Critique author	**Ed Whitney**

Bibliographic Data	
Authors	Chou R, Hashimoto R, et al
Title	Epidural Corticosteroid Injections for Radiculopathy and Spinal Stenosis: A Systematic Review and Meta-analysis
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Other information if relevant	

Methods	
Aim of study	To assess the effectiveness of epidural corticosteroid injections in patients with lumbar radiculopathy or spinal stenosis
Design	Meta-analysis of randomized clinical trial

PICOS	
Population from which participants are drawn	- Patients with diagnoses of radicular low back pain or lumbar spinal stenosis of any duration - Back pain due to fracture, high-impact trauma, cancer, and infection was excluded from consideration
Intervention being evaluated	Epidural injection of corticosteroids by any approach (transforaminal, interlaminar, or caudal Transforaminal injections which did not enter the epidural space (periradicular injections)
Comparison or control intervention	- Injections in which a placebo is used in place of a corticosteroid - Placebo could be either saline, a local anesthetic, or a soft tissue injection - Injections for radiculopathy using different approaches (transforaminal versus interlaminar versus caudal)

Outcomes	- Pain scores, with priority given to leg pain over back pain - Function - Outcomes classified as immediate (5 days to 2 weeks), short term (2 weeks to 3 months), intermediate term (3 months to 1 year), and long term (more than one year) - Minimum clinically important differences were defined as an improvement of 15 points on a pain scale 0 to 100, 10 points on the Oswestry Disability Index, and 5 points on the Roland-Morris Disability Questionnaire (RMDQ)
Study types	Randomized clinical trials for measures of effectiveness Observational studies for measures of adverse outcomes and harms

Study selection	
Search date of literature review	Through May 2015
Databases in literature search	MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, reference lists from included articles, and clinicaltrials.gov
How authors assessed study quality (risk of bias and other considerations	The authors assessed risk of bias by asking the following questions relating to each study, based on criteria suggested by Furlan 2009: Was the method of randomization adequate? Was the treatment allocation concealed? Was knowledge of the allocated interventions adequately prevented during the study? Was the patient blinded to the intervention? Was the care provider blinded to the intervention? Was the outcome assessor blinded to the intervention? Were incomplete outcome data adequately addressed? Was the drop-out rate described and acceptable? Were all randomized participants analyzed in the group to which they were allocated? Are reports of the study free of suggestion of selective outcome reporting? Were the groups similar at baseline regarding the most important prognostic indicators? Were co-interventions avoided or similar? Was the compliance acceptable in all groups? Was the timing of the outcome assessment similar in all groups?

Additional information if relevant	The same journal recently published a meta-analysis on epidural steroids for radiculopathy (sciatica) (Pinto 2012), and this review essentially replicates the results of the earlier meta-analysis Pinto did not separate out studies on spinal stenosis Only data on ESI for spinal stenosis is reviewed below

Results	
Number of studies screened	679 articles were screened for both radiculopathy and spinal stenosis
Number of studies selected for analysis of results	- 30 studies of radiculopathy - 8 studies of spinal stenosis (771 randomized patients)
Whether authors elected to perform meta-analysis to pool study results statistically and type of meta-analysis done (fixed effect or random effects, heterogeneity, etc)	- Although only one study of spinal stenosis was of high quality, the authors pooled results of all studies which reported the outcome of interest - The authors used random effects models to pool studies - Since the heterogeneity was very low for the meta-analyses of pain and most functional outcomes, the pooled analyses can be treated as if they had arisen from fixed effect meta-analyses - That is, the results from the high-quality study were not materially altered by the inclusion of results from the lower quality studies
Quality of studies as assessed by authors	- Only one study of spinal stenosis was considered good quality (Friedly 2014); all the other studies were fair or poor
Effect sizes reported for primary outcomes (mean differences, standardized mean differences, response ratios, etc)	- Pain scores were pooled using weighted mean differences on a scale from 0 to 100 - For none of the pain scores (short, intermediate, or long term) was there a statistically significant difference for steroid injection versus placebo - Functional scores were reported as standardized mean differences for short term followup and as weighted mean differences for intermediate term and long term followup - For none of these functional measures was there a statistically significant difference for steroid injection versus placebo
Effect sizes reported for additional outcomes (mean differences, standardized mean differences, response ratios, etc)	- Some composite outcomes were examined but were not well defined; however, for none of them were there statistically significant difference for steroid injection versus placebo

