Washington State Health Care Authority
Health Technology Assessment

Health Technology Assessment Program: Selected Technologies 2015

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STATE OF WASHINGTON
HEALTH CARE AUTHORITY
626 8th Avenue, SE • P.O. Box 45502 • Olympia, Washington 98504-5502

February 4, 2015

To Whom It May Concern:

SUBJECT: Health Technology Assessment Topic Selection 2015

As the Director of the Health Care Authority (HCA) and per the Health Technology Assessment (HTA) law (70.14 RCW), I select technologies for review by the program in consultation with other agencies and the Health Technology Clinical Committee. Technologies are selected when there are concerns about safety, efficacy or value (cost-effectiveness), when state expenditures are or could be high, and there is adequate evidence to conduct a review. Technologies are selected for re-review when new evidence is available that could change a previous determination. In addition, anyone may petition for a technology review.

For the current selection cycle, I have reviewed the proposed topics as well as the comments received from the interested individuals and groups who responded in the first comment period January 5 through January 20, 2015. Based on the information provided by the HTA program, and the recommendations from staff in the HCA, Department of Labor and Industries and Department of Corrections, I have selected the following technologies for review:

		Primary Criteria Ranking[1]		
	Technology	**Safety**	**Efficacy**	**Cost**
1	**Extracorporeal Membrane Oxygenation (ECMO)**	**High**	**High**	**High**
	Policy Context/Reason for selection: ECMO is a critical care treatment that provides heart-lung bypass support outside of a patient's body. In adult populations there are high concerns related to the evidence of the safety, efficacy and cost-effectiveness of this treatment.			
2	**Bronchial Thermoplasty for Asthma**	**High**	**High**	**Medium**
	Policy Context/Reason for selection: Bronchial thermoplasty is a procedure used to treat asthma that is not well-controlled by medication. Smooth muscle in the lungs is altered by placement of a radiofrequency catheter that heats the muscle tissue reducing the likelihood of bronchocontriction during an asthma reaction. The specific catheter for the procedure was approved for marketing by the FDA in 2010. There are high concerns related to the safety and efficacy of bronchial thermoplasty, and medium concerns for the cost-effectiveness of the procedure.			

	Technology	Primary Criteria Ranking[1] Safety	Efficacy	Cost
3	**Novocure**	**Low**	**High**	**High**
	Policy Context/Reason for selection: Novocure (rebranded as Optune®) is a medical device currently approved for use in adult patients with glioblastoma multiforme that has recurred following chemotherapy. The device is worn on the head and applies alternating electric field therapy also referred to as tumor-treating fields (TTF). The mechanism of action for this therapy involves interfering with tumor cell replication through application of electric field therapy. Concerns for this treatment are considered low for safety, and high for efficacy and cost-effectiveness.			
4	**Pharmacogenetics**	**Low**	**High**	**Medium/High**
	Policy Context/Reason for selection: A growing number of new laboratory tests and computer based predictive algorithms are available to assess an individual patient's potential metabolic response to various drugs. Potential benefits include better application of the drugs or chemotherapy choices that will work for a specific individual. Concerns relate to whether specific tests result in improved treatment decisions and health outcomes, as well as rapid emergence and uptake of pharmacogenetic tests generally. Concerns are considered low for the safety of these tests, high for efficacy, and medium/high for cost-effectiveness.			
5	**Platelet-Rich Plasma Injections for Healing**	**Medium**	**Medium/High**	**Medium**
	Policy Context/Reason for selection: Platelet rich plasma (PRP) injections are proposed for a variety of wound healing applications. Concerns are considered medium for safety, medium/high for efficacy, and medium for cost-effectiveness.			
6	**Negative-Pressure Wound Therapy (Home Use)**	**Medium**	**Medium/High**	**Medium**
	Policy Context/Reason for selection: Negative pressure wound therapy (NPWT) is used in the treatment of slow or non-healing wounds. Home use of NPWT includes use of a portable device. Concerns are considered medium for safety, medium/high for efficacy, and medium for cost-effectiveness.			
7	**Fecal Microbiota Instillation**	**Medium**	**High**	**Low**
	Policy Context/Reason for selection: Primary use is to treat individuals with difficult to treat infections caused by C*lostridium difficile (C. difficile).* Frozen stool from health donors is transplanted to the infected individual's bowel to restore the normal balance of bacteria in the gut. Concerns are considered medium for safety, high for efficacy, and low for cost-effectiveness.			

