September 11, 2015
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
International Spine Intervention Society
North American Neuromodulation Society
North American Spine Society
Society of Interventional Radiology

Dear Medical Specialty Societies,

Thank you for your thoughtful comments on the Agency for Healthcare Research and Quality (AHRQ) Technology Assessment entitled *Pain Management Injection Therapies for Low Back Pain*. The report was conducted at the request of the Centers for Medicare and Medicaid Services (CMS) to review current evidence on injection therapies for low back pain. In accordance with AHRQ Technology Assessment Program’s standard protocols for conducting Technology Assessment Reports, the review followed the Evidence-based Practice Center (EPC) Program’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews (http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=318). The Methods Guide describes the process for grading the strength of evidence and applicability of evidence. Individual studies have different strengths and weaknesses and are assessed along multiple domains. Results are communicated with a rating of confidence in the findings. As with all Technology Assessment Reports, the findings and conclusions in the review are those of the authors who have scientific independence and are responsible for its contents.

Your letter points out the importance and challenges of defining the population and interventions under examination within a systematic review. The TA used a systematic approach which was based on predefined inclusion/exclusion criteria (determined with the input of key informants and subject to public comment) and systematic evaluation of patient and technical factors. The TA included an overall pooled analysis, but also to the
extent possible based on information in the studies, the TA analyzed the impact of specific techniques and patient selection criteria.

We very much appreciate your careful review and comments in your letter of July 29 on the AHRQ report Pain Management Injection Therapies for Low Back Pain. In response to general issues you raise:

1. **Potential differential effectiveness in patient populations with symptoms of "Non-specific" low back pain vs patients diagnosed with identified pathoanatomic cause**

   We agree the patient selection is an important factor in determining the effectiveness of an intervention, particularly when there may potentially be heterogeneity in treatment effectiveness. We recognize that there are tests such as selective nerve blocks that may assist in further identification of pathoanatomic causes. The TA did attempt to evaluate how use of diagnostic blocks to select patients impacted estimates of effectiveness in addition to the overall pooled analysis. The clinical trials included in the TA had different criteria for enrolling patients, sometimes including patients without diagnosed pathoanatomic causes. While the TA pre-specified inclusion criteria to include all studies of patients with only symptoms as well as those with diagnosed pathoanatomic causes, it also analyzed separately studies restricted to all the variables that you mention. These issues are discussed in the section on applicability and implications for clinical and policy decision making on pages 49-50: “Trials also differed in methods used to select patients for inclusion. For example, trials of radiculopathy and spinal stenosis differed in the clinical symptoms required for enrolment as well as in whether concordant imaging findings were required, and trials of presumed facet joint pain varied in whether a positive response to diagnostic blocks were required as well as methods for performing blocks (e.g., single or double block). Potential strategies to enhance the effectiveness of epidural injections would be to perform them using techniques shown to be more effective, or to selectively perform injections in patients more likely to benefit. However, our review found no clear evidence of greater benefits based on technical factors such as the specific epidural technique used, use of fluoroscopic guidance, the specific corticosteroid, the dose, or the number or frequency of injections. Evidence on patient factors was also too limited to identify subgroups of patients more likely to benefit.”

2. **Potential differential effectiveness in injections with image guidance vs those without**

   We agree with the importance of identifying any modifying factors that may affect the effectiveness of therapies for LBP. The TA attempted to analyze the effect of imaging guidance on patient-centered
outcomes, but (as you noted in your letter), no randomized studies examined the use of image guidance as a variable. Indirect comparisons from the randomized controlled trials could not be made because the TA found that the use of imaging guidance was highly correlated with epidural technique used. The observational studies you cited assessed anatomical delivery of medication but not patient-centered outcomes of interest. In the analysis in the TA, trials of transforaminal injections (which uniformly utilized imaging guidance) reported results that were similar to trials that used other approaches (which generally did not utilize imaging guidance). For radicular pain and spinal stenosis, the TA performed analyses based on whether imaging correlation was required, and it had no impact on estimates. Please note that all of the studies you cite about imaging guidance (references 18-22 and 9) were included in the analysis in the TA.

3. **Potential differential effectiveness in technical approach to reach the target epidural space**

In an attempt to identify modifying factors that may affect the effectiveness of therapies for LBP, the TA included a stratified analyses for different approaches or other variables in addition to an overall analysis that looked at all injection types. In the overall analysis, combining all injection types had small immediate effects that disappeared with longer-term follow-up. The analysis restricting to transforaminal injections had results that were the same or worse compared to the outcomes for all injection types. For the TFESI vs. ILESI comparisons, the pooled estimate shows no differences. Excluding trials that used different doses of steroid or didn't clearly enter the epidural space had no impact on the estimates.

We also note a few specific comments on issues you raised:

1. Thank you for pointing out the Ghahreman trial. While the analysis for the final report did acknowledge that the Ghahreman trial used imaging guidance, the text was inadvertently left uncorrected. We will be publishing an addendum/correction.
2. We appreciate your mention of RCTs on lateral parasagittal ILESI vs midline ILESI and vs RFESI. Both studies were included and called out in bullets on page 31.
3. The TA included studies with both continuous outcomes and dichotomous outcomes. We agree that there are limitations of the data, however in the TA, one type of outcome was not emphasized over another, and in fact, results using either type of outcome were similar.
Underlying all of your questions is a concern that the pooled effects from RCTs do not reflect best clinical practice, and that benefits may be obscured by including studies that used poor techniques or did not appropriately select patients. The TA did a sensitivity analysis excluding poor quality studies and found similar results. This technology assessment recognizes that there is variation in clinical practice in patient selection criteria and technical approach. This report adds the results of many new studies and analyses of technical and patient factors compared to previous systematic reviews, but there is a need for more research to inform practice and to better understand the impact of these variations on patient outcomes. As described above, the TA did try to analyze the limited data by all of the variables that you mention.

I have spoken with Dr. Maus about the possibility of the professional societies establishing a registry that could capture real-world information on variation of techniques, patient selection factors, and important outcomes for patients (including quality of life and avoidance of surgery). AHRQ offers a conference grant mechanism that might be appropriate to bring together stakeholders to discuss the design of the registry and ensure that the data elements and data collection methods will be rigorous enough to provide actionable information to various stakeholders. I would be happy to talk with you further about this. Here is a link to the conference grant announcement: http://grants.nih.gov/grants/guide/pa-files/PA-13-017.html.

We appreciate your input on this important topic.

Regards,

Elise Berliner, PhD

Director, Technology Assessment Program