

**Health Technology Clinical Committee**

**Date: March 18, 2011**

**Time: 8:00 am – 6:30 pm**

**Location: SeaTac Airport Conference Center – Central Auditorium**

**Adopted: June 17<sup>th</sup>, 2011**

**HTCC MINUTES**

**Members Present:** Dr. Carson Odegard; Dr. Richard Phillips; Dr. Craig Blackmore; Dr. Marie Annette-Brown; Dr. Kevin Walsh; Dr. Christopher Standaert; Dr. Michelle Simon; Dr. Joann Elmore; Dr. Michael Souter; Dr. Seth Schwartz and Dr. Megan Morris.

**HTCC FORMAL ACTION**

1. **Call to Order:** Dr. Blackmore, Chair, called the meeting to order. Sufficient members were present to constitute a quorum.
2. **December 10<sup>th</sup>, 2010 Meeting Minutes:** Chair referred members to the draft minutes; motion to approve and second, and adopted by the committee.
  - *Action: Nine committee members approved the December 10<sup>th</sup>, 2010 meeting minutes. Two committee members abstained from voting.*
3. **Vertebroplasty, Kyphoplasty and Sacroplasty (VKS) draft Findings & Decision:** Chair referred members to the draft findings and decision and called for further discussion or objection. The VKS findings & decision was approved and adopted by the committee.
  - *Action: Nine committee members approved the VKS findings & decision document. Two committee members abstained from voting.*
4. **Glucose Monitoring for Insulin Dependent Individuals under 19 years of age:** The HTCC reviewed and considered the Glucose Monitoring technology assessment report; information provided by the Administrator; state agencies; public members; and heard comments from the evidence reviewer, HTA program, an invited clinical expert, the public and agency medical directors. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

| <b>HTCC COMMITTEE COVERAGE DETERMINATION VOTE</b> |                    |                                |   |
|---|--------------------|--------------------------------|---|
|   | <b>Not covered</b> | <b>Covered Unconditionally</b> | <b>Covered Under Certain Conditions</b> |
| Self-Monitoring Blood Glucose (SMGB)              | 0                  | 11                             | 0                                       |
| Continuous Glucose Monitoring (CGM)               | 5                  | 1                              | 5                                       |

- ✓ *Discussion:* The Chair called for discussion on conditions related to CGM due to the majority voting for coverage. The following conditions were discussed and approved by a majority:
  - *Limitations of Coverage:* Continuous Glucose Monitoring (CGM) is a covered benefit for diabetes mellitus (DM) patients under 19 using insulin when the following conditions are met:
    1. Suffering from one or more severe episodes of hypoglycemia; or

Version Officially Adopted on 6-17-2011

2. Enrolled in an IRB approved trial

✓ *Action:* The committee chair directed HTA staff to prepare a Findings and Decision document on Glucose monitoring reflective of the majority vote.

**5. Spinal Injections:** The HTCC reviewed and considered the Spinal Injections technology assessment report; information provided by the Administrator; state agencies; public members; and heard comments from the evidence reviewer, HTA program, an invited clinical expert, the public and agency medical directors. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

| <b>HTCC COMMITTEE COVERAGE DETERMINATION VOTE</b> |                    |                                |   |
|---|--------------------|--------------------------------|---|
|   | <b>Not covered</b> | <b>Covered Unconditionally</b> | <b>Covered Under Certain Conditions</b> |
| Lumbar Epidural Injection                         | 1                  | 0                              | 10                                      |
| Cervical-thoracic Epidural Injection              | 3                  | 0                              | 8                                       |
| Nerve Block Injections                            | 11                 | 0                              | 0                                       |
| Sacroiliac Joint Injections                       | 1                  | 3                              | 7                                       |
| Intradiscal Injections                            | 10                 | 0                              | 1                                       |
| Facet Injections                                  | 9                  | 1                              | 1                                       |

✓ *Discussion:* The Chair called for discussion on conditions related to the spinal injections where the majority voted for coverage with conditions. The following conditions were discussed and approved by a majority:

- *Limitations of Coverage:* Therapeutic Epidural Injections in the lumbar or cervical-thoracic spine for chronic pain is a covered benefit when all of the following conditions are met:
  1. For treatment of radicular pain
  2. With fluoroscopic guidance or CT guidance
  3. After failure of conservative therapy
  4. No more than two without clinically meaningful improvement in pain and function, and
  5. Maximum of 3 in 6 months
- *Limitations of Coverage:* Therapeutic Sacroiliac Joint Injections for chronic pain is a covered benefit when all of the following conditions are met:
  1. With Fluoroscopic guidance or CT guidance
  2. After failure of conservative therapy, and
  3. No more than one without clinically meaningful improvement in pain and function, subject to agency review
- *Action:* The committee chair directed HTA staff to prepare a Findings and Decision document on Spinal Injections reflective of the majority vote.

## **SUMMARY OF HTCC MEETING TOPICS, PRESENTATION, AND DISCUSSION**

### **Agenda Item: Welcome & Introductions**

- ✓ The Health Technology Clinical Committee (HTCC) met on March 18<sup>th</sup>, 2011

### **Agenda Item: Meeting Open and HTA Program Update**

Dr. Craig Blackmore, HTCC Chair, opened the public meeting.

- ✓ New committee members, Dr. Seth Schwartz and Dr. Joann Elmore, were introduced
- ✓ Leah Hole-Curry, HTA Program Director, provided an overview of the agenda, meeting guide and purpose, room logistics and introductions.

### **Agenda Item: Previous Meeting Business**

December 10<sup>th</sup>, 2010 Meeting Minutes: Chair referred members to the draft minutes and called for a motion and discussion. Minutes were circulated prior to the meeting and posted.

- *Action: Nine committee members approved the December 10<sup>th</sup>, 2011 meeting minutes. Two committee members abstained from voting.*

Vertebroplasty, Kyphoplasty and Sacroplasty (VKS) Findings and Decision: Chair referred members to the draft findings and decision and called for further discussion. The draft findings and decision document was circulated prior to the meeting and posted to the website for a two week comment period. Five public comments were received, included in the meeting materials, and were reviewed and discussed.

- *Action: Nine committee members approved the Vertebroplasty, Kyphoplasty and Sacroplasty findings & decision document. Two committee members abstained from voting.*

### **Agenda Item: HTA Program Review**

- Leah Hole-Curry, HTA Program Director, provided the HTA context for the meeting and an update on program activities including:
  - State purchasing context and budget reductions and reform efforts, medical technology is driver of increased medical costs and has quality gaps
  - HTA is designed to use reliable science and independent committee to get best information on what works, what is safe and what provides value
  - HTA outcomes include transparency; reports and articles reviewed; and coverage decisions made
  - Comparison with private industry and Medicare decisions completed
  - Program has received recent recognition from public media, clinical press, and various medical and health policy groups with either story highlights or invited presentations

### **Agenda Item: Glucose Monitoring for Insulin Dependent Individuals under 19 years of age Topic Review**

Leah Hole-Curry, HTA Program Director, introduced the technology topic up for discussion:

- ✓ Staff provided an overview of the timeline and referred HTCC members to the included key questions and population of interest for Glucose Monitoring review.
- ✓ Staff welcomed, per HTCC request, an invited clinical expert, Dr. Patricia Fechner an Endocrinologist from Seattle Children's Hospital. Dr. Fechner completed a conflict of interest and indicated no conflicts.

**Agenda Item: Public Comments**

The Chair called for public comments.

- ✓ Scheduled Public Comments: Seven stakeholders scheduled time for public comments.
  - Joan Sanders, Juvenile Diabetes Research Foundation (JDRF), expressed her concerns regarding glucose monitoring (GM) being reviewed by the Health Technology Clinical Committee (HTCC).
  - Melinda Woods, parent, believes that GM is incredibly important for the well-being and quality of life of both of children suffering from diabetes.
  - Dr. Irl B. Hirsch, Washington Diabetes Care Center, expressed concern regarding the topic of glucose monitoring up for review by the committee. Stated that home blood glucose monitoring is not a cure, but it has dramatically improved both the quality of life and the risk for long-term complications in children with diabetes.
  - Dr. Catherine Pihoker, Seattle Children's Hospital, expressed concern regarding the topic of glucose monitoring up for review by the committee. Stated that intensive management is associated with better outcomes, and glucose monitoring is an integral part of management; and that guidelines recommend individualized frequency of monitoring (at least 4-6 tests/day).
  - Kathleen Schneider, RN, Seattle Children's Hospital, expressed concern regarding the topic of glucose monitoring up for review by the committee. Stated that very young children need more frequent monitoring (more susceptible to hypoglycemia, unable to express symptoms); growth, pubertal changes affect insulin needs; and adolescents are taught to check their glucose levels before driving. Furthermore, she indicated scenarios which would require more frequent monitoring (i.e., sick days; insulin pumps; menstrual periods; pregnancy; etc).
  - Dr. Lori Laffel, American Diabetes Association, expressed concern regarding the topic glucose monitoring up for review by the committee. Stated that intensive insulin therapy leads to more optimal glycemic control (measured as A1c). Type 1 diabetes is difficult to manage in youth who experience frequent, wide glycemic excursions.
  - Dr. Bruder Stapleton, Seattle Children's Hospital, expressed concern regarding the topic glucose monitoring up for review by the committee. Stated that the standard of care is intensive management for children; and that glucose monitoring is safe and effective. Patients admitted for severe acute complications are usually those who do not monitor glucose levels.
- ✓ Open Public Comments: five individuals provided comments during the open portion.
  - Faith Lumsden, Washington state citizen, expressed her concern regarding the HTA process which she felt was confusing. Urged the committee to not make a decision, but rather convene a special panel to be able to increase the amount of GM children are able to use.
  - Christine Acarregui, Bayer Healthcare, expressed her concern regarding the topic up for review by the committee. Moved by the parents trying to help their children monitor their

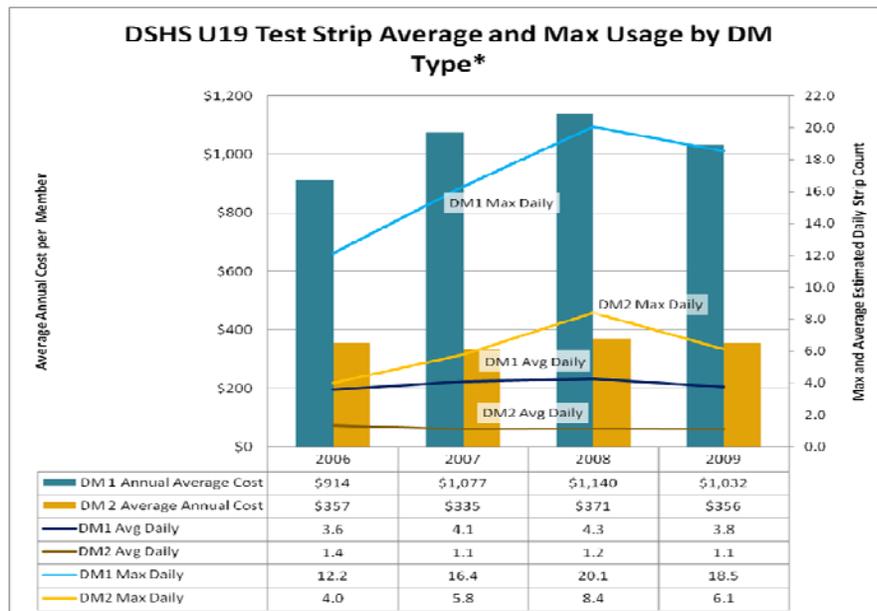
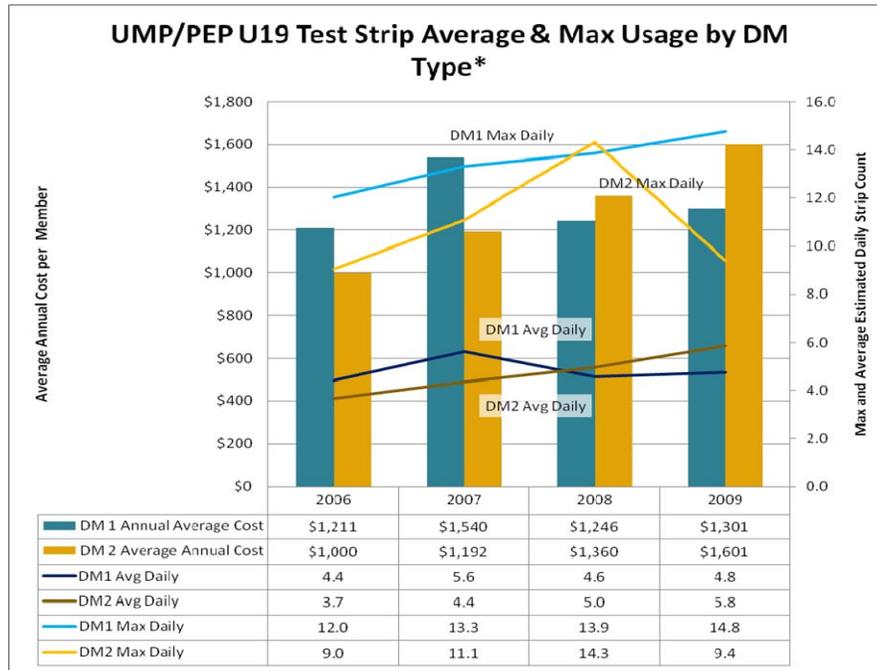
glucose levels. Encouraged the committee to provide more opportunities for children to check their insulin levels for a more quality life.

- Linnea Molder, parent, stated that intensive diabetes and insulin management has been the standard of care for the last 23 years, and should continue forward as the standard of care.
- Angela Badard, MD, Seattle Children's Hospital, expressed her concern regarding children not being able to monitor insulin levels, which is a standard of care in the United States and nationally. By limiting GM, Washington State would be moving away from the standard of care. Stated that it is unethical to put kids in studies that don't allow children to check insulin levels properly.
- Joni Campbell, Abbott Diabetes, concerned that if children can't check their insulin levels, how are they going to keep things leveled and be able to live as normal children? Concerned about taking this away. Stated that diabetes is manageable; however, but only with the right tools.

