

September 15, 2015

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Submitted via e-mail: shtap@hca.wa.gov

Dear Ms. Teeter:

Representatives of 15 medical specialty societies, comprising physicians who perform spinal injection procedures and those whose practices rely on them in determining appropriateness of more invasive surgical treatments, have convened to review and comment on the proposed key questions for the Washington State Health Care Authority's (WA HCA) Health Technology Assessment Program's re-review of spinal injections. These medical specialty societies share a common goal with the WA HCA: identifying spinal injections that provide value to the patient and society through measurable improvements in pain and physical functioning with no or minimal adverse events.

We extend to the committee an offer to provide national and international expert input as a resource for this process. We are fully cognizant of the issues of overutilization and inappropriate utilization, and therefore also wish to bring into focus which interventions are effective when treating the various causes of back and neck pain. We have concerns, however, that the questions posed, along with the review's proposed inclusion/exclusion criteria, will not assist in making such determinations, and that the report's conclusions may lead to egregious denial of access to these procedures for many patients suffering from back and neck pain. We trust that due consideration will be given to our comments and that the key questions and inclusion/exclusion criteria will be revised to ensure that the **best available evidence** is addressed scientifically in order to provide an accurate assessment of the procedures reviewed.

Our primary concerns relative to inclusion/exclusion criteria and framing of the key questions fall into four main categories:

- Assertions Regarding the Nonspecific Nature of Back and Neck Pain
- Evidence Base Restriction to Randomized Controlled Trials (RCTs)
- Importance of Subgroup Analyses for Each Question
 - Specific Diagnoses
 - Image Guidance
 - Approach/Access
- Importance of Reliance on Categorical Data, Not Continuous Data

Assertions Regarding the Nonspecific Nature of Back and Neck Pain

The background information provided begins with the assertion that, "Approximately 90% of low back pain is of the nonspecific type, and a similar majority of neck pain is nonspecific." There is no reference cited to support this statement, and this is not substantiated in clinical practice.

Systematic application of controlled anesthetic blocks or provocation procedures can achieve somewhat less sensitive, but far more specific diagnoses than simply relying on symptoms. (1) Radiculopathy has specific observable physical examination and electrophysiologic findings. Radicular pain without radiculopathy can be diagnosed by a combination of history [pain travelling or shooting down the leg in a narrow band (lumbar) or radiating to the distal arm (cervical)], physical exam [e.g. straight leg raising test (lumbar), Spurling's maneuver (cervical)] and controlled selective nerve blocks. Somatic axial pain experienced in the lumbar region can be specifically attributed to the facet joints (dual comparative medial branch blocks), the intervertebral discs (disc stimulation), paraspinal muscles and fasciae (trigger point injections), or the sacroiliac joints (controlled intra-articular blocks and multi-site, multi-depth lateral branch blocks). Cervical axial pain can be attributed to the facet joints by dual comparative medial branch blocks and to the intervertebral discs by disc stimulation. Numerous studies over the past 20 years have established prevalence rates for these specific pain generators and their relationship to age and gender. (2-8) Asserting that 90% of back and neck pain is nonspecific is erroneous and fails to recognize decades of progress in the specific diagnosis of the processes causal of the symptoms of back and neck pain. We feel it is inappropriate to ignore this body of evidence and accept trials whose inclusion criteria are mere symptoms, resulting in heterogeneous patient populations. The review should assess the effectiveness and risks of these procedures in treating patients with specific diagnoses, which have been confirmed by physical examination findings and appropriate diagnostic blocks.

Evidence Base Restriction to Randomized Controlled Trials (RCTs)

With a restriction to randomized controlled trials (RCTs) as the sole evidence to address questions of efficacy, the ensuing report will ignore the **best available** evidence. The exclusion of high quality observational studies of clinical effectiveness removes important information and context from a synthesis of the literature. (9-11) Recent methodology literature suggests that effect estimates from high quality observational trials do not differ significantly from RCTs. (11) Many of the RCTs that will meet the inclusion criteria include patients selected only by symptoms or in whom image guidance has not been utilized. These failings, further discussed below, make such trials irrelevant to current clinical practice and not unexpectedly show poor outcomes. Judging optimal practice of precise needle placement to a 1 - 2mm target zone in three dimensional space with confirmation of medication distribution by real-time observation of contrast flow, by using data from blind injections into an unknown tissue compartment has no validity. There are very few RCTs that utilize current practice standards. Hence examination of current large observational studies adds important information that is more relevant to current standards of practice.

