total of 5-6 injections were administered over a period of 2 years.
Riew et al, 2000 & 2006 (275,276) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Total = 55 Bupivacaine alone (1 mL, 0.25%) = 27 Bupivacaine (1 mL, 0.25%) with steroid (1 mL betamethasone) = 28 Number of injections = 1-4	Need for operative treatment, North American Spine Society Questionnaire Follow-up: 1 months to 28 months	71% of steroid group chose not to have surgery and 33% of bupivacaine group chose not to have surgery	71% of steroid group chose not to have surgery and 33% of bupivacaine group chose not to have surgery	71% of steroid group chose not to have surgery and 33% of bupivacaine group chose not to have surgery	N/A	P	P	P	N/A	• Epidural bupivacaine with steroids was significantly more effective than transforaminal bupivacaine with steroids was significantly more effective than epidural bupivacaine alone in avoiding surgery.

Table 4 (con't). *Characteristics of fluoroscopic randomized controlled trials of lumbar transforaminal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Tafazal et al, 2009 (881) RA, AC, F Disc herniation or radiculopathy and spinal stenosis Quality Scores: Cochrane = 11/13 IPM-QRB = 32/48	Total: 150 patients Lumbar disc herniation: 76 Local anesthetic = 34 Local anesthetic with steroid = 42 Local anesthetic group: Injection of 2 mL of 0.25% bupivacaine Local anesthetic with steroid group: Injection of 2 mL of 0.25% bupivacaine and 40 mg of methylprednisolone. Bupivacaine only: Lumbar disc herniation: 34 Foraminal stenosis: 25 Bupivacaine with steroids Lumbar disc herniation: 42 Foraminal stenosis: 23 Number of injections = 1 to	VAS, ODI, LBOS Avoidance of surgery Outcomes: 12 weeks 1 year for surgery Excellent outcome	ODI: LA 13.8 ± 3.7 versus LA with steroid 13.6 ± 3.1 VAS leg pain: LA 24.3 ± 5.5 versus LA with steroid 27.4.6 ± 4.7	N/A	Disc herniation group showed greater reduction in the ODI with a mean change of 15 points from baseline of 46.6 in the bupivacaine only group and 43.4 in bupivacaine and steroid group. There was a mean change in the VAS of 26 mm in the disc prolapse group.	N/A	Excellent to good outcomes in 54% Bupivacaine alone and bupivacaine with steroid are both effective	N/A	The requirements for treatments were the same in local anesthetic alone group or local anesthetic with steroids. Overall surgery rates was 18%, the surgery rate was 22% in the bupivacaine only group and 14% in the bupivacaine and steroid group.	N/A	• There was no significant difference between both groups. Surgery was avoided in both groups. • Corticosteroid addition to local anesthetic failed to provide any additional benefit when compared to local anesthetic injection alone.
Vad et al, 2002 (879) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 5/13 IPM-QRB = 16/48	Total: 50 patients Transforaminal: 25 Trigger point injections: 25 Transforaminal injections were performed by safe triangle approach or sacral foramen injection utilizing contrast followed by 1.5 mL of betamethasone acetate 9 mg and 1.5 mL of 2% preservative free Xylocaine. Trigger point injections were performed with 3 mL of normal saline	Outcome measures included visual numeric score, Roland-Morris score, finger to floor distance, and patient satisfaction score. Outcomes were measured at 3 weeks, 6 weeks, 3 months, 6 months, and 12 months.	In transforaminal group 84% showed improvement in trigger point injection group 48% showed improvement	In transforaminal group 84% showed improvement. in trigger point injection group 48% showed improvement	In transforaminal group 84% showed improvement in trigger point injection group 48% showed improvement.	N/A	Transforaminal steroids with lidocaine effective	Transforaminal steroids with lidocaine effective	Transforaminal steroids with lidocaine effective	N/A	This is a randomized trial, but randomization was by patient choice with patients receiving either a high dose transforaminal epidural steroid injection or saline trigger point injection. Study yielded positive results for transforaminal epidural injections at one-year follow-up.