### **Agenda Item: Glucose Monitoring Topic – Agency Comments**

Dr. Steve Hammond, Medical Director, Department of Corrections, presented the agency utilization and outcomes for Glucose Monitoring to the committee, full presentation published with meeting materials.

- ✓ Glucose Monitoring Background:
  - Routine SMBG is considered the standard of care among diabetic patients, particularly those treated with insulin. The cost of SMBG has been estimated to be about 40-50% of the total cost of care for diabetes in children.
  - Despite widespread use, there is no high-grade evidence addressing optimal frequency and strategy of SMBG. Continuous glucose monitoring (CGM) is a relatively resource-intensive technology for which even less evidence is available; CGM is not considered the standard of care in typical cases. Utilization of SMBG among pediatric patients is highly variable.
  - Guidelines, based primarily on expert opinion, typically recommend frequency of SMBG of 4 or more times/day in children with type 1 DM.
- ✓ Agency Concerns:
  - Safety (Medium) -- excessive utilization of SMBG may reflect inadequate professional clinical supervision of diabetic care and/or ineffective glycemic management.
  - Efficacy (High) -- benefits of excessive SMBG (>4-5 times/day) in terms of improved clinical outcomes are unclear.
  - Cost (High) -- the cost of SMBG is a major component of overall costs of diabetic care; unrestricted and excessive utilization carries potential for waste of limited healthcare resources (especially in the setting of inadequate professional clinical supervision and/or ineffective glycemic management).
- ✓ Agency Coverage Overview: Currently covered without quantity restrictions by UMP. Currently covered without quantity restrictions by Medicaid. Only rare coverage at L&I
  - UMP to 2006 to 2009: patients increased from 75 to 113; GM strip spending increased from \$85,000 to \$144,000. Medicaid trend from 2006 to 2009 -- patients increased from 667 to 829; GM strip spending increased from \$187,000 to \$390,000
- ✓ UMP and Medicaid Test Strip Utilization



✓ UMP / PEP U19 Diabetic Patients and Adverse Events

| UMP/PEP U19 Diabetic Population | 2006 |        | 2007 |        | 2008 |        | 2009 |        |
|---------------------------------|------|--------|------|--------|------|--------|------|--------|
|                                 | #    | % mbrs |
| DM Type 1                       | 71   | 83.5%  | 84   | 81.6%  | 118  | 89.4%  | 110  | 90.9%  |
| DM Type 2                       | 14   | 16.5%  | 19   | 18.4%  | 14   | 10.6%  | 11   | 9.1%   |
| <b>Adverse Events*</b>          |      |        |      |        |      |        |      |        |
| ER visits                       | 17   | 20.0%  | 14   | 13.6%  | 22   | 16.7%  | 15   | 12.4%  |
| Critical Care                   | 4    | 4.7%   | 2    | 1.9%   | 6    | 4.5%   | 3    | 2.5%   |
| Ketoacidosis                    | 13   | 15.3%  | 7    | 6.8%   | 5    | 3.8%   | 6    | 5.0%   |
| Hyperglycemia                   | 1    | 1.2%   | 2    | 1.9%   | 2    | 1.5%   | 4    | 3.3%   |
| Diabetic coma                   | 0    | 0.0%   | 0    | 0.0%   | 3    | 2.3%   | 2    | 1.7%   |

✓ DSHS U19 Diabetic Patients and Adverse Events

| DSHS U19 Diabetic Population | 2006 |        | 2007 |        | 2008 |        | 2009 |        |
|------------------------------|------|--------|------|--------|------|--------|------|--------|
|                              | #    | % mbrs |
| DM Type 1                    | 416  | 62.1%  | 452  | 66.6%  | 530  | 66.3%  | 547  | 65.9%  |
| DM Type 2                    | 241  | 36.1%  | 222  | 32.7%  | 255  | 31.9%  | 273  | 32.9%  |
| Adverse Events*              |      |        |      |        |      |        |      |        |
| ER visits                    | 229  | 34.3%  | 311  | 45.8%  | 352  | 44.0%  | 471  | 56.8%  |
| Critical Care                | 42   | 6.3%   | 67   | 9.9%   | 59   | 7.4%   | 95   | 11.54  |
| Ketoacidosis                 | 75   | 11.2%  | 104  | 15.3%  | 106  | 13.3%  | 135  | 16.3%  |
| Hyperglycemia                | 19   | 2.9%   | 33   | 4.9%   | 37   | 4.6%   | 34   | 4.1%   |
| Diabetic coma                | 3    | 0.5%   | 2    | 0.3%   | 7    | 0.9%   | 4    | 0.5%   |

✓ AMDG Concerns:

- There is little evidence regarding optimum frequency of SMBG. There is no evidence that >5 SMBG checks per day improve clinical outcomes. There is concern that excessive use of SMBG may reflect ineffective clinical management.
- There is evidence in the Washington State UMP and Medicaid fee-for-service populations of substantial morbidity among pediatric diabetic patients reflected in use of ER and critical care services and episodes of diabetic ketoacidosis.
- Evidence for clinically significant improvement in outcomes resulting from CGM in pediatric diabetic patients is very weak

✓ AMDG Recommendations:

- Optimal management of diabetes in pediatric patients should be multimodal, guided by qualified clinicians, to include: effective glycemic management through careful attention to diet, exercise, medication, and blood glucose levels, and consideration of intensive insulin therapy as appropriate.
  - Intensive insulin therapy should be guided by regular SMBG, usually 4-5 times daily. Results of SMBG should be used appropriately to adjust diet, exercise, and insulin dosing to achieve appropriate glycemic control
- Coverage of unrestricted quantities of SMBG test strips for all cases is not justified; cover with condition of up to 5 tests/day. Coverage of >5 tests/day should require case review and justification as medically necessary.
  - Could be made available as exception to rule in Medicaid, and consider requiring specialty consultation.
- CGM should not be a covered benefit by Washington State purchased health plans (however, it could be provided in the setting of IRB-approved clinical trials).

**Agenda Item: Evidence Review Presentation**

Spectrum Research presented an overview of their evidence report on Glucose Monitoring, full presentation in meeting materials.

- ✓ Diabetes mellitus (DM) is a serious chronic condition for which there is no definitive cure. DM is categorized into 3 major types, based on etiology:
  - **Type 1 (T1DM):** is an autoimmune disorder that destroys pancreatic beta cells which make insulin. It is the most common form in person's ≤ 18 years old. Insulin therapy is required.
  - **Type 2 (T2DM):** Is most common in adults and is caused by insulin resistance, disordered and inadequate insulin release and excessive glucose production by the liver. Diet, exercise and oral

- medications may be effective in the first years; however, it is progressive and insulin therapy may eventually be required.
  - **Gestational (GDM):** defined as glucose intolerance with pregnancy onset/first recognition of pregnancy.
- ✓ Background – Complications: Chronic complications are strongly related to DM duration and glycemic control (T1 and T2DM). Diabetic ketoacidosis (DKA): severe hyperglycemia; leading cause of hospitalizations in children with T1DM nationally; can lead to coma, death. Hypoglycemia: 3 X more common in children (vs. adults), may be difficult to detect (unawareness); can damage brain, lead to seizures, coma, death.
- ✓ Background – DM duration is associated with chronic complications, thus, person's ≤ 18 years old may have the most to gain from maintaining good glycemic control yet have some of the greatest challenges in achieving and maintaining it.
  - Goal: Achieve/maintain glucose and A1C levels as close to normal as possible while minimizing episodes of severe hypoglycemia.
  - Intensive management with tight control has become standard of care. Self-monitoring plays an integral part since it provides data for decision making; assists in identifying and preventing hypoglycemia; provides “peace of mind” to care givers; and/or influences activities and quality of life.
- ✓ Self-monitoring of blood glucose (SMBG) is intermittent monitoring. First FDA approval was in 1975. Capillary blood drop placed on reagent-impregnated paper strips; monitor reads and provides “snap shot” of blood glucose levels. Recommended for use at least 4 times per day; individualized.
- ✓ Real-time Continuous Glucose Monitor (CGM) – FDA approval (7-17 years): Guardian and MiniMed Paradigm REAL-Time devices (later used w/pumps). Subcutaneously placed, enzyme-embedded sensor samples interstitial fluid glucose every 1-20 minutes. Trend information; alarms for high and low levels.
- ✓ Primary Outcomes (based on available literature):
  - Efficacy and Effectiveness
    - Mean A1C, Achieving, maintaining target A1C levels
    - ADA goals: <6 years old 7.5% -8.5%; age 6-12 <8.0%; adolescents <7.5%
    - Clinically meaningful change 0.5%
    - Hypoglycemia, hyperglycemia, ketoacidosis
    - Microvascular complications
    - Quality of life
  - Safety
    - Device-related, Morbidity, Mortality
- ✓ Literature Search: 240 unique potentially relevant citations. Final number of included study reports = 49 and 3 FDA SSED; multiple studies contributed information to several key questions. No full economic studies were found.
  - Primary evidence – efficacy and effectiveness
    - SMBG: 1RCT (DCCT) and 2 associated observational follow-up studies (EDIC) provide indirect evidence; 1 large registry study and 7 cross-sectional studies
    - CGM: 4 RCTS; JDRF trials' associated additional analyses; Data not uniformly available for those ≤ 18 years old
- ✓ Key Question 1: Efficacy and Effectiveness of SMBG –
  - 1 RCT (LoE II) - Diabetes Complications and Control Trial (DCCT); N = 195 ages 13-17 years; 7.4 yrs f/u
    - SMBG ≥ 4/day *as part* of comprehensive, intensive care (insulin dose adjustment, diet, exercise) vs. SMBG or urine testing 1/day (insulin 1-2 injections/day; no daily changes of insulin or diet)
    - Provides indirect evidence on efficacy of SMBG
    - Primary prevention (PP) cohort (n = 125); participants with no retinopathy or nephropathy
    - Secondary intervention (SI) cohort (n = 70, 1-15 years); participants with mild to moderate non-proliferative retinopathy.

- Epidemiology of Diabetes Interventions and Complications (EDIC) - 2 reports (LoE II).
  - Follow-up of DCCT participants 4 and 10 years after DCCT end;
  - Original IT group encouraged to continue regimens
  - Original CT group offered instruction on intensive therapy
- N =175 (91% of surviving DCCT adolescents) enrolled; 80% follow-up at year 10.
- Testing ≥ 4/day at 4 years: 24% IT, 29% CT and at 10 years and 64.5% IT 38.9% CT (means not provided)

✓ Key Question 1: Effectiveness of SMBG – EDIC results summary:

|                                | <b>Intensive</b>  | <b>Conventional</b> | <b>Effect size</b>               |
|--------------------------------|-------------------|---------------------|----------------------------------|
| <b>Mean A1c (%)</b>            |                   |                     |                                  |
| <b>Year 4</b>                  | <b>8.38 ± 1.7</b> | <b>8.45 ± 1.6</b>   | <b>NS</b>                        |
| <b>Year 10</b>                 | <b>8.2 ± 2.1</b>  | <b>8.2 ± 1.3</b>    | <b>NS</b>                        |
| <b>Severe Hypoglycemia</b>     |                   |                     |                                  |
| <b>Year 4</b>                  | <b>51/100 p-y</b> | <b>57/100 p-y</b>   | <b>RR 0.9, p = 0.749</b>         |
| <b>Retinopathy Progression</b> |                   |                     |                                  |
| <b>Year 4</b>                  | <b>7.1%</b>       | <b>25.4%</b>        | <b>77% (39, 92) p = 0.004</b>    |
| <b>Year 10*</b>                | <b>50.9%</b>      | <b>53.4%</b>        | <b>10% (-104, 60) p = 0.8395</b> |

- Severe non-proliferative diabetic retinopathy (NPDR) or worse and proliferative retinopathy:
  - Year 4: Lower NPDR for IT 1.4% vs. CT 14.5%, p = 0.005; 1.4% IT vs. 8.7% for proliferative
  - Year 10: no significant differences between groups
  - NS differences: macular edema, laser therapy at both times
- Nephropathy (in those without microalbuminuria or albuminuria at DCCT baseline or close; page 95 of report).
  - Year 4: IT group rates were less, but NS; no one on dialysis or with renal transplant
  - Year 10 rates were similar
- ✓ Summary and Overall Strength of Evidence for Key Question 1
  - **Efficacy of SMBG ( 1 RCT) – SoE is low**
    - Indirect evidence from DCCT: SMBG ≥ 4/day as part of intensive, tight control program:
    - Short term (6-12 months): Lower A1C and daily blood glucose;
    - Longer (mean 7.4 years): sustained lower A1C, daily blood glucose; retinopathy and microalbuminuria risk reduction and; faster nerve conduction velocities
    - Higher rate of hypoglycemic events with intensive treatment
  - **Effectiveness (Observational) SMBG–SoE low**
    - EDIC -2 follow-up reports 4 and 10 years post DCCT:
    - 4 years: No differences in mean A1c between groups; IT group- lower rates of retinopathy progression, lower but NS difference in microalbuminuria or albuminuria prevalence
    - 10 years: No differences in mean A1C, retinopathy progression or microalbuminuria or albuminuria
- ✓ Key Question 2: Efficacy by frequency or mode –
  - **SMBG**: DCCT results (indirect evidence, ≥ 4/day)
  - **Continuous Glucose Monitoring (CGM)**

- 5 reports from 4 RCTs of real-time CGM; bulk of evidence comes from two RCTs. Limited data; stratified by age in 2 studies. One RCT compared CGM/pump vs. SMBG/MDI.
  - CGM (+ SMBG for calibration and decision making) versus SMBG alone
  - Participants educated on data use for management decisions
- ✓ Key Question 2: Efficacy of CGM (+SMBG) vs. SMBG alone --- Participants achieving A1c targets:

| <b>A1C levels (26 weeks)</b>             | <b>CGM</b>  | <b>SMBG</b> | <b>Effect Size</b> |
|--|-------------|-------------|--------------------|
| <b>JDRF 2008 (n = 114)</b>               |             |             |                    |
| <7.0%                                    | 27% (15)    | 12% (7)     | RD 15%; p = 0.01   |
| <7.0% with no severe hypoglycemic events | 25% (14)    | 10% (6)     | RD 15%; p = 0.02   |
| ≥ 10% relative ↓                         | 29% (16)    | 12% (7)     | RD 17%; p = 0.04   |
| ≥ 0.5% absolute ↓                        | 54% (30)    | 31% (18)    | RD 23%; p = 0.009  |
| <b>Hirsch 2008 (n = 40)</b>              | <b>% NR</b> | <b>% NR</b> | <b>P = 0.052</b>   |