Additional information if relevant	

Conclusions	
Key conclusions of study authors	- Limited evidence suggests that epidural steroid injections are not effective for spinal stenosis - For spinal stenosis, research is needed to determine whether there may be specific subgroups who would benefit from ESI
Additional information if relevant	- Most of the meta-analysis focused on ESI for radiculopathy, and repeated the recent analysis of Pinto 2012, concluding that ESI confers immediate improvements in pain, but that benefits are small and are not sustained

Comments by DOWC staff

- Neither the main article nor the online appendix display a chart showing how the authors assessed the individual studies on the risk of bias criteria from Furlan 2009
- The largest study of spinal stenosis was Friedly 2014; this was also the only study rated as high quality
- The patients in the Friedly study all had central lumbar spinal stenosis
- Friedly found a small difference in favor of ESI over lidocaine in physical function at 6 weeks when results were adjusted for the duration of pain at baseline, but no difference in leg pain
- One potentially relevant adverse effect of ESI not mentioned by the authors relates to systemic effects on the hypothalamic-pituitary-adrenal axis
- However, Friedly 2014 reported on morning cortisol levels 3 weeks and six weeks after injection; in the lidocaine only group, only 1 of 151 patients had a morning cortisol less than 3 mcg/dl at 3 weeks, compared to 16 of 163 patients in the lidocaine-steroid group
- At 6 weeks, no patient in their lidocaine group had an AM cortisol less than 3 mcg/dl, and 5 of 152 patients in the ESI group had AM cortisol less than 3 mcg/dl
- The primary outcome for Friedly, the RMDQ, has 24 items relating to back disability, all of which are equally weighted
- However, in the setting of spinal stenosis, not all 24 items are equally relevant or sensitive to changes in stenosis-related functional difficulties
- For example, an item like “my appetite is not very good because of my back problems or leg pain” is weighted equally with an item like “”I am not doing any of the jobs I usually do around the house”
- For this reason, there was some concern that the RMDQ could fail to capture some variables, such as balance and weakness, which are common limitations of spinal stenosis, and this could be an important limitation to the conclusions of the Friedly study
- Accordingly, the authors (Makris 2017) reanalyzed the trial data using patient priority weighting, assigning weights to the RMDQ items which reflect their differential relevance to spinal stenosis patient-important outcomes, so that an item like having to hold onto something to get out of an easy chair carries 8.2 points while an item relating to appetite carries only 3.7 points
- The authors hypothesized that the re-analysis would change the primary outcome data and would affect the conclusion of the original study
- When this re-analysis was done, however, the conclusions of the original study were unchanged; the authors again concluded that there were no clinically important differences between ESI and lidocaine injection

Assessment by DOWC staff	

Overall assessment as suitability of evidence for the guideline ☒ High quality ☐ Adequate ☐ Inadequate	High quality meta-analysis supporting strong evidence that in the setting of lumbar spinal stenosis, an epidural injection of corticosteroid plus local anesthetic confers no clinically important benefits compared to injection with local anesthetic alone. There is good evidence from one high quality randomized trial that morning cortisol may be suppressed to less than 3 mcg/dl in up to 10% of patients undergoing epidural steroid injections when measured three weeks after the injection
If inadequate, main reasons for recommending that the article not be cited as evidence	

Additional references if relevant

- Friedly JL, Comstock BA, et al. A randomized trial of epidural glucocorticoid injections for spinal stenosis. New Engl J Med. 2014;371(1):11-2
- Furlan AD, Pennick V, et al. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine 2009;34:1929-41
- Makris UE, Edwards TC, et al. Patient Priority Weighting of the Roland Morris Disability Questionnaire Does Not Change Results . Spine of the Lumbar Epidural Steroid Injections for Spinal Stenosis Trial. Spine 2017;42:(1):42-48.
- Pinto RZ, Maher CG, et al. Epidural corticosteroid injections in the management of sciatica: a systematic review and meta-analysis. Ann Intern Med. 2012;157:865-77.