Table 4 (con't). *Characteristics of fluoroscopic randomized controlled trials of lumbar transforaminal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Ackerman & Ahmad, 2007 (783) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total=90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Steroid and saline with local anesthetic Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	N/A	N/A	Effective in all arms	Effective in all arms	N/A	N/A	• Positive mid-term results in a relatively small trial. • Shows effectiveness of steroids with all approaches with superiority of transforaminal
Rados et al, 2011 (821) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 9/13 IPM-QRB = 30/48	Total=64 Interlaminar = 32 Transforaminal = 32 Lidocaine with methylprednisolone Number of injections = 1 to 3	VAS, ODI, 50% pain relief Follow-up: 6 months	N/A	Interlaminar lidocaine with methylprednisolone = 53% Transforaminal lidocaine with methylprednisolone = 63%	N/A	N/A	N/A	Effective with both approaches	N/A	N/A	• Positive results with short follow-up period in comparison of 2 approaches with lidocaine with methylprednisolone
Jeong et al, 2007 (857) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 31/48	Total=193 Ganglionic = 104 Preganglionic = 89 0.5 mL of bupivacaine hydrochloride and 40 mg of 1 mL of triamcinolone Number of injections = 1	VAS Follow-up: 7-30 days 6 months	Preganglionic = 88.4% Ganglionic = 70.9%	Preganglionic = 60.4% Ganglionic = 67.2%	N/A	N/A	Both approaches effective	Both approaches effective	N/A	N/A	Moderate quality study with mid-term positive results.
Ghai et al, 2014 (617) RA, DB, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 42/48	Total = 62 Parasagittal interlaminar = 32 Transforaminal = 30 2 mL of methylprednisolone (80 mg) mixed with 2 mL of normal saline for both PIL and transforaminal groups Number of epidural steroid injections: Transforaminal group: 60 PIL group: 58 Average procedures: 2	Visual analog scale, Oswestry Disability questionnaire, significant improvement, greater than 50% pain relief from baseline, Patient Global Impression	PIL group: 78% Transforaminal group: 77%	PIL group: 75% Transforaminal group: 77%	PIL group: 69% Transforaminal group: 77%	N/A	Effectiveness in both arms	Effectiveness in both arms	Effectiveness in both arms	N/A	This relatively small active control trial with a long-term follow-up assessed the role of parasagittal interlaminar epidural injections and transforaminal epidural injections showing equal improvement with steroids without local anesthetic.

Table 4 (con't). *Characteristics of fluoroscopic randomized controlled trials of lumbar transforaminal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Friedly et al, 2014 & 2017 (278,818) RA, AC, F Spinal stenosis Quality Scores: Cochrane = 8/13 IPM-QRB = 30/48	Total = 400 Lidocaine Group: Interlaminar = 139 Transforaminal = 61 Glucocorticoids plus lidocaine Group: Interlaminar = 143 Transforaminal = 57 Lidocaine alone or glucocorticoid plus lidocaine Variable doses	NRS, RMDQ Follow-up: 6 weeks	Significant improvement. At 3 weeks and 6 weeks RMDQ scores were significantly less in glucocorticoid-lidocaine group compared to lidocaine group. Leg pain was also significantly less in the steroid group compared to lidocaine alone group.	No significant differences or improvement in observational study	No significant differences or improvement in observational study	N/A	Both treatments effective	Neither treatment was effective	Neither treatment was effective	N/A	Large trial with flawed design and assessment with positive results at 3 months. Even though based on flawed analysis it shows negative results. Multiple flaws include not only the design and analysis of the data, but patient selection, technical considerations, and inherent bias.
Kennedy et al, 2014 (273) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 30/48	Total patients = 78 Dexamethasone 15 mg or 1.5 mL = 41 patients Triamcinolone 60 mg or 1.5 mL = 37 patients Number of Injections: 1 to 3	NRS, ODI, at least 50% reduction in pain and disability scores	Dexamethasone group 73% reduction in pain scores, 68% reduction in ODI scores Triamcinolone group 73% reduction in pain scores, 68% reduction in ODI scores	Dexamethasone group 73% reduction in pain scores, 71% reduction in ODI scores Triamcinolone group 76% reduction in pain scores, 65% reduction in ODI scores	N/A	N/A	Both drugs effective	Both drugs effective	N/A	N/A	• This is one of the studies showing effectiveness of steroids without local anesthetic. • Relatively small study with short-term follow-up only
Kamble et al, 2016 (770) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	N/A	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	N/A	N/A	All 3 techniques were effective; however, transforaminal group showed superiority. There was no difference between caudal and interlaminar approaches	N/A	N/A	N/A	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.

Table 4 (con't). *Characteristics of fluoroscopic randomized controlled trials of lumbar transforaminal epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Pandey, 2016 (769) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	N/A	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	N/A	P	P	P	N/A	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.