- ✓ Key Question 2: Efficacy of CGM (+SMBG) vs. SMBG alone:
- Hypoglycemia – JDRF 2008 (N = 114)
    - ≥ 1 severe event: CGM 4 (7%), SMBG 6 (10%)
    - Rates of severe hypoglycemia: p = 0.06
    - CGM 17.9/100,000 p-y; SMBG 24.4/100,000 p-y
    - Min/day ≤ 50 mg/dl: CGM 10, SMBG 13; p = 0.50
    - Min/day ≤ 70 mg/dl: CGM 47, SMBG 59; p = 0.29
  - Hyperglycemia – JDRF 2008 (N = 114)
    - Min/day ≥ 180 mg/dl: CGM 643, SMBG 635; p = 0.58
    - Min/day ≥ 250 mg/dl: CGM 242, SMBG 268; p = 0.18
  - Quality of Life (26 weeks) -- Combined populations of JDRF 2008 (>7.0% A1C at baseline) and JDRF 2009 (<7.0% A1C).
    - Participants and parents completed diabetes-specific and general assessments of QOL
    - Measures: Hypoglycemia Fear Survey subscale (HFS), Pediatric Quality of Life Inventory (PDLQL) generic and diabetes specific editions; Problem areas in Diabetes (PAID; parents only completed).
    - No differences by treatment in mean values for any measure for either participants or parents.
- ✓ Summary and Overall Strength of Evidence for Key Question 2 is low.
- JDRF 2008 (N =114) and Hirsch 2008 (n = 40):
    - Short term (26 weeks): No differences in mean A1C; JDRF – CGM participants twice as likely to achieve A1C targets
    - JDRF: Lower rate of hypoglycemic events with CGM (but NS); % of participants achieving targets w/o such events significantly greater for CGM
    - Longer term: no studies found
  - Combined JDRF 2008 and 2009 data
    - No differences in quality of life measures at 26 weeks for either participants or parents
- ✓ Effectiveness of CGM (+SMBG): Frequency of Use -- Extension studies JDRF 2008 and sub-analysis of JDRF 2009. Observational studies (LoE II and III)
- JDRF 2008 extension studies
    - Original CGM cohort (n = 80): Lower mean A1C (maintained by 12 months) and larger percentage of participants meeting targets with use ≥ 6 days/week
    - Original SMBG cohort offered CGM (with less intensive training; n = 47): no consistent pattern of improvement in A1C or for meeting target levels based on use. Lower hypoglycemia rates reported following 6 month CGM use (p not reported).

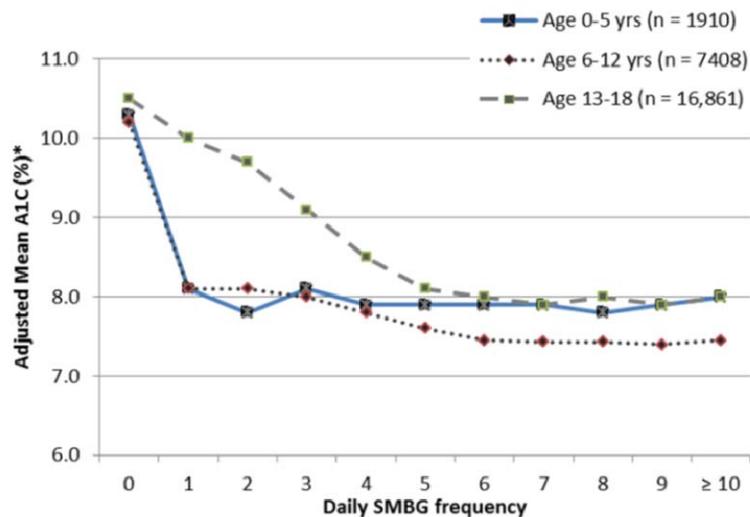
- JDRF 2009 subanalysis of those with baseline  $\leq 7.0\%$  A1C: mean change in A1C of  $-0.72\%$  with  $\geq 6$  days/week
- ✓ Effectiveness – Frequency of SMBG: 6 cross-sectional studies (LoE III).
  - N ranged from 89-2,743; 5 report statistically significant associations between number of SMBG per day and lower A1C in multivariate analyses. Testing at least 4 - 5 times per day.
  - Hypoglycemia and DKA (Ziegler):

|                                     | Hypoglycemic events             | Diabetic Ketoacidosis events                               |
|-------------------------------------|---------------------------------|--|
| <b>SMBG 0-4/day</b>                 | <b>13-20 events/100 p-years</b> | <b>6-12 events/100 person-years (except for 1SMBG/day)</b> |
| <b>SMBG <math>\geq 5</math>/day</b> | <b>20-37 events/100 p-years</b> | <b>4-6 events/100 person-years</b>                         |

- ✓ Summary and overall strength of evidence for key question 2 -- Frequency:
  - **Effectiveness CGM Frequency – SoE low**
    - JDRF 2008 extensions. Original CGM cohort: use  $\geq 6$  days/week appears to have maintained lower A1C and more met age appropriate targets. Original SMBG cohort provided with CMG: no consistent pattern of benefit with frequency of use
  - **Effectiveness SMBG Frequency – SoE low**
    - One large registry, six additional cross-sectional studies. SMBG 4-5 times per day associated with lower mean A1C. Causality cannot be inferred
- ✓ Key Question 3 – Safety:
  - SMBG: No data for current devices
  - CMG: (7 RCTs, 7 observational, 3 FDA SSED). No mortality in  $\leq 18$  year olds reported. Insertion site problems: Redness/itching (16%-45%); dry skin (21%); mild, moderate skin changes (14% each); irritation, bruising or pain (0-53%). Sensor/Device concerns: alarm interferes with daily routine (38%); alarm irritating (38%-50%); sensor too bulky (22%-75%); sensor pulled out (10%-13%). Many studies had small sample sizes.
- ✓ Overall strength of Data = Moderate.
  - CGM: RCTs, observational studies, SSED. Primary concerns reported: Insertion site problems, alarm related. No deaths in age group or major adverse events reported.
  - SMBG: No studies on current devices. Older reports: sore finger, difficulty obtaining samples.
- ✓ Key Question 4 – Differential Outcomes for subpopulations:
  - CGM – JDRF 2008 RCT; Participants 8-14 years old and those 15-24 years old had similar results with regard to mean A1C, hypoglycemia.
  - SMBG: Zeigler (LoE III) N = 26,723. Association between SMBG frequency and average improvement in A1C varied by age and insulin regimen.

|                       | 0-5 years<br>(n = 1989)             | 6-12 years<br>(n = 7568)            | > 12 years<br>(n = 17,166)          |
|-----------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| <b>Mean A1C</b>       | <b>7.59% <math>\pm</math> 1.34</b>  | <b>7.61 <math>\pm</math> 1.32</b>   | <b>8.46 <math>\pm</math> 1.85</b>   |
| <b>SMBG frequency</b> | <b>6.0/day <math>\pm</math> 1.9</b> | <b>5.3/day <math>\pm</math> 1.8</b> | <b>4.4/day <math>\pm</math> 1.4</b> |
|                       | CT<br>(n = 5016)                    | MDI<br>(n = 18,565)                 | CSII<br>(n = 3142)                  |
| <b>Mean A1C</b>       | <b>7.64% <math>\pm</math> 1.67</b>  | <b>8.24% <math>\pm</math> 1.75</b>  | <b>8.01% <math>\pm</math> 1.60</b>  |
| <b>SMBG frequency</b> | <b>5.3/day <math>\pm</math> 1.8</b> | <b>4.7/day <math>\pm</math> 1.5</b> | <b>5.3/day <math>\pm</math> 1.8</b> |

- ✓ General trend for the relationship between frequency of SMBG and adjusted mean A1c by age group (estimated by Ziegler):



- ✓ Overall Strength of Evidence for Key Question 4 = Low
  - **CGM:** 1 RCT; 8-14 year olds and 15-24 year olds had similar patterns for most results
  - **SMBG:** Registry study
    - Age: For 13-18 year olds, greater average improvement in A1C for each additional SMBG up to 5 per day. In 0-5 and 6-12 year olds, less improvement for each additional SMBG beyond the first.
    - Insulin Regimen: CSII: tests up to 10 times per day closest to targets.
- ✓ **KQ #5: Economic – no evidence, no full studies**
- ✓ Observations and Implications:
  - Diabetes management in children and adolescents presents a number of challenges and influences quality of life for the child and care givers.
  - As DM duration contributes to development of complications, this younger age group may have the most to gain from good control.
  - Self-monitoring is viewed as a critical component of management.
  - Studies did not provide specifics regarding how data from self-monitoring (SMBG or CGM) are used to influence decisions on insulin dose/regimens, diet or exercise; thus it is not possible describe the independent influence of monitoring on outcomes.
  - Adherence to monitoring and taking appropriate action based on the data are necessary to effect outcomes.
  - SMBG is part of CGM use protocol. CGM's role for pediatric use is not yet defined in the literature. No long term studies in this population were found.

## **Agenda Item: HTCC Glucose Monitoring Discussion and Findings**

Dr. Blackmore, Committee Chair, led a discussion of the evidence related to the safety, efficacy, and cost-effectiveness of Glucose Monitoring beginning with identification of key factors and health outcomes, and then a discussion of what evidence existed on those factors.

### **1. Evidence availability and technology features**

The evidence based technology assessment report indicates:

- 1.1 Diabetes mellitus or diabetes is a serious chronic disease characterized by elevation of blood glucose. The predominated form of diabetes in children is from an autoimmune disorder that destroys the pancreatic cells where insulin is made. There is no cure; insulin injections are required and the primary goals for treatment of youth with insulin requiring diabetes are to maintain plasma glucose and A1C levels as close to normal as possible. Diabetic ketoacidosis (very high glucose level) is the leading acute complication and can result in

morbidity and mortality. A seminal diabetes study (DCCT) results suggest that maintaining near normal levels of A1C are ideal to minimize the risk of chronic complications, but the lower the A1C puts individuals at risk of severe hypoglycemia. Children and adolescents have challenges related to varying physical capability, physiological and psycho-social changes that influence metabolism and adherence to self care behaviors.

- 1.2 Self monitoring of blood glucose has become a standard practice recommendation due to the link between good glycemic control and lower chronic complications; however, the method and optimal frequency of self-monitoring of blood glucose in patients remains controversial. Several lines of evidence have suggested an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self-monitoring, along with a lack of clinically relevant improvement in diabetes-related outcomes in patients who self-test. On the other hand, children and adolescents can be especially at risk for some diabetes related complications. Information about the best options for glucose monitoring in diabetic persons 18 and under, including evidence of efficacy and safety and cost; and correlation of frequency (including strip frequency and continuous monitoring) to improved outcomes is needed.
- 1.3 Self-monitoring of blood glucose (SMBG) uses meters to analyze small amounts of capillary blood on reagent-coated test strips to provide immediate documentation of glycemic status. This allows one to implement strategies to address and avoid out of range glucose values. It provides only a snapshot of the blood glucose level and thus, cannot provide information on whether there is a trend toward higher or lower levels. Continuous glucose monitors (CGM) are more recent technology where a minimally-invasive device is worn to measure interstitial fluid glucose concentration via sensors which have been inserted subcutaneously. These devices take samples every 1-20 minutes over the time that the device is worn. CGM is not approved for insulin dosing decisions, so individuals using CGM must still conduct SMBG several times a day.
- 1.4 Evidence included in the technology assessment review was obtained through a structured, systematic search of the medical literature; economic studies; and clinical guidelines. 240 potentially relevant studies were identified; 49 were included; no economic studies found. The evidence is indirect because SMGB is not separately studied. Primary evidence for SMBG is 1 randomized control trial (DCCT) and 2 associated observational follow up (EDIC); 1 larger registry study and 7 cross-sectional studies. For CGM, 4 RCTs and JDRF's analysis were included, though data is not uniformly available for 18 and under.
- 1.5 The evidence based technology assessment report identified six expert treatment guidelines and no National Coverage decision (NCD) policy addressing children.
- 1.6 The committee also reviewed information provided by the state agencies, and public members; and heard comments from the evidence reviewer, clinical expert, HTA program, agency medical directors and the public.

## **2. Evidence about the technology's safety**

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is safe. Summary of committee considerations follows.

- 2.1 The evidence based technology assessment report indicates that the strength of evidence of safety is moderate based on number and quality of studies. SGBM and CGM have no major adverse events or deaths. (*Adverse events from severe high and low glucose are described in efficacy*).
- 2.2 The evidence based technology assessment report indicates that the primary issues for SGBM are from older studies that reported sore fingers and difficulty obtaining samples.
- 2.3 The evidence based technology assessment report indicates that for CGM, primary issues from small RCT and observational studies included skin irritation (0%- 53%); sensor dislodging (10% - 13%); alarms interfering with daily routine (38%) and irritation with alarms

(38% - 50%). The primary safety issue with CGMs are false alerts and missed alerts (false negatives); rates varied across blood glucose thresholds and devices – false negatives rates for hypoglycemia (below threshold) ranged from 14% to 75% and false negative rates for hyperglycemia (above threshold) ranged from 5% to 37%).

### 3. Evidence about the technology's efficacy and effectiveness

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is effective. Summary of committee considerations follows.