[1] ***Link to Primary Criteria Ranking.***

Additionally, I have selected **Cardiac Stents** and **Spinal Injections** for re-review based on the newly available published evidence.

Upon publication of the selected list of technologies, a 30-day comment period will begin whereby any interested person or group may provide information relevant to review of these topics. HTA will begin work to review these technologies following this comment period.

Should you have any questions or concerns, please contact Josh Morse, HTA Program Manager, by telephone at 360-725-0839 or via email at josh.morse@hca.wa.gov.

Sincerely,

Dorothy F Teeter

Dorothy F. Teeter, MHA
Director

Washington State Health Care Authority
Health Technology Assessment

Selected Technologies

	Technology	Primary Criteria Ranking[1] Safety	Efficacy	Cost
1	**Extracorporeal Membrane Oxygenation (ECMO)**	**High**	**High**	**High**
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2	**Bronchial Thermoplasty for Asthma**	**High**	**High**	**Medium**
	Policy Context/Reason for selection: Bronchial thermoplasty is a procedure used to treat asthma that is not well-controlled by medication. Smooth muscle in the lungs is altered by placement of a radiofrequency catheter that heats the muscle tissue reducing the likelihood of bronchocontriction during an asthma reaction. The specific catheter for the procedure was approved for marketing by the FDA in 2010. There are high concerns related to the safety and efficacy of bronchial thermoplasty, and medium concerns for the cost-effectiveness of the procedure.			
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	Policy Context/Reason for selection: Novocure (rebranded as Optune®) is a medical device currently approved for use in adult patients with glioblastoma multiforme that has recurred following chemotherapy. The device is worn on the head and applies alternating electric field therapy also referred to as tumor-treating fields (TTF). The mechanism of action for this therapy involves interfering with tumor cell replication through application of electric field therapy. Concerns for this treatment are considered low for safety and high for efficacy and cost-effectiveness.			
4	**Pharmacogenetics**	**Low**	**High**	**Medium/High**
	Policy Context/Reason for selection: A growing number of new laboratory tests and computer based predictive algorithms are available to assess an individual patient's potential metabolic response to various drugs. Potential benefits include better application of the drugs or chemotherapy choices that will work for a specific individual. Concerns relate to whether specific tests result in improved treatment decisions and health outcomes, as well as rapid emergence and uptake of pharmacogenetic tests generally. Concerns are considered low for the safety of these tests, high for efficacy and medium/high for cost-effectiveness.			
5	**Platelet-Rich Plasma Injections for Healing**	**Medium**	**Medium/High**	**Medium**
	Policy Context/Reason for selection: Platelet rich plasma (PRP) injections are proposed for a variety of wound healing applications. Concerns are considered medium for safety, medium/high for efficacy and medium for cost-effectiveness.			
6	**Negative-Pressure Wound Therapy (Home Use)**	**Medium**	**Medium/High**	**Medium**
	Policy Context/Reason for selection: Negative pressure wound therapy (NPWT) is used in the treatment of slow or non-healing wound. Home use of NPWT includes use of a portable device.			

	Technology	Primary Criteria Ranking[1] Safety	Efficacy	Cost
	Concerns are considered medium for safety, medium/high for efficacy and medium for cost-effectiveness.			
7	**Fecal Microbiota Instillation**	**Medium**	**High**	**Low**
	Policy Context/Reason for selection: Primary use is to treat individuals with difficult to treat infections caused by C*lostridium difficile (C. difficile).*Frozen stool from health donors is transplanted to the infected individual's bowel to restore the normal balance of bacteria in the gut. Concerns are considered medium for safety, high for efficacy and low for cost-effectiveness.			