RA = Randomized; AC = Active Control; F = Fluoroscopy; PC = Placebo Control; DB = Double-Blind; P = Positive; N = Negative; NA = Not Applicable; LA = local anesthetic; IPM-QRB = Interventional Pain Management techniques -- Quality Appraisal of Reliability and Risk of Bias Assessment; NRS = Numeric Rating Scale; ODI = Oswestry Disability Index; VAS = Visual Analog Scale; LBOS = Low Back Outcome Score; PIL = Parasagittal Interlaminar; RMDQ = Roland Morris Disability Questionnaire; JOA = Japanese Orthopaedic Association; BDI = Beck Depression Inventory

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Table 5. *Effectiveness of percutaneous adhesiolysis assessed by randomized controlled trials and observational studies.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
LUMBAR POST-SURGERY SYNDROME											
Manchikanti et al, 2009, 2012 (893,894) RA, AC, DB Post-lumbar surgery syndrome Quality Scores: Cochrane: 11/13 IPM-QRB: 42/48	Total = 120 Percutaneous adhesiolysis = 60 Caudal epidural = 60 - Percutaneous adhesiolysis with lidocaine, betamethasone and 10% hypertonic solution; - Caudal epidural injection with lidocaine, betamethasone and 0.9% NaCl solution	NRS, ODI, employment status, opioid intake	78% in adhesiolysis group experienced >50% relief compared to 23% in control group	73% in adhesiolysis group experienced >50% relief compared to 7% in control group	70% in adhesiolysis group experienced >50% relief compared to 5% in control group	82% in adhesiolysis group vs. 5% in caudal group	P	P	P	P	Short- and long-term effectiveness of adhesiolysis on post-lumbar surgery syndrome
Chun-jing et al, 2012 (896) RA, AC, DB Post-lumbar surgery syndrome Quality Scores: Cochrane: 12/13 IPM-QRB 34/48	Total = 76 Percutaneous adhesiolysis = 38 Epidural injection = 38 - Percutaneous adhesiolysis with saline and dexamethasone; - Epidural injection of dexamethasone	VAS, McNabb lumbar disease evaluation, opioid use	NA	Intervention group VAS score >3 VAS points lower than baseline, control group VAS score <1 point lower than baseline	NA	NA	P	NA	NA	NA	Short-term effectiveness of adhesiolysis in patients with failed back surgery syndrome
Manchikanti et al, 2004 (897) RA, PC, DB Predominantly post-surgery syndrome Quality Scores: Cochrane: 12/13 IPM-QRB: 37/48	Total = 75 Control with normal saline = 25 Adhesiolysis with normal saline = 25 Adhesiolysis with hypertonic saline = 25 - One-day adhesiolysis with 0.9% saline and local anesthetic and steroid; - One-day adhesiolysis with 10% saline and local anesthetic and steroid; - Epidural injection with local anesthetic, steroid and 0.9% saline	VAS, ODI, employment status, opioid intake, range of motion, psychological evaluation by P-3	72% of 10% saline group, 64% of 0.9% group and 0% of control group had >50% pain relief	72% of 10% saline group, 60% of 0.9% group and 0% of control group had >50% pain relief	72% of 10% saline group, 60% of 0.9% group and 0% of control group had >50% pain relief	NA	P	P	P	NA	Short- and long-term effectiveness and equivalency between normal and hypertonic saline adhesiolysis in chronic low back pain
Veihelmann et al, 2006 (898) RA, AC Post-surgery syndrome and disc prolapse Quality Scores: Cochrane: 8/13 IPM-QRB: 30/48	Total = 99 Adhesiolysis = 47 Physiotherapy = 52 - One-day adhesiolysis with 10% saline, ropivacaine and triamcinolone; - Physical therapy 99 patients with chronic low back pain and sciatica based on disc protrusion/prolapse or failed back surgery	VAS, ODI, GHS, use of analgesics	Mean improvement of the adhesiolysis group was >50% in VAS and >40% in ODI. Physical therapy group had ~10% relief	Mean improvement of the adhesiolysis group was >50% in VAS and >40% in ODI. Physical therapy group had ~10% relief	Mean improvement of the adhesiolysis group was >50% in VAS and >40% in ODI. Physical therapy group had ~10% relief	NA	P	P	P	NA	Short and long- term effectiveness of adhesiolysis over physiotherapy in patients with sciatica