- 3.1 Efficacy of SMBG – the evidence based technology assessment report indicated that no studies evaluated current methods of SMBG testing alone or as an independent component of diabetes management. The Diabetes Complications and Control Trial (DCCT-1994) is the primary study of 195 patients aged 13 to 17 providing indirect evidence regarding the efficacy of SMBG as part of a package of comprehensive, intensive diabetes care, which included SMBG four or more times per day and education on how to use the information to adjust insulin, diet and exercise compared with the then standard of care (urine or SMBG once/day, only periodic insulin adjustment).
  - Mean A1c levels 8.06% for intensive care arm vs. 9.7% for conventional arm; a 61% risk reduction in sustained at least three step retinopathy in intensive arm; no difference in nephropathy; no difference in ketoacidosis (18% vs. 20%); and a threefold higher risk of hypoglycemia resulting in coma/seizure in intensive care arm.
- 3.2 Effectiveness of SMBG – the evidence based technology assessment report indicated indirect evidence on the effectiveness of SMBG is based on the Epidemiology of Diabetes Interventions and Complications (EDIC-2001) the observational follow-up to the DCCT at four and ten years with 175 patients. All participants in the conventional treatment arm were offered instruction in the use of intensive therapy and intensive treatment group patients were encouraged to continue such treatment. No significant differences between the groups identified except related to retinopathy at 4yr.
  - Mean A1c levels 8.38% for intensive arm vs. 8.45% in conventional at 4yr; and 8.2% for both groups at 10yr;
  - Retinopathy progression worse in 7% of intensive arm vs. 25% in conventional at 4yr and 51% for intensive arm vs. 53% in conventional at 10yr;
  - Severe hypoglycemia; macular edema; and nephropathy had no significant differences
- 3.3 Efficacy and effectiveness by frequency or mode of test -- there were no clinical trials that directly evaluated the efficacy of SMBG frequency. Indirect evidence from the DCCT provides information with respect to frequency in that the intensive group was instructed to test at least four times per day compared with the conventional care groups once per day (see above). The bulk of the evidence on efficacy of mode of self-monitoring comes from comparisons with continuous glucose monitors (CGM).
- 3.4 CGM used with SMBG (for calibration and verification per FDA recommendations) was compared with SMBG alone; three RCTs form primary basis; overall *Strength of Evidence is low*. Data from one JDRF 2008 report on CGM (result stratified by age (n = 114, 8-14 year olds)) and one smaller Hirsch RCT (n = 40, 12-18 year olds) are primary studies. Another JDRF (2009) study has few outcomes stratified by age. In the JDRF studies, 84% of both CGM and SMBG groups used insulin pumps (which did not communicate with the CGM) and 100% of patients in the Hirsch study used pumps integrated with the CGM device in the CGM arm only. Different in population and study design preclude pooling of data.
  - Mean differences in HbA1C levels were not clinically or statistically significant in short term.
  - No study reported significant differences in episodes of hypoglycemia for CGM vs. SMBG.

- 2 RCTs reporting on hyperglycemia reported no significant differences for CGM vs. SMBG.
- Results on the effect of CGM vs. SMBG on medication or nutritional management conflicted: 2 studies reported significant differences in insulin doses where one study reported no change in insulin doses.
- There are currently no long-term comparative studies on these devices for evaluation of benefits, complications or diabetes-related co-morbidities on those  $\leq 18$  years old.

#### 4. Special Populations

- 4.1 The evidence based technology assessment report reported one RCT and one large registry study directly assessed differential outcomes for either CGM or SMBG by age subpopulations. The overall strength of evidence is low.
- 4.2 The evidence based technology assessment report included one RCT comparing CGM with SMBG in patients 8-14 years old and those 15-24 years old - each had similar results with regard to A1C and achieving targets for CGM and SMBG with no evidence of differential efficacy by age was demonstrated.
- 4.3 The evidence based technology assessment report reported that there is limited evidence for differential effect of frequency of SMBG testing by age from one large registry study.
  - For 13-18 year olds an average improvement in A1C of  $0.3\% \pm 0.011$  for each additional SMBG was reported. This appears to apply up to tests five per day.
  - In contrast, for ages 0-5 and 6-12, beyond one test per day, improvement in A1C was much less and averaged  $0.04\% \pm 0.018$  and  $0.12\% \pm 0.010$  respectively beyond one SMBG per day.

#### 5. Evidence about the technology's value and cost-effectiveness

The committee discussed multiple key factors that were important for consideration in their overall decision on whether the technology has value and is cost-effective. Summary of committee considerations follows.

- 5.1 The evidence based technology assessment report indicated that no evidence is available to assess the cost effectiveness of SMBG or CMG in persons with diabetes  $\leq 18$  years old who require insulin. No full economic studies which focused on the cost-effectiveness of CGM or the frequency of SMBG were found.

#### 6. Evidence on Medicare Decision and Expert guidelines

Committee reviewed and discussed the expert guidelines as identified and reported in the technology assessment report.

- 6.1 Centers for Medicare and Medicaid Services (CMS) – no NCD policy addressing children.
  - For adults, to be eligible for coverage of home blood glucose monitors and related accessories and supplies, the patient (or patient's care-giver) must meet all the following criteria:
    - Diagnosed with diabetes that is being treated by a physician
    - Glucose monitor and related supplies ordered by the treating physician with documentation of medical necessity for the prescribed frequency of testing
    - Successfully completed training or is scheduled to begin training in the use of these items
    - Capable of using the test results to assure appropriate glycemic control
    - Device is designed for home use
  - Supplies covered: Up to 100 test strips and lancets every month for beneficiaries who are insulin dependent and every 3 months for those who are non-insulin dependent, and one lancet device every 6 months for both indications.

6.2 Guidelines – the evidence based technology assessment report identified six guidelines though a search of the *National Guideline Clearinghouse*.

- American Diabetes Association (ADA), 2010 – Frequency of self-monitored blood glucose (SMBG): SMBG in general has been extensively reviewed by the ADA and is recommended for patients of all ages with type 1 diabetes. The 2010 report did not specifically address frequency for children; however, in a statement published in 2005 by the ADA entitled Care of Children and Adolescents with Type 1 Diabetes it is recommended that SMBG be performed at least four times daily. *Continuous glucose monitoring (CGM)*: CGM in conjunction with intensive insulin regimens can be a useful tool to lower A1c in selected adults (age ≥ 25 years) with type 1 diabetes. Although the evidence for A1c lowering is less strong in children, teens, and younger adults, CGM may be helpful in these groups. Success correlates with adherence to ongoing use of the device. CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes. *Glycemic goals*: consider age when setting glycemic goals in children and adolescents with type 1 diabetes, with less stringent goals for younger children.
- Diabetes Coalition of California, California Diabetes Program, 2008 – this guideline addresses adults, children and adolescents with type 1 and type 2 diabetes mellitus. *SMBG testing*: typically test at least 4x / daily. *Lab exams*: A1c should be checked 1-2 times year if stable, quarterly if treatment changes or if not meeting goals. Target goal < 7.0% or < 1% above lab norms. For children, modify as necessary to prevent significant hypoglycemia. Furthermore, microalbuminuria should be checked beginning with puberty once the duration of diabetes is > 5 years unless proteinuria has been documented. *Self-care behaviors*: as appropriate for child’s developmental stage.
- International Society for Pediatric and Adolescent Diabetes (ISPAD), 2009 – In summary, SMBG is an essential tool in the optimal management of childhood and adolescent diabetes and, when financially possible, should be made available for all children with diabetes. The cost of BG monitoring is very expensive and in many countries the cost relative to the cost of living may make this technology unavailable. *Frequency of SMBG*: SMBG should be prescribed at a frequency to optimize each child’s diabetes control, usually 4-6 times a day, because frequency of SMBG correlates with glycemic control. *CGM*: CGM devices are becoming available that may particularly benefit those with hypoglycemic unawareness, as the devices will alarm when glucose is below a specified range or with rapid rate of fall of glucose. *Glycemic goals*: the target A1c for all child age-groups is recommended to be < 7.5%. Every child should have a minimum of one measurement of A1c per year. Ideally, there should be four to six measurements per year in younger children and three to four measurements per year in older children.
- National Institute for Health and Clinical Excellence (NICE), 2004 -- *SMBG*: who are trying to optimize their glycemic control and/or have intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day. Should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care team. *CGM*: who have persistent problems with hypoglycemia awareness or repeated hypoglycemia or hyperglycemia should be offered CGM systems. *Glycemic goals*: should be encouraged to use blood glucose measurements for short-term monitoring of glycemic control. The target for long-term glycemic control is an A1c level of less than 7.5% without frequent disabling hypoglycemia and the child’s care package should be designed to attempt to achieve this.
- American Association of Clinical Endocrinologists (AACE), 2010 – Personal CGM is recommended for patients with type 1 DM and following characteristics: hypoglycemic unawareness or frequent hypoglycemia; A1c over target, or with excess glycemic variability; requiring A1c lowering without increased hypoglycemia; during preconception or pregnancy. Personal CGM use is recommended for children and adolescents with type 1

DM who have achieved A1c levels less than 7.0%; youth with type 1 DM who have A1c levels of 7.0% or higher and are able to use the device on a near-daily basis. The following patients might be good candidates for personal CGM, and a trial of 2 to 4 weeks is recommended: youth who frequently monitor their blood glucose levels; committed families of young children (< 8 years old), especially if the patient is having problems with hypoglycemia.

- o British Society of Pediatric Endocrinology, 2009 – *Proven clinical indication*: to lower A1c, when this remains above the individual’s target despite optimized use of intensive insulin regimens. *Potential clinical indications – Diagnostic*: suspected nocturnal hypoglycemia and/or early morning hyperglycemia; suspected unrecognized hypoglycemia; A1c above individualized target despite intensified insulin therapy apparently optimized with self-monitoring; persistent disabling hypoglycemia despite conversion from MDI to CSII. *Potential clinical indications – Therapeutic*: further optimization of pump therapy regimens when A1c cannot be consistently lowered below 7.5%; protection against recurrent disabling hypoglycemia, and for those with hypoglycemia unawareness or debilitating fear of hypoglycemia.

## **Committee Conclusions**

Having made findings as to the most significant and relevant evidence regarding health outcomes, key factors and identified evidence related to those factors, primarily based on the evidence based technology assessment report, the committee concludes:

### **1. Evidence availability and technology features**

The committee concludes that the best available evidence on Glucose Monitoring has been collected and summarized.

- 1.1. The evidence review summarized the evidence on the safety and efficacy of SMBG and CGM in individuals with insulin dependent diabetes, 18 years of age or under. SMBG plays an important role in the key treatment goal to managing diabetes; maintenance of good glycemic control without increase in the frequency of hypoglycemic events; there is direct evidence that optimizing glucose levels decreases both short and long term diabetes related complications; and managing glucose levels requires self checking.
- 1.2. Current best evidence is available primarily from 1 randomized control trial (DCCT) and 2 associated observational follow up (EDIC); 1 larger registry study and 7 cross-sectional studies. For CGM, 4 RCTs and JDRF’s analysis were included.
- 1.3. Self monitoring of blood glucose is a standard practice recommendation due to the link between good glycemic control and lower chronic complications; however the evidence about SMBG optimal frequency is unknown and additional methods (CGM) benefit is unclear.

### **2. Is it safe?**

The committee concludes that the comprehensive evidence indicates that SMBG is safer than alternatives (limited or no self testing); and CGM is unproven to be equally or more safe to SMBG. Key factors to the committee’s conclusion included:

- 2.1. The committee unanimously agreed that moderate quality evidence demonstrates SMBG is more safe than conventional treatment (including limited or no self testing): minor skin irritations related to testing site were only reported harm; major morbidity or mortality is not anticipated with this intervention, and none was reported in the literature.
- 2.2. A majority of the committee agreed that the safety of adding CGM is unproven when compared to conventional treatment or SMBG. Low quality evidence included documented adverse events of skin irritation in up to 53% of patients; sensor dislodging (10% - 13%) and alarms interfering with daily routine (38%) and irritation with alarms (38% - 50%). Additionally, the primary safety issue with CGMs are false alerts and missed alerts (false negatives)

because a primary potential benefit of CGM is the ability to lower events of hypoglycemia; rates varied across blood glucose thresholds and devices – false negatives rates for hypoglycemia (below threshold) ranged from 14% to 75% and false negative rates for hyperglycemia (above threshold) ranged from 5% to 37%.

### **3. Is it effective?**

The committee concludes that the comprehensive evidence shows that SMBG is a more effective treatment than alternatives (limited or no self testing); and CGM is unproven to be equally or more effective treatment than SMBG. Key factors to the committee's conclusion included:

- 3.1. The committee unanimously agreed that sufficient evidence exists to conclude that SMBG is a more effective treatment compared to conventional treatments or CGM.
- 3.2. The committee agreed that insufficient evidence exists to conclude that CGM is an effective treatment.

### **4. Evidence about the technology's special populations, patient characteristics and adjunct treatment**

The committee agreed that no compelling evidence exists to differentiate sub groups or special populations.

- 4.1. The evidence based technology assessment report compared CGM with SMBG and indicated one RCT. Patients 8-14 years old and those 15-24 years old had similar results with regard to A1C and achieving targets for CGM and SMBG with no evidence of differential efficacy by age was demonstrated, based on one RCT.
- 4.2. The evidence based technology assessment report reported that the SMBG frequency evidence is from one large registry study. There is limited evidence for differential effectiveness for frequency of SMBG by age. For 13-18 year olds an average improvement in A1C of  $0.3\% \pm 0.011$  for each additional SMBG was reported. This appears to apply up to tests five per day. In contrast, for ages 0-5 and 6-12, beyond one test per day, improvement in A1C was much less and averaged  $0.04\% \pm 0.018$  and  $0.12\% \pm 0.010$  respectively beyond one SMBG per day.

### **5. Is it cost-effective?**

The committee concludes that the SMBG is more cost effective than conventional treatments and CGM. CGM is unproven to be cost effective; agreeing with the comprehensive evidence review that no evidence based conclusions about cost effectiveness can be drawn.

- 5.1. The evidence report adequately summarized the very low quality evidence on cost which helped the committee conclude that CGM is not a cost effective treatment.