[1] Primary Criteria Ranking

Technologies Considered, Not Proposed

	Technology
1	Trans Catheter Aortic Valve Replacement
2	Non-Pharmacologic Treatments for ADHD
3	Non-Pharmacologic Treatments for Pain in Primary Care
4	Saturation Biopsy for Prostate
5	Circumcision

Technologies for Re-review

Technologies are considered for re-review at least once every 18 months and may be selected for update if new evidence is identified by any interested person or stakeholder that could change a previous decision. All technologies that have previously been selected and reviewed by the Health Technology Clinical Committee (HTCC) are listed below, along with information on whether they have been selected for re-review.

	Technologies	Originally Reviewed	Recommended for Re-review
1	**Cardiac Stents** New literature identified, changing standard practices and new absorbable stent devices support a re-review. Surveillance report attached.	May 2009	**Yes**
2	**Spinal Injections** New literature identified. New safety concerns emerged for epidural injections (FDA).	March 2011	**Yes**

	Technologies	Originally Reviewed	Recommended for Re-review
3	**Artificial Disks (Cervical & Lumbar)**	March 2011	No
4	**Femoroacetabular Impingement Syndrome (FAI)**	September 2011	No
5	**Stereotactic Radiation Surgery/ Stereotactic Body Radiation Therapy**	November 2012	No
6	**Applied Behavioral Therapy for Autism**	June 2011	No

For the current period, the program has not received or identified new evidence to support review of the following topics in at least 18 months:

	Topic	Date of Last Search or Re-Review
1	Arthroscopic Knee Surgery	October 2008
2	Bone Growth Stimulators	October 2009
3	Computed Tomographic Angiography	May 2009
4	Calcium Scoring	May 2010
5	Breast MRI	October 2010
6	Knee Joint Replacement or Knee Arthroplasty	December 2010
7	Vertebroplasty, Kyphoplasty, Sacroplasty	March 2011
8	Glucose Monitoring	June 2011
9	Positron Emission Tomography Scans for Lymphoma	November 2011
10	Microprocessor-controlled Lower Limb Prosthetics	March 2012
11	Osteochondral Allograft / Autograft Transplantation	March 2012
12	Sleep Apnea Diagnosis and Treatment	May 2012
13	Bone Morphogenetic Protein	May 2012
14	Upright/Positional MRI	June 2012
15	Robotic Assisted Surgery	September 2012
16	Upper Endoscopy for GERD and GERD-like symptoms	September 2012
17	Virtual Colonoscopy or Computed Tomographic Colonography	December 2012
18	Vitamin D Screening and Testing	March 2013
19	Hyperbaric Oxygen	May 2013
20	Cervical Fusion	May 2013

Washington State Health Care Authority
Health Technology Assessment

2015 HTA Proposed Technologies (New and Re-review): Response to Public Comments

January 30, 2015

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This document responds to all comments received on the 2015 Proposed HTA Technology Topics. Public comment periods were accepted from January 4 through January 20, 2015. Comments were received from the following individuals and groups:

- Robert E. Harbaugh, MD, President, American Association of Neurological Surgeons
  Nathan R. Selden, MD, PhD, President, Congress of Neurological Surgeons
  Farrokh Farrokhi, Vice-President, Washington State Association of Neurological Surgeons

- Jeffery Summers, MD, President International Spine Intervention Society

- Kelly M Shriner, Director, Health Economics & Reimbursement, Pulmonary Endoscopy, Boston Scientific