Table 5 (con't). *Effectiveness of percutaneous adhesiolysis assessed by randomized controlled trials and observational studies.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
Heavner et al, 1999 (899) RA, DB Post-surgery syndrome and disc prolapse Quality Scores: Cochrane: 10/13 IPM-QRB: 23/48	Total = 59 Group I (hypertonic saline plus hyaluronidase) = 17 Group II (hypertonic saline) = 15 Group III (isotonic saline) = 17 Group IV (isotonic saline plus hyaluronidase) = 10 3-day adhesiolysis with either 0.9% or 10% saline and with or without hyaluronidase	SFM, VAS for back, right leg, and left leg pain	About 50% of subjects had more than 10/100 improvement in VAS	About 50% of subjects had more than 10/100 improvement in VAS	About 50% of subjects had more than 10/100 improvement in VAS	NA	P	P	P	NA	Short- and long-term effectiveness and equivalency between adhesiolysis groups with 0.9% and 10% saline and with or without hyaluronidase in patients with low back pain and radiculopathy
Akbas et al, 2018 (901) RA, AC Post-lumbar surgery syndrome Quality Scores: Cochrane: 9/13 IPM-QRB: 35/48	60 patients 3 groups: Caudal = 20 S1 foraminal = 20 L5 transforaminal = 20 All patients underwent placement of 16 gauge RX Coude needle in the Racz catheter with 3 approaches along with adhesiolysis. They also received exercises with neural flossing 3-4 times daily for 3 months.	VAS, ODI 1 month, 3 months, 6 months after the procedure	Significant improvement was seen with pain and functional status with reduction in scores with all 3 approaches with no significant differences between the approaches.	Significant improvement was seen with pain and functional status with reduction in scores with all 3 approaches with no significant differences between the approaches.	Significant improvement was seen with pain and functional status with reduction in scores with all 3 approaches with no significant differences between the approaches.	NA	P	P	P	NA	The 3 approaches result in the same outcome with regard to pain relief and complication rate. Adhesiolysis is an effective technique in managing post-lumbar surgery syndrome pain.
LUMBAR SPINAL STENOSIS											
Manchikanti et al, 2009, 2013 (891,892) Central spinal stenosis RA, AC Quality Scores: Cochrane: 11/13 IPM-QRB: 36/48	Total = 50 Percutaneous adhesiolysis = 25 Additional 45 patients followed for 2 years in adhesiolysis group Caudal epidural = 25 - Percutaneous adhesiolysis with lidocaine, 10% NaCl solution and betamethasone; - Caudal epidural injection with catheterization, lidocaine, normal NaCl solution and betamethasone	NRS, ODI, opioid intake, employment status	80% of adhesiolysis had >50% relief vs 28% for caudal	80% of adhesiolysis had >50% relief vs 12% for caudal	76% of adhesiolysis had >50% relief (3.5 average injections) vs 4% for caudal	71% of patients in adhesiolysis group only	P	P	P	P	Short- and long-term effectiveness of adhesiolysis on chronic intractable pain secondary to lumbar central spinal stenosis

Table 5 (con't). *Effectiveness of percutaneous adhesiolysis assessed by randomized controlled trials and observational studies.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	≥ 12 mos.	24 mos.	
Karm et al, 2018 (900) RA, AC, DB Refractory central lumbar spinal stenosis who suffered from chronic lower back pain and/or lumbar radicular pain Quality Scores: Cochrane: 11/13 IPM-QRB: 34/48	Total = 44 Balloon adhesiolysis = 24 Balloon-less adhesiolysis = 20 2-day percutaneous adhesiolysis with inflatable balloon catheter or balloon-less catheter	NRS, ODI, GPES, MQS	Successful response of 40% in balloon-less group and 58% in inflatable balloon group	Successful response of 25% in balloon-less group and 58% in inflatable balloon group	NA	NA	N = (balloon-less), P = (inflatable balloon)	NA	NA	NA	Negative study for adhesiolysis with balloon-less catheter, positive study for inflatable balloon catheter on chronic lower back pain and/or lumbar radicular pain
Choi et al, 2016 (908) Single arm, prospective observational study Severe spinal stenosis Quality Score: IPM-QRBNR = 28/48	61 patients Adhesiolysis with a single combined treatment with balloon inflatable catheter ZiNeu.	NRS, ODI measures at 1, 3, 6, and 12 months, 30% or more than 2-point reduction in NRS	61%	57%	36%	NA	P	P	P	NA	Patients with severe stenosis and also significant proportion of patients with foraminal stenosis, 31%, were included. There was large number of patients missing followup at end of one-year. Improvement of 30% or NRS of 2 considered
Choi et al, 2013 (910) Retrospective assessment Post-lumbar surgery syndrome or spinal stenosis Quality Score: IPM-QRBNR = 24/48	78 patients studied with percutaneous adhesiolysis with caudal approach. Following appropriate adhesiolysis, 5 mL of 0.25% ropivacaine containing 1,500 units or hyaluronidase was injected in the recovery room. 6 mL of 10% sodium chloride solution was injected. Following this, 2 mL of 0.9% sodium chloride solution containing 40 mg of triamcinolone was injected.	Pain relief. Assessment of proportion of patients based on severity of the stenosis.	51.1% successful response	49% successful response	NA	NA	P	NA	NA	NA	Small retrospective assessment in 78 patients with positive results with a single treatment in 51% of the patients at 3 months and 49% of the patients at 6 months. Authors also included a large number of patients with previous surgery of 37% of the patients. They also included 33% with foraminal stenosis. In addition severe stenosis was seen in 13% of the patients and root compression in 46% of the patients providing somewhat mixed results.