### **Committee Decision**

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and agency and state utilization information. The committee concluded that the current evidence on Glucose Monitoring demonstrates that there is sufficient evidence to cover self-monitoring of blood glucose (SMBG) for insulin dependent individuals under the age of 19. The committee agreed that there is sufficient evidence on continuous glucose monitoring for insulin dependent individuals under the age of 19 to cover with conditions. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. Based on these findings, the committee voted to cover self-monitoring of blood glucose (SMBG). Based on these findings, the committee voted to cover with conditions continuous glucose monitoring (CGM).

## **Glucose Monitoring Coverage Vote**

The clinical committee utilized their decision tool to first gauge committee judgment on the status of the evidence in the three primary areas of safety, efficacy, and cost.

### ***Self-monitoring of blood glucose (SMBG) --***

**Is there sufficient evidence under some or all situations that self-monitoring of blood glucose for insulin dependent individuals under the age of 19 is:**

|                                   | <b>Unproven<br/>(no)</b> | <b>Equivalent<br/>(yes)</b> | <b>Less<br/>(yes)</b> | <b>More<br/>(yes)</b> |
|-----------------------------------|--------------------------|-----------------------------|-----------------------|-----------------------|
| <b>Effective</b>                  | 0                        | 0                           | 0                     | <b>11</b>             |
| <b>Safe</b>                       | 0                        | 0                           | 0                     | <b>11</b>             |
| <b>Cost-effective<br/>Overall</b> | <b>3</b>                 | 0                           | 0                     | <b>8</b>              |

### ***Continuous Glucose Monitoring (CGM) --***

**Is there sufficient evidence under some or all situations that continuous glucose monitoring for insulin dependent individuals under the age of 19 is:**

|                                   | <b>Unproven<br/>(no)</b> | <b>Equivalent<br/>(yes)</b> | <b>Less<br/>(yes)</b> | <b>More<br/>(yes)</b> |
|-----------------------------------|--------------------------|-----------------------------|-----------------------|-----------------------|
| <b>Effective</b>                  | <b>11</b>                | 0                           | 0                     | 0                     |
| <b>Safe</b>                       | <b>9</b>                 | <b>2</b>                    | 0                     | 0                     |
| <b>Cost-effective<br/>Overall</b> | <b>11</b>                | 0                           | 0                     | 0                     |

Glucose Monitoring Coverage Vote: Based on the evidence provided and the information and comments presented, the committee moved to a vote on coverage.

| <b>HTCC COMMITTEE COVERAGE DETERMINATION</b>   |                    |                                |   |
|--|--------------------|--------------------------------|---|
|  | <b>Not covered</b> | <b>Covered Unconditionally</b> | <b>Covered Under Certain Conditions</b> |
| <b>Self-monitoring of blood glucose (SMBG)</b> | 0                  | 11                             | 0                                       |
| <b>Continuous Glucose Monitoring (CGM)</b>     | 5                  | 1                              | 5                                       |

- Action: The committee vice-chair directed HTA staff to prepare a Findings and Decision document on glucose monitoring reflective of the majority vote for final approval at the next public meeting.
- ✓ *Limitations of Coverage:* Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, Continuous Glucose Monitoring (CGM) is a covered benefit for diabetes mellitus (DM) patients under 19 using insulin when all of the following conditions are met:
  - Suffering from one or more severe episodes of hypoglycemia
  - Or involved in an IRB approved trial

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The committee discussed Clinical guidelines and Medicare decision, and their coverage determinations are consistent with the clinical guidelines and Medicare decision. The committee found that the evidence review summarized the most recent, relevant evidence and assessed its quality along with addressing key questions relevant to the committee's statutory criteria including evidence on safety, efficacy, effectiveness and cost that were addressed or transparent in clinical guidelines.

## **Agenda Item: Spinal Injections Topic Review**

Leah Hole-Curry, HTA Program Director, introduced the technology topic up for discussion:

- ✓ Staff provided an overview of the timeline and referred HTCC members to the included key questions and population of interest for the Spinal Injections review.
- ✓ Staff welcomed, per HTCC request, an invited clinical expert, Dr. Craig Hartrick, clinical anesthesiologist and researcher at William Beaumont Hospital in Michigan. Dr. Hartrick prepared a COI with no conflicts listed, other than his professional affiliation as Editor in Chief of Pain Practice.

## **Agenda Item: Public Comments**

The Chair called for public comments.

- ✓ Scheduled Public Comments: Eighteen stakeholder groups requested scheduled time for public comments.
  - The following clinicians provided comment in support of spinal injections based on their clinical experience and observation and belief that spinal injections are effective and safe. The commenters believe that spinal injections increase function; reduce need for other interventions that are riskier; and/or are accepted by medical and specialty societies. Restrictions on spinal injections could lead to more unnecessary spinal surgeries. Believe that evidence report inclusion/exclusion criteria are inappropriate and authors have conflict. Issues with overuse are not related to the treatment but are caused by increased providers without adequate training or controls or not using imaging guidance. No additional clinical evidence was cited.
    - Paul Dreyfuss, MD; Ray Baker, MD; Way Yin, MD; Nikolia Bogduk, MD; Richard Rosenquist, MD; John Carrino, MD; Carolyn Marquardt, MD; Andrew J. Cole, MD; Jason Attaman, DO; Jeffrey Roh, MD; Llewellyn N. Packia Raj, MD; Irene Young, MD; Yung J. Lee, DO; Michael Hatzakis, Jr., MD; Alison Stout, DO and Trent L. Tredway, MD collectively.
  - Elin Bjorling, American Pain Foundation (APF), provided comment in support of spinal injections based on concern that Washington State has a one size fits all decision making approach, which disregards the individual needs of the pain population. No additional clinical evidence was cited.
  - Deryk Lamb, patient, provided comment in support of spinal injections based on his personal experience with failed back surgery syndrome; spinal injections are part of his regimen and concerned those barriers to finding pain care will decrease his quality of life and that Washington state patients deserve appropriate pain management care access, including spinal injections.
- ✓ Open Public Comments: Six individuals provided comments during the open portion.
  - The following clinicians provided comment in support of spinal injections based on their clinical experience and observation and belief that spinal injections are effective, increase function; reduce need for other interventions that are riskier; and/or are accepted by medical and specialty societies. Several commenters did acknowledge that overutilization occurs and appropriate candidates need to be identified. No additional clinical evidence was cited.
    - Carlos Moravek, MD, Franciscan Medical Group
    - Zachary Abbott, MD, Olympia clinician
    - Brett Quave, MD, Medical Director at Watersedge Yakima Memorial
    - Doug Burns, MD, Evergreen hospital

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- Andrew Engle, MD
- Mary Winkler, Washington state employee and patient receiving spinal injections provided comment in support of spinal injection based on her personal experience. Believes that while spinal injects are unpleasant, they have allowed her to remain working and does not believe other options are available.

**Agenda Item: Spinal Injections – Agency Data**

Josh Morse, Department of Labor & Industries, presented to the committee the agency utilization and outcomes for Spinal Injections. Full PowerPoint slides in meeting materials.

- ✓ Spinal Injections Background: Up to 75% of the population will have an episode of pain at some point in life. Spinal injections may be used to treat and/or isolate the source of back or neck pain, typically when: it has become chronic (more than 3 or 6 months w/o relief), and Conservative measures have failed to provide relief.
- ✓ Agency Concerns:
  - Safety Concerns (Low): Spinal injections are invasive techniques to infiltrate tissues in the vicinity of major nerves of the CNS with anesthetic or anti-inflammatory agents. Though risk is reportedly low, infection and allergic reactions are safety concerns.
  - Efficacy Concerns (Medium): The efficacy of spinal injections is rated medium. It is unclear what effect spinal injections may have on long term improvement in back pain and function.
  - Cost Concerns (Medium): Back pain is common among Washington insured. The cost-effectiveness of spinal injections is unknown, yet the volume of utilization significant and rising.
- ✓ Coverage Overview: Currently covered by UMP, Medicaid and Labor and Industries. UMP and Medicaid have no limits and prior authorization is not required.
- ✓ LNI Coverage has limits - Overview:
  - Epidural injections may be authorized when there is evidence of nerve root irritation or radiculopathy. The intent is to identify the involved nerve root(s), or to reduce inflammation of same.
  - Epidural steroid injections are limited to 3 in the first 30 days. No more than 6 per episode.
  - Must be under fluoroscopic guidance, or performed in an accredited facility.
  - Facet joint injections are covered when provided by qualified specialists in orthopedics, neurology, and anesthesia. Injections must be performed in an accredited hospital under radiographic control. Not more than four facet injection procedures are authorized in any one patient.
- ✓ Utilization Cost for all agencies (\*average per patient per year; \*\*average per patient per 4 years):

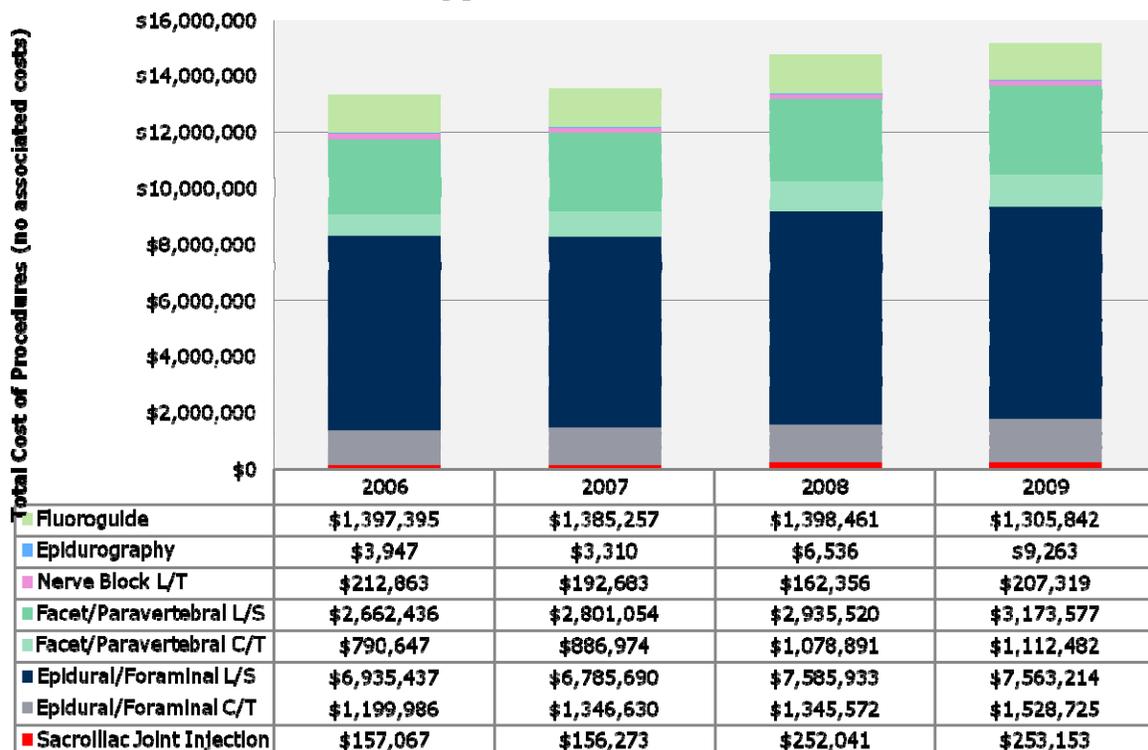
|                           | 2006   | 2007   | 2008   | 2009   | 4 Year Total |
|---------------------------|--------|--------|--------|--------|--------------|
| Procedures                | 34,298 | 33,994 | 39,667 | 44,128 | 152,087      |
| Patients                  | 9,010  | 9,072  | 10,025 | 11,078 | 36,846       |
| Avg Cost L&I per patient  | \$2231 | \$2353 | \$2336 | \$2161 | \$2268*      |
| Avg Cost DSHS per patient | \$517  | \$503  | \$520  | \$523  | \$648**      |
| Avg Cost UMP per patient  | \$1429 | \$1418 | \$1507 | \$1491 | \$1925**     |

✓ Utilization Costs for all agencies:

| Direct Costs (millions) | 2006   | 2007   | 2008   | 2009   | 4 Year Total |
|-------------------------|--------|--------|--------|--------|--------------|
| Total                   | \$13.1 | \$13.3 | \$14.5 | \$14.9 | \$55.7       |
| L&I                     | \$10.4 | \$10.4 | \$10.8 | \$10.6 | \$42.1       |
| DSHS                    | \$1.3  | \$1.3  | \$1.5  | \$1.8  | \$6.0        |
| UMP                     | \$1.4  | \$1.56 | \$2.2  | \$2.4  | \$7.7        |

✓ Agency Utilization – combined agency costs of Spinal Injections by Type, 2006 – 2009:

### Combined Agency Costs of Spinal Injections by Type, 2006-2009



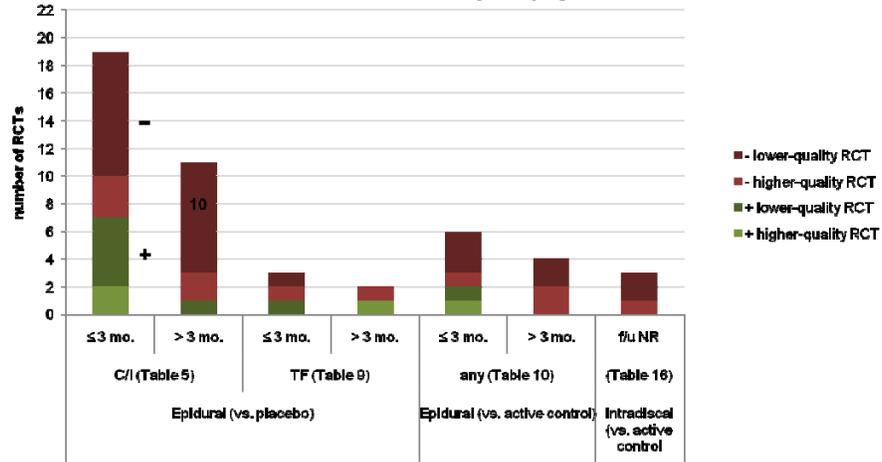
- ✓ Increase in Utilization: Spinal injection costs increased in all agencies between 6 and 16% from 2008 to 2009. 6.1% increase in L&I despite 15% decrease in claim volume. 76% of utilization, \$42 million, is in workers' compensation.
- ✓ Summary: The best evidence from the Spectrum report shows only 'mixed results' for the most common spinal injections for back pain with sciatica or radiculopathy including: Lumbar caudal or interlaminar epidural steroid injections and transforaminal steroid injections.
  - A large body of evidence appears to show no benefit from a variety of different injection techniques for a number of conditions including: Spinal stenosis; low back pain without sciatica or radiculopathy; failed back surgery syndrome; facet joint pain and discogenic back pain.
- ✓ AMDG Considerations:
  - Is there a category of injections where coverage with conditions makes sense?
  - If there is, should it be only for monoradiculopathies and/or for multiple levels? Single root injections for monoradiculopathies? Injections for multiple roots (bilateral or multiple levels)?
  - Is there any evidence for coverage of any injection for chronic, non-radicular back pain?
- ✓ Agency Recommendations based on the available evidence and agency experience: Coverage with conditions for of spinal injections.
  - Limitations of coverage: 1 Epidural steroid injection for radiculopathy when:
    - Conservative treatment has failed
    - There is documentation of clinical evidence of sciatica or radiculopathy (e.g., altered sensation, inability to heel-toe walk)
    - Additional injections may be covered the first injection is demonstrated to provide relief (pain and function) for the expected duration
  - Non-coverage for therapeutic facet joint injections; therapeutic intradiscal injections or any injections for chronic, non-radicular back pain