Importance of Subgroup Analyses for Each Question

Specific Diagnosis

It is critical to perform subgroup analyses by specific diagnoses. Many studies fail to adequately specify the process under treatment. For example, there is no physiologic process beyond systemic effect by which steroids delivered to the epidural space would be expected to relieve axial back pain arising from nociception in the intervertebral discs, facet joints, sacroiliac joints, or supporting musculature. There is ample experimental and clinical evidence that radicular pain has an inflammatory basis and is potentially susceptible to targeted delivery of an anti-inflammatory agent to the interface of neural tissue and the compressive lesion. (12) For this reason, it is

imperative that studies included in the assessment have diagnostic specificity, with correlative imaging findings as a requirement for inclusion.

For perspective, consider a hypothetical systematic review of prescription medication for the treatment of cough, a common symptom like low back pain. Studies may show beneficial effects from antibiotics in a group of patients with bacterial pneumonia, a specific diagnosis, whereas pooled data from heterogeneous groups of patients with cough– including viral bronchitis, chemical pneumonitis, asthma, lung cancer, *etc.* – would produce different effects. If these pooled effects showed that many different medications had minimal impact on cough from various sources, would we abandon prescription antibiotics for pneumonia?

Additionally, the identification of the underlying etiologies of pain is essential as different pathologies not only have varying responses to treatment, but also have different natural histories, impacting prognosis. Thus, the time frame of follow-up to determine clinical utility becomes imperative. Some conditions, such as intervertebral disc herniation, can result in debilitating pain, but have an overall favorable natural history. This would be in contrast to neurogenic claudication due to central canal stenosis, which is less likely to resolve spontaneously with time. Thus short-term relief would be very appropriate and expected for pain caused by a disc herniation. To evaluate the long-term effects in this population would be as flawed as evaluating the long-term effectiveness of antibiotics for pneumonia. Again, should we withhold all antibiotics for pneumonia given the largely favorable natural history, or should we state antibiotics are ineffective because all subjects were better at 1 year follow-up? Similarly, should we withhold pain medications from patients with fractures or after orthopedic surgery, as these conditions only result in pain and have favorable natural histories?

Image Guidance

The techniques utilized in the administration of epidural steroids are also critical. Studies have demonstrated that up to 74% of “epidural” steroid injections performed without image guidance either deposit medication external to the epidural space or do not reach the targeted pathology within the ventral epidural space. (13-16). It is critical that studies included in the review are restricted to those that use image guidance to ensure that medications have been delivered to the target.

Image guidance is absolutely essential for the safe and efficacious performance of spinal injection procedures, based on a large body of non-RCT evidence. Failure to do so would place WA HCA in conflict with the Food and Drug Administration’s Safe Use Initiative, which recommends image guidance for epidural steroid injections of all types. (17)

Approach/Access

While image guidance is essential, the technique of delivery is equally important. Many midline interlaminar epidural steroid injection (ILESI) and caudal injection studies suffer from the lack of image guidance; and even when performed with image guidance, these procedures may deliver medication distant from the site of pathology, without certainty that the steroid will reach, or in what concentration it will reach, the target zone in the ventral epidural space. In contrast, transforaminal epidural steroid injection (TFESI) procedures place the needle in direct proximity to the target nerve and verify delivery to that site by observing contrast media flow. (18) Recently described lateral parasagittal ILESI have also been shown to preferentially deliver injectate to the

target ventral epidural space. (19) It is not reasonable to combine these injection techniques in an evaluation of “epidural steroid injections”.

Importance of Reliance on Categorical Data, Not Continuous Data

In addition to image guidance and injection technique, another important study characteristic is the method of reporting outcomes data. Many studies report only continuous data as a comparison between group means in reference to a minimum clinically important difference. However, pain and functional disability data are not normally distributed. Rather, responses are often bimodal, with segregation into responder and non-responder populations that will be concealed by evaluating group means. Categorical outcomes that define the proportion of patients reaching a predefined responder status are critical to meaningful interpretation, as noted in the recent NIH Task Force recommendations on research standards for chronic low back pain. (20)

COMMENTS ON SPECIFIC QUESTIONS

Question 1:

What is the evidence of efficacy and effectiveness of spinal injections?

Suggest that Question 1 is not needed. Question 3 should be the only question relative to efficacy and effectiveness. Assess the evidence by diagnosis, use of image guidance, and approach, relying on the best available literature, not restricting to RCTs of heterogeneous patient populations. Aggregating multiple procedures, or heterogeneous techniques of a class of procedures, is useless.