Table 5 (con't). *Effectiveness of percutaneous adhesiolysis assessed by randomized controlled trials and observational studies.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	≥ 12 mos.	24 mos.	
DISC HERNIATION											
Gerdesmeyer et al, 2013 (895) RA, PC, DB Chronic lumbar radicular pain lasting longer than 4 months Quality Scores: Cochrane: 13/13 IPM-QRB 44/48	Total = 90 Percutaneous adhesiolysis = 46 Placebo = 44 - Percutaneous adhesiolysis with steroids and 10% saline solution; - Placebo (no spinal canal insertion, saline solution)	ODI, VAS	26/45 of treated group had >50% improvement in ODI compared to 7/42 of placebo group	31/42 of treated group had >50% improvement in ODI compared to 4/37 of placebo group	28/31 of treated group had >50% improvement in ODI compared to 9/26 of placebo group	NA	P	P	P	NA	Short- and long-term effectiveness of adhesiolysis on chronic lumbar radicular pain Most relevant placebo-controlled trial

RA = randomized; DB = double-blind; AC = active control; PC = placebo-controlled; P = positive; N = negative; NA = not applicable; NRS = Numeric Rating Scale; ODI = Oswestry disability index; VAS = Visual Analog Scale; GHS = Gerbershagen score; SFM = Short Form McGill Pain Questionnaire; GPES = Global Perceived Effect of Satisfaction; MQS = Medication Quantification Scale III; IPM-QRB = Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment; IPM-QRBNR = Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment for Nonrandomized Studies