### **Agenda Item: Evidence Review Presentation**

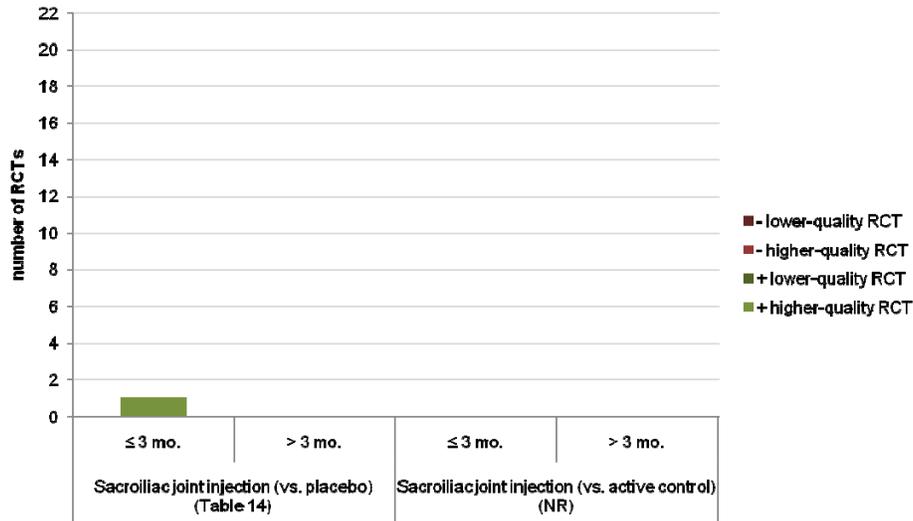
Spectrum Research presented an overview of their evidence report on Spinal Injections. A full set of slides and information is included in the meeting materials.

- ✓ Spinal Injections Background: typically considered only after failure of conservative treatment. Injection of anti-inflammatory agent (steroid) and local anesthetic into spine or surrounding nerves and joints. Injection often monitored with fluoroscopic or CT visualization. Deliver treatment directly to pain source (theoretical advantage).
- ✓ Literature Search: For key questions 1-3 (n = 1 SR; n = 22 RCTs); (n = 7 cohort studies) and (n = 24 case series). For key question 4 (n = 2 economic analyses).
- ✓ Key Question 1 inclusions: RCTs published in English. For lumbar injections: RCTs ≤ 2008 as reported in the APS / Chou et al (2009) SR and RCTs ≥ 2008. Exclusions: unreported diagnosis; < 75% of patients had excluded diagnosis; study type other than RCT and/or abstracts, letters and editorials. Key Question 1 outcomes = pain relief; physical function; opioid use; return to work; quality of life and patient satisfaction. Comparisons include 5 variables = injection type; injection approach (epidural only); diagnosis; control intervention (placebo, active control); and study quality.
- ✓ Lumbar Spinal Injections:

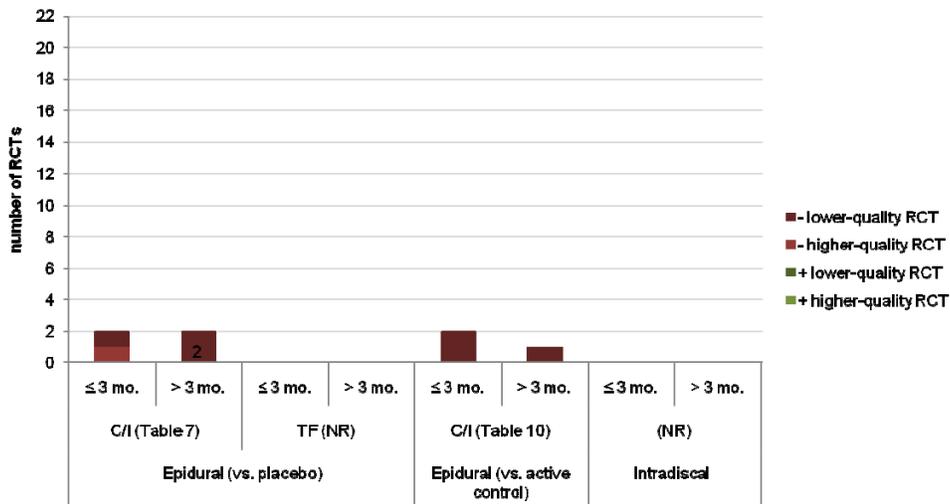
### Sciatica/radiculopathy: pain



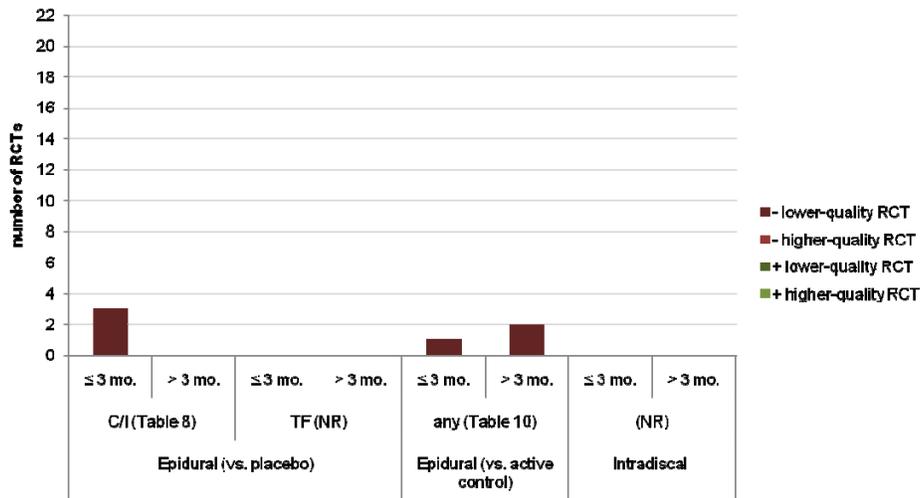
### Lumbar pain from SI joint: pain



### Spinal stenosis: pain & function

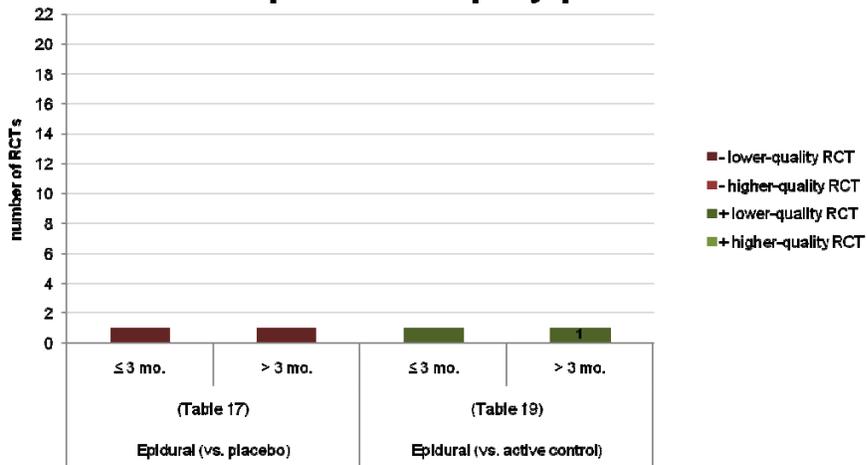


### FBSS: pain & function

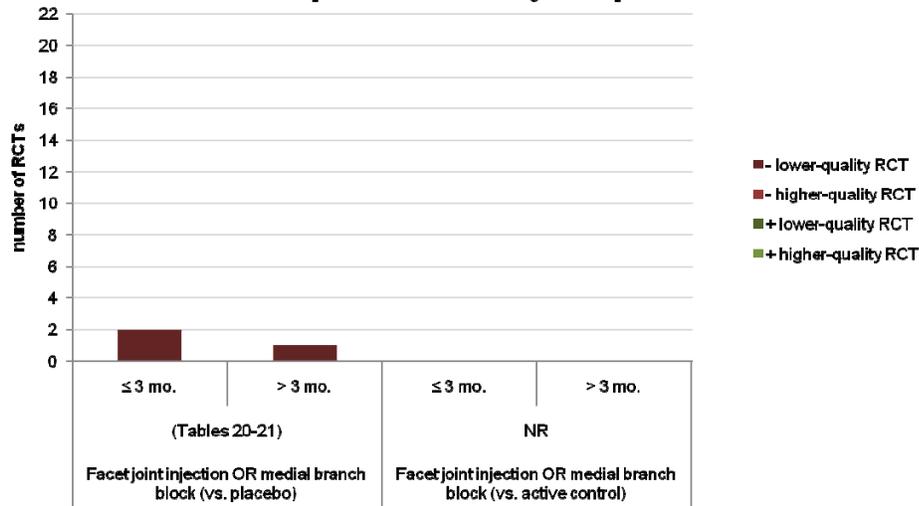


✓ Cervical Spinal Injections

### Neck pain + radiculopathy: pain



### Cervical pain from facet joint: pain



- ✓ Key Question 2 inclusions: RCTs + APS SR as included in Key Question 1. Case series designed to report complications (n ≥ 100). Exclusions = case reports.
- ✓ Major complications: lumbar spinal injections (SoE = High [major complications are rare])

|                               | <b>RCTs</b><br>(APS/Chou SR + 14 RCTs) | <b>Case series</b><br>(6 studies) |
|-------------------------------|--|-----------------------------------|
| Death attributed to procedure | 0/1146 patients                        | 0/10,416 injections               |
| Paralysis                     | 0/1146 patients                        | 0/10,416 injections               |
| Dural puncture                | 1/1556 injections or patients          | 1/10,416 injections               |
| Subarachnoid puncture         | 1/1556 injections or patients          | 1/10,416 injections               |
| Angina pectoris               | 1/1556 injections or patients          | 0/10,416 injections               |

- ✓ Key Question 2 – major complications: cervical spinal injections (SoE = High [major complications are rare])

|   | <b>RCTs</b><br>(5 RCTs)      | <b>Case series</b><br>(4 studies) |
|---|------------------------------|-----------------------------------|
| Death attributed to procedure           | 0/326 patients               | 0/7240 injections or patients     |
| Paralysis                               | 0/326 patients               | 0/7240 injections or patients     |
| Dural puncture                          | 0/710 injections or patients | 2/6330 patients                   |
| Subarachnoid puncture                   | 3/710 injections or patients | NR                                |
| Life-threatening anaphylactice reaction | NR                           | 1/7240 injections or patients     |
| Grand-mal seizure                       | NR                           | 1/7240 injections or patients     |
| Local hematoma                          | NR                           | 1/7240 injections or patients     |

- ✓ Key Question 2 – minor complications. Overall rate of minor complications: 0.06% - 16.3% injections or patients (19 RCTs, 14 case series).
- ✓ Key Question 3 inclusions: comparative clinical studies (RCTs, cohort studies with concurrent controls). Exclusions = Non-clinical (e.g., technical reports); case reports; unreported diagnosis; and < 75% of patients had excluded diagnosis.
- ✓ Key Question 3 – no strong evidence of differential efficacy or safety in subpopulations based on the following characteristics: injection approach (lumbar epidural) = 8 RCTs, 2 retrospective cohort studies; diagnosis = 1 RCT, 4 retrospective cohort studies; baseline pain and dysfunction = 1 RCT, 1 prospective and 3 retrospective cohort studies; injectate characteristics = 1 RCT; sex = 3 retrospective cohort studies; age = 3 retrospective cohort studies; and imaging = 2 retrospective cohort studies.
- ✓ Economic conclusions = SoE very low (no evidence of cost effectiveness)
- ✓ Points to Consider – Efficacy:
  - On one hand: Large number of RCTs. No clear benefit of epidural steroid injections in sciatica patients. In general, no benefit of spinal injections for other types of back pain; fewer trials reporting.
  - On the other hand: Heterogeneity relating to injection types and approaches, diagnosis, control groups and study quality. Heterogeneity between control interventions makes interpretation of results somewhat challenging. Possible benefit in the following cases (1 study each): LBP from

the SI joint treated with SI joint blocks. Cervical radiculopathy treated with epidural steroid injections.

- ✓ Points to Consider – Safety:
  - On one hand: major complications are rare. Minor complications are more common.
  - On the other hand: Major complications have been reported in case reports; incidence unclear. Minor complications are generally transient in nature.
- ✓ Point to Consider – Cost Effectiveness:
  - Based on 2 RCTs: epidural versus placebo injections in patients with LBP + sciatica. Higher quality study showed no cost benefit. Short-term cost benefit (3 – 4 weeks) in lower quality study not sustained. Other injection types not evaluated.