Technology	Comment	HCA Response
Topic: Novocure		
Robert E. Harbaugh, MD, President, American Association of Neurological Surgeons **Nathan R. Selden**, MD, PhD, President, Congress of Neurological Surgeons **Farrokh Farrokhi**, Vice-President, Washington State Association of Neurological Surgeons	Complete comments with information attached below.	Thank you for your comments. We appreciate that studies are on-going and additional evidence may become available. However, the technology is in use and questions about the safety, efficacy and cost-effectiveness are relevant considerations for state purchased health care. No change to proposed technologies.
Topic: Pharmacogenetics		
Robert E. Harbaugh, MD, President, American Association of Neurological Surgeons **Nathan R. Selden,** MD, PhD, President, Congress of Neurological Surgeons **Farrokh Farrokhi,** Vice-President, Washington State Association of Neurological Surgeons	Complete comments with information attached below.	Thank you for your comments. We recognize that the breadth of this topic may be too expansive for a single evidence review and policy. The scope of the review will be refined and may focus on tests proposed to improve clinical management and medication use based on genetic variability and where there is published evidence adequate for consideration. The key question phase of the review will include opportunity for further comment on the proposed scope. No change to proposed technologies.
Topic: Spinal Injections		
Jeffery Summers, MD, President International Spine Intervention Society	Complete comments with information attached below.	Thank you for your comments on the proposed re-review of the Spinal Injections topic. This review was triggered by new information related to the safety of certain medications used for epidural steroid injections and the publication of a comparative trial of epidural steroid injections. A complete literature search will be conducted by an evidence-based review group when the update is performed to identify if new evidence (other than the information already cited) has emerged that could change the prior evidence report conclusions. This will ensure that the basis for any new determination considers all relevant, newly available information. No change to proposed technologies.

Technology	Comment	HCA Response
Topic: Bronchial Thermoplasty		
Kelly Shriner, Director Economics & Reimbursement, Pulmonary Endoscopy Boston Scientifi	Complete comments with information attached below.	Thank you for your comments. References provided will beincluded for consideration in the evidence review. No change to proposed technologies.

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Portland, Oregon

January 20, 2015

Josiah Morse, MPH
Program Director
Washington State Healthcare Authority
Health Technology Assessment Program
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Re: AANS/CNS Comments on Washington State HTA Review of Novocure and Pharmacogenetics

Dear Mr. Morse:

On behalf of the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the Washington State Association of Neurological Surgeons (WSANS), we appreciate the opportunity to provide comments regarding the Washington State Healthcare Authority (WCA) Health Technology Assessment (HTA) program decision to place Novocure and pharmacogenetics on its 2015 proposed list of technologies to review. As such, we would like to share the following remarks.

Literature

We strongly agree that safety, quality, and cost are important considerations for any procedure and understand the agency's requirement to balance these considerations. We believe the early evidence for Novocure and pharmacogenetics is promising but studies are on-going and we would recommend that you wait to place these technologies on the program's agenda until additional scientific evidence becomes available.

NovoTTFTTM [NovocureTM]

Specifically for Novocure, Tumor Treating Fields (TTFields) delivered by the NovoTTF-100ATTM System in combination with standard-of-care temozolomide chemotherapy was recently assessed in a Company sponsored phase III trial [EF-14] with 2:1 randomization. Interim analysis of the first 315 patients, representing approximately 50 percent of the targeted study population, was presented on November 15, 2014 at the Society for Neuro-Oncology Annual Meeting. The patients treated with TTF demonstrated a significant increase in progression free survival compared to temozolomide alone (median PFS of 7.1 months compared to 4.0 months, respectively, hazard ratio=0.63, p=0.001); and a significant increase in overall survival compared to temozolomide alone (median OS of 19.6 months compared to 16.6 months, respectively, hazard ratio=0.75, p=0.034). Based on the interim analysis results, the Independent Data Monitoring Committee (IDMC) for the EF-14 trial recommended that the trial be stopped early and that Novocure provide access to TTFields for patients on the temozolomide alone arm. This was granted by the FDA. We anticipate that a full review of the study and publication of the results will be completed in the next few months.

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Pharmacogenetics

Pharmacogenetics holds the promise to both prognosticate patient outcomes, as well as identify which targeted treatment options work for an individual based on their specific tumor or disease. In general, we support the development of tests that would give treating physicians and their patients more information about the response to a particular treatment. However, the topic is very general with numerous biomarkers of various types currently under consideration for a variety of diseases with additional potential biomarkers under development at any given time. We hope that, should this topic be selected for review, the scope would be narrowed to consideration of specific biomarkers for specific conditions rather than a broad evaluation of the entire field.