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Table 6. *Characteristics of fluoroscopic cervical/thoracic interlaminar epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Manchikanti et al 2013 (922) RA, AC, DB, F Cervical disc herniation or radiculopathy Quality Scores: Cochrane = 12/13 IPM-QRB = 43/48	Total = 120 Local anesthetic = 60 Local anesthetic with steroids = 60 Local anesthetic or with Celestone Average number of injections = 5 to 6 for 2 years	NRS, NDI, employment status, opioid intake Significant improvement > 50% pain relief and > 50% functional status improvement	Overall: LA 83% vs LA with steroid 70% Responsive: LA 91% vs LA with steroid 84%	Overall: LA 82% vs LA with steroid 73% Responsive: LA 91% vs LA with steroid 86%	Overall: LA 72% vs LA with steroid 68% Responsive: LA 77% vs LA with steroid 82%	Overall: LA 72% vs LA with steroid 68% Responsive: LA 77% vs LA with steroid 80%	P	P	P	P	•Positive results in a randomized large trial performed under fluoroscopy with long-term follow-up. •Similar results with local anesthetic or with local anesthetic and steroids. •Overall, a total of 5-6 injections were administered over a period of 2 years.
McCormick et al, 2017 (941) RA, SB, AC, F Unilateral cervical radicular pain C5-C6 Quality Scores: Cochrane = 10/13 IPM-QRB = 37/48	Total = 76 Standard interlaminar epidural injection at C5-C6 = 40 Targeted cervical interlaminar epidural steroid injections = 36 Injectate was 2 mL of triamcinolone acetonide (80 mg) diluted in 1 mL of 1% preservative free lidocaine in both groups.	NRS, ONDI, PDI, MPQ, PGIC, DME, MQS	NRS standard group: Baseline: 6 3 months: 2.5 NRS targeted catheter group: Baseline: 7 3 months: 2 ONDI standard group: Baseline: 21 3 months: 15.5 ONDI targeted group: Baseline: 19 3 months: 10.5	NRS standard group: 6 months: 2 NRS targeted catheter group: 6 months: 2 ONDI standard group: 6 months: 8 ONDI targeted group: 6 months: 7.5	NA	NA	P	NA	NA	NA	This is a prospective randomized comparative trial of standard interlaminar epidural injection compared to targeted steroid injection via epidural catheter approach in unilateral cervical radicular pain showing effectiveness of both modalities and no significant difference noted between the modalities. The relief with one injection lasted almost 6 months in responsive patients, which is unusual based on the other studies.
Cohen et al, 2014 (932) RA, AC, F Cervical disc herniation or radiculopathy Quality Scores: Cochrane = 6/13 IPM-QRB = 24/48	Total = 169 Conservative treatment group = 59 (medical therapy and physical modalities) Epidural steroid injection group = 58 (3 mL of solution containing 60 mg of depo-methylprednisolone and normal saline) Combination therapy group = 55 (epidural steroid injection and pharmacotherapy with gabapentin and physical modalities)	Within group changes and between group changes, pain, NRS, NDI	Positive outcome: Conservative group: 26.8% Epidural group: 36.7% Combination therapy group: 56.9%	Positive outcome: Conservative group: 23.6% Epidural group: 25.5% Combination therapy group: 44%	NA	NA	U	NA	NA	NA	•Undetermined results at 3 months for epidural steroid injection without local anesthetic combined with conservative management, with borderline response in 36.7% at 3 months and 25.5% at 6 months with epidural injections. •This trial included acute and chronic pain patients. Number of injections provided is not shown. Local anesthetic was not utilized. There was a large number of patients who were not compliant in conservative and combination groups.

Table 6 (con't). *Characteristics of fluoroscopic cervical/thoracic interlaminar epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Manchikanti et al, 2012 (925) RA, AC, F Cervical spinal stenosis Quality Scores: Cochrane = 11/13 IPM-QRB = 42/48	Total = 60 Local anesthetic only = 30 Local anesthetic with steroids = 30 Local anesthetic or with Celestone Average number of injections = 3 to 4 for 1 year	NRS, NDI, employment status, opioid intake Significant improvement > 50% pain relief and > 50% functional status improvement Responsive was defined as those patients responding with at least 3 weeks of improvement with the first 2 procedures.	Overall: LA 77% vs LA with steroid 87% Responsive: LA 79% vs LA with steroid 82%	Overall: LA 87% vs LA with steroid 80% Responsive: LA 79% vs LA with steroid 92%	Overall: LA 73% vs LA with steroid 70% Responsive: LA 90% vs LA with steroid 89%	NA	P	P	P	NA	•Preliminary results of a large randomized trial performed under fluoroscopy with positive results. •Similar results with local anesthetic or with local anesthetic and steroids. •Overall, 3-4 injections were provided over a period of 1 year.
Manchikanti et al 2014 (924) RA, DB, AC, F Cervical axial or discogenic Quality Scores: Cochrane = 11/13 IPM-QRB = 44/48	Total = 120 Local anesthetic only = 60 Local anesthetic with steroids = 60 Local anesthetic or with Celestone Average number of injections = 5 to 6 for 2 years	NRS, NDI, opioid intake, employment, changes in weight Significant improvement > 50% pain relief and > 50% functional status improvement	Overall: LA 68% vs LA with steroid 77% Responsive: LA 75% vs LA with steroid 82%	Overall: LA 67% vs LA with steroid 73% Responsive: LA 73% vs LA with steroid 79%	Overall: LA 72% vs LA with steroid 68% Responsive: LA 78% vs LA with steroid 83%	Overall: LA 73% vs LA with steroid 70% Responsive: LA 78% vs LA with steroid 75%	P	P	P	P	•Positive results of a large RCT performed under fluoroscopy. •Similar results with local anesthetic or with local anesthetic and steroids. •A total of 5-6 injections on average were provided over a period of 2 years.
Manchikanti et al, 2018 (927) RA, AC, F Cervical post-surgery syndrome Quality Scores: Cochrane = 11/13 IPM-QRB = 42/48	Total = 116 Local anesthetic only = 58 Local anesthetic with steroids = 58 Local anesthetic or with Celestone Average number of injections = 5 to 6 for 2 years	NRS, NDI, employment status, opioid intake Significant improvement > 50% pain relief and > 50% functional status improvement Responsive was defined as those patients responding with at least 3 weeks of improvement with the first 2 procedures.	NA	Overall: LA 69% vs LA with steroid 74% Responsive: LA 74% vs LA with steroid 81%	Overall: LA 74% vs LA with steroid 69% Responsive: LA 79% vs LA with steroid 81%	Overall: LA 69% vs LA with steroid 71% Responsive: LA 74% vs LA with steroid 79%	P	P	P	P	•An active-control trial conducted with fluoroscopy with positive results. •Similar results with local anesthetic or with local anesthetic and steroids. •On average, 3-4 injections were provided during one-year and 5-6 injections for 2 years.