### **Agenda Item: HTCC Spinal Injections Discussion and Findings**

C. Craig Blackmore, Committee Chair, led a discussion of the evidence related to the safety, efficacy, and cost-effectiveness of Spinal Injections beginning with identification of key factors and health outcomes, and then a discussion of what evidence existed on those factors.

#### **1. Evidence availability and technology features**

- 1.1 The evidence based technology assessment report estimates 75% of the population has an episode of back pain at some point in their life. While most acute back pain resolves within a few months, surveys report that approximately 5% of the population has chronic back pain, with significant social and economic impacts. Those affected can have disabling symptoms that can dramatically affect their quality of life and ability to perform a variety of activities. The source and pathology of chronic spinal pain is not well understood but has been attributed degenerative disc disease (DDD), herniated nucleus pulposus (HNP) (or herniated/slipped disc), spinal stenosis, radiculopathy, failed back surgery syndrome (FBSS), facet joint syndrome, among other causes.
- 1.2 The evidence based technology assessment report indicates treatment for chronic back pain typically begins with the identification (or ruling out) of underlying cause of pain and beginning conventional medical management (CMM). CMM may include conservative/ non-invasive interventions such as physical therapy and rehabilitation, pharmaceutical pain management, psychological therapy and coping skills, exercise, education, antidepressants, cognitive behavioral therapy and supported self-management, spinal manipulation, electrical stimulation, injections outside the spine, implanted devices, acupuncture/acupressure, and modified work.
- 1.3 The evidence based technology assessment report indicates that a small percentage of non-responsive patients may proceed to invasive therapies, including spinal injections. Spinal injections are not curative but are intended to provide pain relief and functional improvement for up to several months. Spinal injections involve the injection of an anti-inflammatory agent such as a steroid and/or an anesthetic into the spine or space around the spinal nerves and joints. One of the theoretical advantages of spinal injections is that they deliver medication directly to the site thought to be the source of pain. Types of spinal injection include epidural, facet joint, intradiscal, and sacroiliac joint injections. Spinal injections can be used for diagnostic and therapeutic purposes. According to one study examining Medicare claims of lumbosacral injections, the number of epidural steroidal injections increased 271% and the number of facet injections increased 231% from 1994 to 2001. A similar study found that lumbar facet joint injections/diagnostic blocks increased 161% from 2002 to 2006.
- 1.4 Despite dramatic growth in procedures, evidence about the impact of spinal injections on important patient oriented outcomes related to impact on pain, physical function, opioid use; return to work; quality of life; patient satisfaction; avoidance of more invasive surgery; expected duration of impact; need for repeat procedures; frequency and type of harms; as well as clinical impacts of multilevel or procedure differences and any evidence about

differential effect based on different patient, social or provider characteristics; different injection types; and impact of cost is needed.

- 1.5 The evidence based technology assessment report indicates that the Spinal injection evidence base is extensive: initial search resulted in over 2,700 potential citations; and based on evaluation against inclusion criteria, 1 Systematic review; 22 RCTs, 24 Observational Studies and two economic studies were included.
- Evidence was identified on five injection types: epidural (lumbar and cervical); facet joint; sacroiliac; intradiscal injections and medial branch blocks.
  - Key strengths of the overall body of evidence are a large evidence base including randomized clinical trials.
  - Limitations in the overall body of evidence: despite well validated measures to evaluate treatment outcomes, evidence is limited by the variety of different measures or non-validated measures used; most studies were limited by a focus on one outcome - impact on short term pain; studies not including a placebo arm are limited when measuring subjective improvement in pain; many studies were limited by short duration (3 month or less) for treatment of a chronic condition; there remains uncertainty over clinically meaningful improvement for pain and function; and the variety of injection methods and types.

## **2. Evidence about the technology's safety**

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is safe. Summary of committee considerations follows.

- 2.1 Major Complications: the evidence based technology assessment report indicated that major reported complications of spinal injection include dural puncture; subarachnoid puncture and angina pectoris, though rates are rare.
- There were no cases of death or paralysis related to the procedure in the included studies, though death unrelated to the procedure was reported in 10 of 1146 patients in the RCTs, and there have been case reports of death and paralysis in the published literature.
  - For dural or subarachnoid punctures, or other life threatening complications, the reported rates ranged from 3 in 710 injections to 5 in 7240 (cervical) and 1 in 1556 injections to 1 in 10,416 injections for lumbar.
  - Vascular Puncture: the evidence based technology assessment report indicated the mean incidence of intravascular puncture following fluoroscopically guided lumbar spinal injections was 10.18% (range, 1.9–22%) as reported in five case series designed to assess its incidence.
- 2.2 Minor Complications: the evidence based technology assessment report indicated that minor complications are more common but are generally transient in nature. The overall minor complication rate ranged from 0.06% to 16.3% of injections or patients in 19 RCTs and 14 case series, and complications included: pain at the injection site, increased radicular pain/numbness/weakness, nerve root irritation, superficial infections, sympathetic blockade, facial flushing, vasovagal reactions/fainting, headache, gastric complaints, dizziness, pruritis, irregular periods, and insomnia.
- 2.3 Radiation Exposure to the Physician: the evidence based technology assessment report indicated the with proper protective measures, total radiation exposure was within normal limits following a mean of 923 procedures (range, 100 – 1819) with an average length of radiation exposure of 9.8 seconds/procedure (range, 4.9 – 15.2) in all five case series we identified.
- The evidence based technology assessment report reported that approximately 50% of four million interventional medical procedures per year are performed under

fluoroscopic guidance. Fluoroscopy for spinal injections is routinely used to ensure correct needle placement, accurate delivery of the injectate, and avoidance of complications. Incorrect needle placement during spinal injections without the use of fluoroscopy has been reported by various studies in 12.5% to 38.3% of patients. A C-arm fluoroscope allows the X-ray tube to be moved around the prone patient and an image intensifier enhances the image, making it easier to interpret. Although studies have shown that radiation exposure to physicians using fluoroscopy for spinal injections is within safety limits, other methods, including ultrasound and CT, are being investigated as non-radioactive or lower radioactive methods of needle guidance.

### 3. Evidence about the technology's efficacy and effectiveness

The committee discussed multiple key factors and health outcomes that were important for consideration in their overall decision on whether the technology is effective. Summary of committee considerations follows.

3.1 Discussion focused on the following categories of injections: lumbar epidural; cervical/thoracic epidural; facet joint injection; sacroiliac joint injection; medial branch block; and intradiscal injection. Further differentiation was not focused on as the evidence based technology report indicated low to very low overall strength of evidence of different impact. The low level of evidence reported no consistent differential impact based on the approach to administering the injection; the diagnosis, pre-injection pain intensity; type of steroid, gender, age or other patient characteristics.

3.2 **Epidural Steroid Injections for lumbar or low back pain with sciatica or radiculopathy** was highly studied and reported on; however, the overall strength of evidence is low based on the individual trial limitations and the inconsistency in results. Low back pain with sciatica or radiculopathy *the evidence is mixed* about the impact of spinal injection on pain (and in some studies function); with some studies showing a inferior results compared to placebo or other interventions and some studies showing a positive result.

- When compared to placebo for caudal or interlaminar: *In the short-term* ( $\leq 3$  months) there was mixed evidence based on data from twenty RCTs, seventeen of which were included in the Chou/APS SR (seven were considered to be higher-quality trials). Seven of seventeen studies included in the SR reported no benefit or inferior results while another seven reported positive results and three reported unclear results. Three LoE IIb RCTs published after the SR were added here, two reported on pain (both negative) and three on function (two negative and one positive) at three months. *In the long-term* ( $> 3$  months) there was mixed evidence based on data from twelve RCTs, nine of which were included in the Chou/APS SR. Seven of nine studies included in the SR reported no benefit or inferior results while positive results were reported by one study and another reported mixed results. Regarding the more recent RCTs included here, two reported on pain (both negative at twelve months, although one was positive at six months) and three on function (mixed results, one positive, one mixed, and one negative). (SoE = Low)
- When compared to placebo for transforaminal: mixed evidence based on data from four RCTs, two of which were included in the Chou/APS SR and considered to be higher-quality and two of which were more recent LoE IIb studies. In terms of pain relief, the data suggest a benefit at two weeks (one study), mixed results at one month (two studies- one positive and one negative), and no benefit by 3 months. No benefit in function was reported at three months by two studies. Long-term data were mixed as reported by two higher-quality RCTs, both of which were reported in the Chou/APS SR, with one study reported positive results while the other showed no benefit. When compared to intramuscular injections, transforaminal steroid injections were superior to intramuscular injections in terms of pain relief at one month based on data from one LoE IIb RCT. (SoE = Low)

- 3.3 **Epidural Steroid Injections for lumbar or low back pain without sciatica or radiculopathy** was also studied and reported on, and the overall strength of evidence is low to moderate based on the individual trial limitations and indication studied. The evidence indicates *no benefit* of spinal injections compared either to placebo, physical therapy, trigger point injection, discectomy or dry needling.
- Low back pain (without sciatica or radiculopathy) compared to placebo showed no benefit based on data from three RCTs, one of which was included in the Chou/APS SR and considered to be a lower-quality trial. The two more recent RCTs rated IIb also reported no benefit in pain, function, or opioid use at three months or in employment at twelve months. (SoE = Moderate)
  - Spinal Stenosis compared to placebo: *In the short-term* (24 hours – 3 months), there was no benefit based on data from four RCTs, three of which was included in the Chou/APS SR; one was considered to be a higher-quality trial. Three of four studies reported no benefit; one study reported improved walking distance at one week. In a recent RCT, LoE IIb there was no benefit in pain, function, or opioid use at three months. (SoE = moderate). *In the long-term* (13 – 30 months), there was no benefit based on data from two RCTs as reported in the Chou/APS SR. (SoE = Low)
  - Failed back surgery syndrome compared to placebo: no benefit based on data from three RCTs, two of which were included in the Chou/APS SR and considered to be lower-quality trials. In the one recent LoE IIb RCT, there was no benefit in pain, function, or opioid use at three months. (SoE = Moderate)
  - Spinal Stenosis compared to physical therapy or control: no benefit in terms of pain, function, or quality of life at three and six months based on data from one LoE IIb RCT. (SoE = Very Low)
- 3.4 **Epidural Steroid Injections for cervical pain** reported overall strength of evidence of very low based on small number of trials, trial limitation and inconsistent results. The evidence indicates *mixed benefit* of epidural cervical spinal injections.
- For neck pain with disc herniation and radiculitis (comparator = placebo): *no benefit* in terms of pain, function, or opioid use at both three and twelve months or on employment at twelve months based on data from one LoE IIb RCT. (SoE = Very Low)
  - Neck pain without disc herniation and radiculitis (comparator = placebo): *no benefit* in terms of pain, function, or opioid use at both three and twelve months or on employment at twelve months based on data from one LoE IIb RCT. (SoE = Very Low)
  - Neck pain with disc compression and radiculitis (comparator = intramuscular injection): epidural injections were *superior* to intramuscular injections in the posterior neck in terms of pain, analgesic use, and employment at one week and twelve months based on data from one LoE IIb RCT. (SoE = Very Low)
- 3.5 **Facet Joint Steroid Injections** overall had low strength of evidence of no benefit based on four RCTs.
- Confirmed or presumed lumbar facet joint pain compared to placebo: no benefit in the first three months based on data from two RCTs included in the Chou/APS SR, one of which was considered to be lower-quality. Although one of the studies reported a statistically meaningful benefit at six months in patient improvement following steroid injection, the rationale for this late response is not clear. (SoE = Low)
  - Non-radicular back pain and facet joint osteoarthritis compared to hyaluronic acid: no benefit in the injection of steroids versus hyaluronic acid into the facet joint at six months based on data from one higher-quality RCT included in the Chou/APS SR. (SoE = Low)
  - Confirmed cervical facet joint pain compared to placebo: no benefit in terms of the length of pain relief based on data from one LoE IIb RCT. No long-term data was reported. (SoE = Very Low)

- 3.6 Sacroiliac Joint Steroid Injections had low overall strength of evidence of benefit based on one RCT.
- For sacroiliac Joint Pain, compared to placebo: sacroiliac joint injections were superior to placebo injections based on data from one higher-quality RCT included in the Chou/APS SR. (SoE = Low)
- 3.7 Intradiscal Injections overall had moderate strength of evidence of no benefit based on seven RCTs.
- For discogenic back pain, steroid injection compared to placebo: no benefit based on data from three RCTs included in the Chou/APS SR, one of which was higher-quality. (SoE = Moderate)
  - For sciatica compared to chemotherapy: no benefit based on data from three RCTs included in the Chou/APS SR, one of which was higher-quality. (SoE = Moderate)
  - For low back pain without radiculopathy using neurolytic agent compared to placebo: intradiscal injections with methylene blue were superior to placebo injections in terms of pain, function, patient satisfaction, and analgesic use in the long-term (6-24 months) based on data from one LoE IIa RCT. (SoE = Low)
- 3.8 Medial Branch Blocks overall had low to very low strength of evidence of no benefit based on four RCTs.
- For confirmed lumbar facet joint pain compared to placebo: no benefit in terms of pain or function at both three and twelve months or on opioid use at twelve months based on data from one LoE IIb RCT. (SoE = Very Low)
  - For presumed lumbar facet joint pain compared to Sarapin: no benefit in injections with Sarapin with or without steroid based on data from one higher-quality and one lower-quality RCT included in the Chou/APS SR. (SoE = Low)
  - For confirmed cervical facet joint pain compared to placebo: no benefit in terms of pain or function at both three and twelve months or on opioid use or employment at twelve months based on data from one LoE IIb RCT. (SoE = Very Low)

#### 4. Special Populations

- 4.1 Approach of the Epidural Steroid Injection: the evidence based technology assessment report indicated no consistent evidence from a systematic review of six RCTs and two additional RCTs published since the systematic review that one approach is more efficacious in administering lumbar epidural steroid. The results of one lower quality RCT suggest that interlaminar injections may not be as efficacious as transforaminal in patients with axial only pain from spinal stenosis. However, more study is needed to verify these findings.
- 4.2 Diagnosis: the evidence based technology assessment report indicated no consistent evidence that epidural steroid injections have differential efficacy or effectiveness among various diagnoses of the lumbar or cervical spine.
- 4.3 Pre-injection pain intensity or duration, type of steroid, sex, age, or MRI findings: the evidence based technology assessment report indicated no consistent evidence that pre-injection pain intensity or duration, type of steroid used as injectate, sex, age or pre-injection MRI findings are associated with outcome in patients receiving epidural steroid injections of the lumbar or cervical spine.