Neurosurgeon Participation in Technical Assessment

As you know, organized neurosurgery has taking an active interest in the Washington State HTA program since it was established in 2006. We urge you to include neurosurgeons in the development of key research questions and in the review of clinical evidence included in the technical assessments prepared for these issues. AANS,CNS,WSANS and the AANS/CNS Joint Section on Tumors are able and eager to provide names of neurosurgeon tumor experts both in the state of Washington and nationally who are trained in evidence based medicine, do not have financial conflicts, and are willing to devote their volunteer time to assisting the agency in the public interest.

Conclusion

Thank you for your time and attention. We look forward to working closely with the agency during the assessment of these new technologies. Again, we are eager to help identify neurosurgeons with tumor expertise from the state of Washington and from our AASN/CNS Joint Section on Tumors to be involved in the effort as we have over the last nine years. We continue to share the agency's dedication to the best possible care for citizens of the state of Washington.

Sincerely,

Robert E. Harbaugh, MD, President
American Association of Neurological Surgeons

Nathan R. Selden, MD, PhD, President
Congress of Neurological Surgeons

Farrokh Farrokhi, Vice-President
Washington State Association of Neurological Surgeons

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January 20, 2015

Dorothy Frost Teeter, Director
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Submitted via e-mail: **shtap@hca.wa.gov**

RE: Washington State Health Care Authority's Recommendation to Re-Review Spinal Injections

Dear Ms. Teeter:

The International Spine Intervention Society, a multi-specialty association of 3,000 physicians dedicated to the development and promotion of the highest standards for the practice of interventional procedures in the diagnosis and treatment of spine pain, would like to comment on the Washington State Health Care Authority's recommendation to re-review spinal injections via the Health Technology Assessment program.

Based on the information shared during the January 9 stakeholder call, it is our understanding that the topic of spinal injections is being considered for re-review based on two new concerns:

1. The July 2014 article by Friedly *et al.* published in the New England Journal of Medicine regarding the use of epidural steroid injections for spinal stenosis.
2. The April 2014 FDA warning regarding the use of steroids in the epidural space, "Epidural Corticosteroid Injection: Drug Safety Communication - Risk of Rare But Serious Neurologic Problems".

Regarding concern #1, the Friedly *et al.* study was a comparative effectiveness study that focused only on the population of patients with primary central spinal stenosis and neurogenic claudication. Therefore, the following considerations should be noted:

- Any re-reviews should focus exclusively on the use of epidural steroid injections for degenerative central spinal stenosis and neurogenic claudication and not for radicular pain due to other causes such as herniated discs, foraminal stenosis, lateral recess stenosis, and synovial cysts. There are no new explanatory trials on the use of epidural steroid injections for the treatment of radicular pain from herniated discs, foraminal stenosis, lateral recess stenosis, and synovial cysts since the prior review by the Washington State Health Technology Clinical

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Committee (HTCC). Thus, a re-review on the use of epidural steroid injections for the treatment of radicular pain from causes other than degenerative central spinal stenosis is not justified.

- The standard of evidence for such a re-review would need to be established, given that the Friedly *et al.* study was not a placebo-controlled trial.

Regarding concern #2, we are very familiar with the issues surrounding the FDA's concerns. Attached for your review is a letter that was submitted by the International Spine Intervention Society on behalf of more than a dozen medical specialty societies to the FDA's Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC). The FDA has yet to issue a decision on this topic following the November 2014 open meeting. If the HTCC chooses to review this topic, the scope of the review should be confined to the *safety* of epidural steroid injection, and not *efficacy*. Consideration in this regard should include route of administration and the specific corticosteroid agents utilized.

We extend to the Committee an offer to provide national and international expert input as a resource in this process. If you have any questions or wish to discuss any of our comments, please contact Margaret Klys, Director of Health Policy, at mklys@spinalinjection.org or 708-505-9416.