Table 6. *Characteristics of fluoroscopic cervical/thoracic interlaminar epidural injections.*

Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Manchikanti et al, 2014 (588) RA, AC, DB, F Thoracic pain Quality Scores: Cochrane = 11/13 IPM-QRB = 43/48	Total = 110 Local anesthetic only = 55 Local anesthetic with steroids = 55 6 mL of local anesthetic only or 6 mL of local anesthetic with 6 mg of nonparticulate betamethasone Average number of injections = 5 - 6 for 2 years	NRS, ODI, employment status, opioid intake Significant improvement > 50% pain relief and > 50% functional status improvement	Overall: LA 78% vs LA with steroid 82% Responsive: LA 88% vs LA with steroid 86%	Overall: LA 74% vs LA with steroid 84% Responsive: LA 84% vs LA with steroid 90%	Overall: LA 71% vs LA with steroid 84% Responsive: LA 80% vs LA with steroid 90%	Overall: LA 71% vs LA with steroid 80% Responsive: LA 80% vs LA with steroid 86%	P	P	P	P	•First large randomized trial with active control design and long-term follow-up. •Similar results with local anesthetic or with local anesthetic and steroids. •On average, 5-6 total procedures were performed over a period of 2 years.
Joswig et al, 2018 (937) R, F Cervical disc herniation	Total = 45 Injectate: 0.5% bupivacaine 1 mL mixed with 40 mg of triamcinolone	VAS, NDI	66.7% responded with pain relief and improvement in disability scores	NA	36 of 45 responded. 7 patients received a second injection and 6 of them responded with one of them be lost to follow-up	NA	P	P	P	NA	This is a study to assess the safety of a second interlaminar epidural injection in the cervical spine. Results are rather amazing that majority of the patients had one-year relief and only 7 of 45 patients required a second injection. However, authors injected 0.5% bupivacaine, which is considered unsafe if subarachnoid leakage or injection happened in advertently.
Beyaz & Eman, 2013 (940) R, F Cervical pain syndrome	Total: 65 Discal pathology = 26 Degenerative pathology = 38 Spinal stenosis = 9 Injectate = a total of 5 mL of 80 mg of triamcinolone acetonide with 3 mL of bupivacaine 0.25%	NRS	Satisfaction scores were average 3.3 ± 0.9 80% of patients were classified as perfect or good satisfaction	Satisfaction scores were average 3.3 ± 0.9 80% of patients were classified as perfect or good satisfaction	Satisfaction scores were average 3.3 ± 0.9 80% of patients were classified as perfect or good satisfaction	NA	P	P	P	NA	This study was a fluoroscopy guided cervical interlaminar steroid injection; however, bupivacaine was injected which is not an appropriate injection for cervical epidural injections which may lead to substantial complications even though they have not reported any complications. Overall, the response was good with positive results.

RA = Randomized; AC = Active Control; F = Fluoroscopy; DB = Double-Blind; SB = Single Blind; R = Retrospective; P = Positive; N = Negative; NA = Not Applicable; U = Unclear; LA = local anesthetic; IPM-QRB = Interventional Pain Management techniques -- Quality Appraisal of Reliability and Risk of Bias Assessment; NRS = Numeric Rating Scale; NDI = Neck Disability Index; ONDI = Oswestry Neck Disability Index; PDI = Pain Disability Index; MPQ = McGill Pain Questionnaire; PGIC = Patient Global Impression of Change; DME = daily morphine equivalents; MQS = Medication Quantification Scale III scores

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