If retaining Question 1, add considerations of:

- Prevention of spine surgery
- Use of epidurals in conjunction with other modalities (evidence of synergy; e.g. mechanical diagnosis and treatment-based physical therapy)
- Analgesic medication use, separately from opioid use
- Subgroup analysis by diagnoses
- Subgroup analysis by use of image guidance
- Subgroup analysis by approach/access

Question 2: What is the evidence of the safety of spinal injections?

Add considerations of:

- This question must take into consideration comparison of the risks of spine surgery, the typical alternative treatment option in patients properly selected for spine injection.
- This question must also take into consideration comparison of the risks of pharmacologic treatment of persisting spine pain, particularly treatment with opioid analgesics.
- Careful consideration when addressing this question must separate adverse event rates in the context of adherence to society guidelines vs. the rate of adverse events when injections are performed without such rigor. In particular, serious irreversible complications have yet to be reported in most spinal injections performed in accordance with Spine Intervention Society Guidelines. (21-23)
- Subgroup analysis by diagnoses
- Subgroup analysis by use of image guidance
- Subgroup analysis by approach/access
- Case reports provide no insight into the frequency of adverse events.

Question 3: What is the evidence that spinal injections have differential efficacy or safety issues in subpopulations?

- Consideration (d) indicates “diagnosis or time elapsed from fracture” – suggest (d) should be “diagnosis” and another consideration should be “subacute or chronic nature of condition”
- Include all considerations listed in Question 1, along with:
 - Prevention of spine surgery
 - Use of epidurals in conjunction with other modalities (evidence of synergy; e.g. mechanical diagnosis and treatment-based physical therapy)
 - Analgesic medication use, separately from opioid use
 - Subgroup analysis by use of image guidance
 - Subgroup analysis by approach/access

Question 4: What is the evidence of cost implications and cost-effectiveness of spinal injections?

- Cost-comparison of spinal injection treatment paired with other conservative measures (e.g., PT, oral analgesics) to spinal surgery paired with other conservative measures (e.g., PT, oral analgesics) must specifically be addressed given that this is the typically realistic clinical picture.
- Comparisons to individual competing therapies: physical therapy, NSAIDs, opioids, surgery: this inevitably requires an assessment of their clinical effectiveness, where such data exist.
- Subgroup analysis by diagnoses
- Subgroup analysis by use of image guidance
- Subgroup analysis by approach/access

Summary

It is imperative to recognize that study methodology is meaningless unless the procedures being assessed are performed on appropriately selected patients with appropriate indications using accurate and current technique. An RCT with sound randomization, excellent blinding, and no losses to follow-up is of no value if the patients did not have the condition under investigation and/or the therapeutic procedure was not conducted accurately. Stratification of studies by appropriate patient selection and acceptable, technical performance of the procedures is critically important and must be considered in parallel with, or even precede, evaluation of study design in assigning value to a study.

The description of the health technology assessment process on the WA HCA website indicates that clinical experts may be consulted at various points throughout the process. The clinical experts serving in any advisory role for the upcoming review must be intimately familiar with the intricacies of proper patient selection and study design, technical ‘nuances’ of proper injection techniques, and the utility of various outcome measures. The process for selecting these experts needs to be rational and transparent. Experts should be highly regarded among their peers in the field of interventional pain management. We propose that Washington State Health Care Authority and its technology assessment center seek guidance from the Multisociety Pain Workgroup (MPW) in identifying appropriate technical experts.

Thank you for considering our comments, which are offered in the spirit of collaboration to ensure an accurate assessment of the injection procedures that can be effective tools in the treatment of appropriately selected patients. If you have any questions or wish to discuss our comments, please contact Belinda Duszynski, Senior Director of Policy and Practice at the Spine Intervention Society, at bduszynski@spinalinjection.org.

Sincerely,

American Association of Neurological Surgeons

American Academy of Pain Medicine

American Academy of Physical Medicine and Rehabilitation

American College of Radiology

American Pain Society

American Society of Anesthesiologists

American Society of Neuroradiology

American Society of Regional Anesthesia and Pain Medicine

American Society of Spine Radiology

Congress of Neurological Surgeons

North American Neuromodulation Society

North American Spine Society

Society of Interventional Radiology

Spine Intervention Society

Washington State Association of Neurological Surgeons

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