Sincerely,

Jeffrey Summers, MD
President
International Spine Intervention Society

November 7, 2014

Randall P. Flick MD, MPH *via Email to AADPAC@fda.hhs.gov*
Chair
Anesthetic and Analgesic Drug Products Advisory Committee
c/o Stephanie L. Begansky, PharmD
Designated Federal Officer
Center for Drug Evaluation and Research
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Dear Dr. Flick and Members of the Committee:

The American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Disorders of the Spine and Peripheral Nerves, American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Pain, American Academy of Pain Medicine, American Academy of Physical Medicine and Rehabilitation, American Association of Neurological Surgeons, American College of Radiology, American Pain Society, American Society of Anesthesiologists, American Society of Regional Anesthesia and Pain Medicine, Congress of Neurological Surgeons, International Spine Intervention Society, North American Neuromodulation Society, North American Spine Society, and Society of Interventional Radiology would like to take this opportunity to comment on the safety and effectiveness of epidural steroid injections. As medical specialty societies representing physicians who perform epidural steroid injections, we are deeply committed to ensuring that patients are safe and that their quality of life is greatly improved with interventional spine care. Our organizations have a strong record of working to eliminate fraudulent, unproven, and inappropriate procedures. At the same time, we are equally committed to assuring that safe and effective treatments are preserved so that patients do not have to unnecessarily suffer or undergo more invasive surgical procedures.

On April 23, 2014, the Food and Drug Administration (FDA) released a Drug Safety Communication warning that injection of steroids into the epidural space of the spine may result in rare but serious neurologic adverse events including stroke, loss of vision, paralysis, and death. We applaud the FDA on their effort to appropriately remind physicians and patients that they should be aware of the side effects and potential complications related to any and all drugs and medications that may be considered for treatment. The risks and benefits of treatments should be openly discussed by physicians, and considered by patients when determining how best to proceed. Unfortunately, the FDA's Drug Safety Communication is also misleading. The statement indicates that the

safety and effectiveness of epidural administration of steroids have not been established. This is clearly not true based on robust literature on this topic.

Safety of Epidural Steroid Injections

While complications with epidural steroid injections (ESIs) have been reported, and are likely underreported, serious complications are limited to isolated case reports. This is despite the large number of injections performed annually.[1] No serious neurological complications have ever been reported in any prospective study of ESIs, regardless of approach or technique used, or anatomical area injected. A recently completed multi-institutional cohort of over 16,000 consecutive ESI procedures at all spine segments also reported no major complications.[2,3,4]

Particulate and Non-Particulate Steroids
Though rare, neurological complications are catastrophic and include stroke, blindness, paralysis, and death. These adverse events likely result from inadvertent injection of a radicular or vertebral artery that perfuses the spinal cord and brain. In all reported cases, particulate steroids have been used, and the mechanism of injury is presumed to be embolism of these particulates resulting in infarction. Light microscopy studies have demonstrated that the particles in these steroid preparations are either larger than red blood cells or form aggregates larger than red blood cells.[5] Additionally, animal studies have shown central nervous system infarction with intra-arterial injection of particulate steroids.[6]

This is in contrast to dexamethasone, which has particles 5 to 10 times smaller than red blood cells on microscopic evaluation, and is effectively non-particulate in this context. Dexamethasone has been shown to have no adverse sequelae with direct injection into the arterial supply of the neuroaxis in animals.[5,6] Non-particulate steroids have been routinely administered via the transforaminal epidural technical approach without a single report of a serious neurologic adverse event to date. It is logical to conclude that increased utilization of this medication will lead to decreased complication rates associated with these procedures. However, use of dexamethasone has not been universally adopted due to the fact that most published studies demonstrating the effectiveness of transforaminal injection of steroid (TFIS) have utilized particulate steroids. However, recent high quality studies have demonstrated the non-inferiority of dexamethasone to the most commonly injected particulate corticosteroid, triamcinolone acetate,[7,8] which should further increase its utilization. Given that the risk of neurologic injury resulting from embolization of particulate steroid may be eliminated with the use of a non-particulate steroid, dexamethasone should be considered the preferred first-line medication option for TFIS. Particulate steroids could be considered as a second-line agent for lumbar TFIS (lumbar region only) if non-particulate steroids do not result in adequate duration of relief. This recommendation is consistent with the FDA Safe Use Initiative's recommendations for safe injection practices which have been submitted for publication, and which all signatories to this letter support to help minimize risks associated with epidural steroid injections. Based on these data, and further supported by the consensus of experts representing fourteen

different specialty societies, we feel non-particulate steroids should be excluded from any FDA action as they have a robust safety profile.

