October 19, 2015

Elise Berliner, PhD **via Email**
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Agency for Healthcare Research and Quality
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Dear Dr. Berliner:

We thank you for your thoughtful reply to our letter, dated July 29, 2015; however, we continue to have concerns, as the methodological flaws and resulting erroneous conclusions of the technology assessment (TA) poorly serve physicians and patients and may inadvertently cause harm. Therefore, please allow us to convey the following comments on your numbered responses:

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

While the issue is acknowledged in the TA report, as well as in your response, it still needs to be adequately addressed. The analysis did not stratify outcomes by the presence of an imaging lesion or a specific diagnosis. The inclusion criteria gave precedence to randomized controlled trial (RCT) methodology above all else and included many dated studies with patients selected based upon symptoms alone. Having failed to examine large, high quality observation trials with superior patient selection and contemporary technically superior procedural performance, while including decades-old, meaningless RCTs, the TA cannot render any useful assessment of efficacy or clinical effectiveness.

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

The TA acknowledges that there are no direct comparative effectiveness trials with image guidance as a primary variable and indirect evidence from RCTs is not applicable. Asserting that there is no evidence of benefit for image guidance ignores the extensive non-RCT body of evidence supporting image guidance, including comparison of outcomes in explanatory trials, as we previously noted. Non-RCT data also show that "epidural" injections performed without image guidance may not universally reach the epidural space, even in expert hands.[1-3] Such off-target medication delivery may not be efficacious and may be dangerous. The TA directly contradicts the FDA Safe Use Initiative on epidural steroid injections that demands image guidance. To suggest to patients and physicians that epidural steroid injections do not require image guidance may create a significant potential for patient harm.

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

The analysis of transforaminal epidural steroid injections (TFESI) vs interlaminar epidural steroid injections (ILESI) evaluates 5 comparative effectiveness trials, and using continuous data as the comparator, finds no differences. However, the Ackerman[4], Thomas[5], and Gharibo[6] trials favored TFESI over ILESI in pain relief with statistical significance. The Rados trial[7] used twice the corticosteroid dose in ILESI vs TFESI, yet the categorical outcomes favored the TFESI group, although without statistical significance. The "nerve root sheath" injections in the Kolsi study[8] are of unknown value. There is extensive evidence in large, high quality observational studies, unevaluated by the TA, supporting TFESI in treatment of radicular pain. In addition, the TA fails to adequately examine the evidence suggesting that delivery of medication to the ventral epidural space, whether by TFESI or lateral parasagittal ILESI, is a determinant of efficacy.

We agree with your assessment that "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's sensitivity analysis was not useful since the assessment of study quality considered only research methodology and not patient selection or technical procedural performance. Hence, the concern you acknowledge went unaddressed.

We would welcome the opportunity to discuss with AHRQ the conference grant to establish a patient registry that might provide patient outcome, safety, and cost effectiveness data in real-world practice, but with rigorous control for patient selection and technical procedural performance, as best clinical practice demands. We would hope that such data would be included in any future assessment of the effectiveness of injections, despite the fact that the published data would not be generated by an RCT.

AHRQ and the undersigned medical specialty societies share a common goal in identifying safe, efficacious, and cost-effective treatments for patients suffering from pain of spinal origin. Unfortunately, the methodological flaws and lack of domain expertise of the TA's authors have resulted in a report that poorly serves key stakeholders -- the AHRQ, CMS, patients, and physicians. As such, we continue to offer our collective expertise on this issue.

Yours 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

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