Comparison to Alternative Treatments for Back Pain
For further comparison, the rates of serious complications from alternative treatments for spine pathology are significantly higher. There were 14,800 opioid related deaths in the United States in 2008.[9] More than 103,000 individuals are hospitalized annually in the United States for NSAID-related serious GI complications, with 16,500 NSAID-related deaths occurring each year in the United States among patients with rheumatoid arthritis and osteoarthritis.[10] Based on these data, we request that the FDA warning be modified to reflect the extremely low risk involved with lumbar ESI in comparison to significantly higher risks of alternative treatment option such as opioids and NSAIDs.

Effectiveness of Epidural Steroid Injections

The second area of concern with the FDA statement is the misleading sentiment that the effectiveness of ESIs has not been determined. While there is always room for more research, there is ample evidence demonstrating the effectiveness of ESIs in reducing and eliminating pain, improving function, decreasing reliance on opioids, and eliminating the need for surgery for many patients.[11]

Particulate and Non-Particulate Steroids
Multiple high quality studies have demonstrated efficacy of ESIs when performed on patients with appropriate indications. A double blind randomized controlled trial (RCT) by Riew *et al* investigated the effect of TFIS on avoidance of surgery for lumbar radicular pain.[12] Only 29% of patients who were treated with transforaminal injection of betamethasone and bupivacaine required surgery during the 13-28 month post-procedure follow-up time period compared with 66% of those who received transforaminal injection of bupivacaine alone ($P < 0.004$). Corroboration of the surgery-sparing effect of lumbar TFIS has been provided in a recent study in which injections were offered to patients with radicular pain who were on a surgical waiting list. A successful outcome, and avoidance of surgery, was achieved in 51/91 (56%, 95% CI ± 10%) patients.[13] Lumbar TFIS have also been shown to be effective for the treatment of radicular pain that has not responded to surgical intervention. Of 156 patients whose radicular pain was not relieved by surgery, 38 (31%, 95% CI ± 7%), responded to TFIS and none of these patients required revision surgery.[14] Another RCT found that after an average follow-up period of 1.4 years, the patients receiving TFIS had an 84% success rate compared to only 48% for the group receiving deep lumbar paraspinal muscle injection with saline ($P < 0.005$).[15] The most scientifically rigorous double blind RCT compared the efficacy of TFIS with transforaminal injection of local anesthetic, transforaminal injection of saline, intramuscular steroids, or intramuscular saline for the treatment of lumbar radicular pain.[16] The authors found that success rates for providing at least 50% pain relief from the various control treatments were statistically indistinguishable at 15% (95% CI +/- 7%) while 54% (+/- 18%) of patients who received TFIS achieved a successful outcome both at 1- month and at 12-month follow-up. Collectively these studies have led to recent systematic reviews[17,18] with meta-analyses that have summarized the large volume of research on this topic. Up to 70%

of patients achieve 50% pain relief for 1-2 months; 30% achieve complete pain relief.[18] For patients with disc herniations, up to 70% may achieve 50% pain relief for six months.[7] Pain relief is accompanied by functional recovery and reduced reliance on other health care resources.[7,18,19]

Recent studies have also demonstrated that non-particulate medications are just as effective as particulate preparations. A large retrospective review of over 3600 lumbar transforaminal injections from the Mayo Clinic showed dexamethasone to be non-inferior to particulate preparations.[8] Also a prospective double blind RCT showed dexamethasone was equivalent to triamcinolone, with over 70% of subjects that received an ESI experiencing at least 50% pain relief and avoiding surgery through the study's 6 month follow-up period.[7]

Diagnosis/Indications

Some studies and reviews, however, do report negative results with ESIs. There are multiple potential reasons for this. First while there is a large preponderance of evidence supporting the effectiveness of image-guided ESIs for radicular pain due to disc herniations, ESIs may not be as effective for other pathologies. Unfortunately, a significant number of studies simply study low back or radicular pain without identifying the underlying etiology. These are merely symptoms and not a diagnosis. For perspective, imagine a hypothetical systematic review of prescription medication for the treatment of cough, a symptom. A few studies may show beneficial effects from antibiotics in a group of patients with bacterial pneumonia, a specific diagnosis, whereas pooled data from heterogeneous groups – 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, it would still be a disservice to abandon prescription antibiotics for pneumonia.

Technique/Image Guidance

Second, when reviewing the literature regarding the effectiveness of ESIs, it is of utmost importance to know what technique was utilized. Multiple studies have demonstrated that non-image guided ESIs have unacceptably high miss rates with as many as 74% of these injections placing medication either outside the epidural space or not reaching the targeted site of pathology within the epidural space.[20] Since placebo controlled studies of intra-muscular steroid injections failed to show any benefits,[21,22,23] it should be no surprise that prospective randomized comparisons of image-guided ESIs to intramuscular steroid injections[16,24] and to blind ESIs[25] unanimously favor image-guided ESIs. In a clinically relevant context, studies of non-image guided ESIs show no benefit over sham treatment with a collective number needed to treat of >90.[26,27,28,29,30,31] In stark contrast, a large number of controlled studies of image-guided TFIS for patients with radiculopathy demonstrate robust positive outcomes[16,32,33,34,35,36,37,38,39,40,41] with a number needed to treat of 3.[18]

Data Analysis

While imprecision in diagnosis and inaccuracy in injections are major contributors to poor reported outcomes, negative studies and reviews are also reported for other reasons.

Unfortunately a preponderance of studies have opted to report clinical relevance by comparing group means for a minimum clinically important difference. While appealingly simplistic, this approach is inherently flawed. This method can result in a misinterpretation of the data, and dismisses clinically important information about the treatment effects of spine injections. Comparison between group means assumes a normal Gaussian distribution of pain and disability in response to spinal injections. In the context of ESIs, the clinical result is often bimodal, with some patients who respond and others who do not. Thus, the treatment effects are best-assessed using categorical data to compare proportions of responders to non-responders. A clear example of the utility of this approach is revealed in a study comparing TFIS to placebo.[16] Comparison of group mean data failed to find any difference between treatment groups, but categorical analysis demonstrated both statistically and clinically meaningful differences in favor of TFIS.

It has also been suggested by some that epidural injections of local anesthetic alone are equivalent to epidural injections that include steroid. We reject this claim. When two treatment arms have similar results, the appropriate conclusion is not necessarily that both treatments are equally effective. Just as likely, the treatments may be equally ineffective. For several indications, the latter is more likely. As cited above, multiple high quality, well-designed studies have demonstrated statistically and clinically significant differences favoring ESIs over local anesthetic alone.[12,15,16]

In conclusion it is clear that indication, technique, data analysis, and treatment medication are all vitally important in determining the effectiveness of ESIs. The data collectively show that for appropriate pathologies, image-guided ESIs with non-particulate steroids are an effective and safe treatment, and it would be inappropriate and biased to conclude that all ESIs are ineffective and unsafe.

We appreciate the opportunity to provide these comments and insights for consideration.

Sincerely,

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From: Shriner, Kelly kelly.Shriner@bsci.com Sent: Tue 1/20/2015 10:46 AM
To: HCA ST Health Tech Assessment Prog
Cc:
Subject: bronchial thermoplasty

Josh:

Thank you for your time earlier today explaining the Washington HTA program. I just want to re-iterate the fact that we support the review of bronchial thermoplasty in this process, and hope that a decision is made to proceed with the assessment.

I understand there will be an opportunity in the future to provide more information for this review, but I thought I would send a list of the publications on BT in the last 5 years as reference, for your decision of whether or not to conduct this assessment. Please note the recent cost effectiveness paper (Cangelosi et al), in addition to 5 year follow-up in 3 studies (Wechsler, Pavord and Thomson). Finally, you may be interested in knowing that both Healthcare Services Corporation (BCBS TX, IL, OK, NM and MT) and Carefirst BCBS have recently decided to cover BT.

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Thank you for your consideration. We look forward to observing and commenting on your assessment process.

Kelly

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