#### 5. Evidence about the technology's value and cost-effectiveness

The committee discussed multiple key factors that were important for consideration in their overall decision on whether the technology has value and is cost-effective. Summary of committee considerations follows.

- 5.1. The evidence based technology assessment report reported no evidence that epidural steroid injections are cost effective based on data from two economic analyses. One moderately well conducted cost utility analysis (QHES 78/100) suggested that one epidural steroid injection is a more cost effective patient management strategy than up to three injections and that cost effectiveness ratios for epidural steroid injections are too high to be considered cost effective by UK conventions. Further, the budget impact of epidural spinal injections is likely large because of high use. Poor economic data (QHES 49/100) from a second trial (Karppinen) suggested that over one year epidural steroid injections do not show cost or outcome advantages compared to saline injections, and that contained herniations may be more responsive to steroid injection than bulges or extrusions.
- 5.2. The evidence based technology assessment report reported no economic data were available for facet injections, medial branch blocks, sacroiliac joint injections, or intradiscal injections or for any type of cervical injection.
- 5.3. Washington state agency utilization and cost information indicated costs for Spinal Injections of \$55M for the past four years with a rising trend.

## 6. Evidence on Medicare Decision and Expert guidelines

Committee reviewed and discussed the Medicare Decision and expert guidelines as identified and reported in the technology assessment report.

- 6.1 The Centers for Medicare and Medicaid Services have no published National coverage determinations (NCD) for any spinal injections.
- 6.2 Guidelines – a search of the core sources and relevant specialty groups identified fourteen guidelines.
  - o American Pain Society (APS), 2009: For patients with nonradicular low back pain, the APS is unable to assess the benefit of epidural steroid injection, facet joint steroid injection, medial branch block, or sacroiliac joint injection based on insufficient or poor evidence. Corticosteroid facet joint injection is not recommended based on moderate evidence. Intradiscal steroid injection is not recommended for treatment of nonradicular low back pain based on good evidence. For patients with radicular low back pain, the APS found moderate evidence for short-term (through three months) benefit from epidural steroid injections based on fair evidence. A recommendation for epidural steroid injection for patients with symptomatic spinal stenosis is not offered based on insufficient or poor evidence.
  - o American Society of Interventional Pain Physicians, 2009: The recommendation for caudal epidural steroid injection in managing lumbar spinal pain with disc herniation and radiculitis or discogenic pain without disc herniation or radiculitis is 1A or 1B, indicating a strong recommendation where the benefits outweigh the risks of treatment. In addition, the recommendation for caudal epidural steroid injection for patients with post-lumbar laminectomy syndrome and spinal stenosis is 1B or 1C, also indicating a strong recommendation. The recommendation for use of cervical interlaminar epidural injection for disc herniation and radiculitis to achieve short-term relief is 1C. For patients seeking long-term relief, the recommendation is 2B (weak recommendation), indicating benefits are balanced with risks and burdens of treatment. In patients with spinal stenosis and discogenic pain without disc herniation and radiculitis the recommendation is 2C (very weak, with uncertainty in estimates of benefits, risk, and burden of treatment). The recommendation for lumbar transforaminal epidural injections is 1C. Intraarticular facet joint injections are not recommended. Cervical, thoracic, and lumbar facet joint nerve blocks are recommended to provide both short-term and long-term relief in the treatment of chronic facet joint pain (recommendation 1B or 1C).
  - o Institute for Clinical Systems Improvement (ICSI), 2009: Epidural steroid injections and facet joint injections are classified as level I (standard, first-line) therapeutic procedures, and are recommended as part of a comprehensive treatment plan that includes

pharmacologic, rehabilitative, and psychological interventions. Evidence is limited when such procedures are used alone.

- American College of Occupational and Environmental Medicine (ACOEM), 2008: Epidural glucocorticosteroid injection is recommended as a treatment option for subacute radicular pain syndromes, and as an option for second-line treatment of acute flare-ups of spinal stenosis associated with true radicular or radiculomyelopathic symptoms based on low potential harm to the patient and low costs (Evidence Rating I: insufficient evidence). Epidural glucocorticosteroid injection is not recommended to treat chronic neck pain or for dorsal spine symptoms that predominate over leg pain based on evidence that harms and cost exceed benefits to the patient (Evidence Rating C: limited evidence). The ACOEM makes no recommendation regarding the use of facet joint injection for flare-ups of neuropathic pain or chronic low back pain (Evidence Rating I: insufficient evidence). Facet joint injection is not recommended for any radicular pain syndrome, chronic non-specific axial pain, and repeat injections are not recommended for patients who failed to achieve lasting functional improvements after a prior injection for neuropathic or chronic low back pain based on evidence that treatment is ineffective or that costs or harms outweigh benefits to the patient (Evidence Rating B: moderate evidence).
- Institute for Clinical Systems Improvement (ICSI), 2008: ICSI recommends epidural steroid injection only after conservative treatment has failed and to avoid surgical intervention. ICSI finds limited evidence for the efficacy of epidural steroid injection, but indicates it may allow patients to progress with conservative treatments. Epidural steroid injection should be performed under fluoroscopy with contrast in order to prevent treatment failure.
- Work Loss Data Institute, Low back – lumbar & thoracic (acute & chronic), 2008: Epidural steroid injection and sacroiliac joint injections are recommended as part of a comprehensive treatment plan for low back pain. Specifically, epidural steroid injection is recommended to avoid surgery for severe cases with radiculopathy, but does not offer long-term functional benefit. “Series of three” epidural steroid injections, facet joint injection (multiple series, thoracic, and medical branch blocks), and intradiscal steroid injection were considered but are not recommended.
- Work Loss Data, Neck and upper back (acute & chronic), 2008: Epidural steroid injection is recommended as part of a comprehensive treatment plan for radicular pain. Specifically, epidural steroid injection is recommended to avoid surgery in severe cases with neurologic findings. Facet joint injection was considered but is not recommended.
- Work Loss Data, Pain (chronic), 2008: Epidural steroid injection is recommended as part of a comprehensive treatment plan. Facet blocks are classified as under study by the Institute and are not currently recommended.
- American Academy of Neurology, 2007: The American Academy of Neurology indicates the use of epidural steroid injections may result in a small magnitude of improvement in radicular lumbosacral pain when evaluated 2-6 weeks post-injection, but the recommendation is classified as a level C (possibly effective) due the small number of relevant studies, highly select patient population, and variation in comparison treatments in the evidence base. Epidural steroid injections are not recommended for radicular lumbosacral pain due to a lack of evidence for improvement of function, need for surgery or long-term pain relief beyond 3 months. This recommendation is classified as level B (probably ineffective based on Class I-III evidence). There was insufficient evidence to make a recommendation regarding the use of epidural steroid injections to treat cervical radicular pain.
- American College of Occupational and Environmental Medicine, 2007: The use of epidural glucocorticosteroid injection is recommended as a second-line treatment of acute spinal stenosis flare-ups, and as a treatment option for acute or subacute radicular pain syndromes lasting at least 3 weeks after treatment with NSAIDs and when pain is

- not trending towards spontaneous resolution. Both treatments are recommended based on low potential harm to the patient and low costs (Evidence Rating I: insufficient evidence). The use of facet joint injections is not recommended for acute, subacute, chronic low back pain, and radicular pain syndrome based on evidence that the treatment is ineffective or that harms and cost exceed benefits to the patient (Evidence Rating B: moderate evidence). Sacroiliac joint corticosteroid injection is recommended as an option for patients with specified known cause of sacroiliitis (Evidence Rating C: limited evidence). The use of epidural glucocorticosteroid injection is not recommended for acute, subacute, or chronic low back pain in the absence of radicular signs and symptoms (Evidence Rating C: limited evidence).
- American College of Physicians and the American Pain Society, 2007: Epidural steroid injection is an option for patients with prolapsed lumbar disc with persistent radicular symptoms who have not responded to noninvasive therapy. No specific recommendation is given for this or any other injection therapy of interest.
  - North American Spine Society (NASS), 2007: The NASS recommends nonfluoroscopically-guided interlaminar epidural steroid injection as a treatment option for short-term symptom relief in patients with neurogenic claudication or radiculopathy. A single radiographically-guided transforaminal injection may also provide short-term symptom relief for patients with radiculopathy (Grade B: fair evidence). A multiple injection regimen of radiographically-guided transforaminal epidural steroid injection or caudal injections may provide long-term symptom relief in patients with radiculopathy or neurogenic intermittent claudication, but evidence supporting this recommendation is of poor quality.
  - EuroCOST: European evidence-based guideline COST B13 Working Group on Guidelines for Chronic Low Back Pain, 2006: Epidural steroid injection, facet joint injection, and facet nerve blocks are not recommended based on a lack of evidence or conflicting evidence. Intradiscal injections are not recommended for the treatment chronic nonspecific low back pain based on evidence they are not effective (level B: moderate evidence).
  - American Association of Neurological Surgeons; Congress of Neurological Surgeons, 2005: Lumbar epidural injections and facet injections are recommended as treatment options for temporary, symptomatic relief in some patients with chronic low back pain, but epidural injections are not recommended for long-term relief of pain, based on Class III evidence (unclear clinical certainty). Facet injections are not recommended as long-term treatment for low back pain based on Class I evidence (high clinical certainty).

## **Committee Conclusions**

Having made findings as to the most significant and relevant evidence regarding health outcomes, key factors and identified evidence related to those factors, primarily based on the evidence based technology assessment report, the committee concludes:

### **1. Evidence availability and technology features**

The committee concludes that the best available evidence on Spinal Injections has been collected and summarized.

- 1.1 The committee appreciated and agrees that chronic back pain is a serious condition that can be debilitating. Causes of chronic back pain are not well understood and current treatment aims to reduce pain and improve function. Spinal injections are advocated as an alternative treatment proposed for patients with chronic back pain who have not responded to conventional medical management. Spinal injections are an invasive procedure, compared to conventional medical management, but are less invasive than surgical interventions. Proposed benefits of spinal injections is that medication is delivered directly to the area thought to be the source of pain; and for individuals that have not responded to conventional

medical management who might otherwise consider surgery, spinal injections may be less invasive, risky, and costly.

- 1.2 The evidence based technology assessment report searched and summarized evidence on common types of spinal injections; to identify any patients most likely to benefit based on patient oriented outcomes including pain, function, long-term effects, prevention of surgery, return to work, opioid use and quality of life. Despite a robust quantity of evidence, including over 30 randomized controlled trials, the strength of evidence on Spinal Injections was overall low to moderate with results showing no benefit; and some low quality evidence showing mixed results (some trials positive, some negative) for certain injections and indications.

## 2. Is it safe?

The committee concludes that the comprehensive evidence indicates that Lumbar Epidural injections are equally safe to alternative treatments. Safety for Cervical Epidural injections; Medial Branch Block injections; Intradiscal injections; Facet Joint injections and Sacroiliac Joint injections are unproven. Key factors to the committee's conclusion included:

- 2.1. The committee agreed that there is insufficient evidence about the safety of most spinal injections, including cervical epidural injections, medial branch block injections, intradiscal injections, facet joint injections, and sacroiliac injections. The committee agreed that the procedures are invasive and have risk, though minor complications are most common.
- 2.2. The committee agreed that the relatively large body of evidence did not include any reports of morbidity following injections in trials, though the trials were unlikely to be powered for this rare event, and there are some case reports.
- 2.3. The committee agreed that the evidence demonstrated that major complications that can be life threatening include dural puncture; subarachnoid puncture; and pectoral angina occur, but are rare following; however trial reporting of complications was variable (some did not report on complications at all), and thus may be underreported.
  - Lumbar spinal injections had more clinical evidence reported where ranges could be identified from at least 14 RCTs (1/1556 event per injection); and 6 non-randomized studies that evaluated complications post procedure with major complications occurring at 1/10,416 injections and minor complications 5.8%.
  - The committee agreed that vascular puncture was identified as an adverse event, reported to occur about 10% (range 1.9-22%) in fluoroscopically guided lumbar injections.
- 2.4. The committee agreed that predominately minor complications are common but are generally transient in nature. The overall complication rate ranged from 0.06% to 16.3% of injections or patients and included: pain at the injection site, increased radicular pain/numbness/weakness, nerve root irritation, superficial infections, sympathetic blockade, facial flushing, vasovagal reactions.

## 3. Is it effective?

The committee concludes that the comprehensive evidence indicates that Lumbar Epidural injections are equally more effective than alternative treatments. Effectiveness for Cervical Epidural injections; medial branch block injections; Intradiscal injections; Facet Joint injections and Sacroiliac joint injections are unproven. Key factors to the committee's conclusion included:

- 3.1. The committee agreed that the evidence for spinal injections is generally low despite a relatively large quantity of trials, leaves many key questions about patient outcomes unanswered; but there has been a sharp rise in use (up to 271%) over the past decade.
  - Overall, the majority of randomized controlled trials *reported no benefit*.

- A subset of trials, mainly around lumbar epidural injections showed mixed results. Strengths of the body of evidence include the relatively larger number of randomized controlled trials that included comparison to placebo for efficacy questions. Limitations weakening the relatively large quantity of trials included: patient sample sizes in trials were small; reported outcomes focused on a small subset of subjective patient oriented outcomes that were not consistently reported; and the overall body of evidence shows no benefit or is inconsistent.
  - The committee agreed that several key questions remain unaddressed: a primary proposed advantage for spinal injections is the prevention of surgery; however, evidence is lacking on this outcome; and the expected duration of effect and number of repeated treatments for this chronic condition (and appropriate follow up time for trials) is a key determinate for overall effectiveness and net benefit, but is not addressed.
  - Patient oriented outcomes such as meaningful impact on function; quality of life; patient satisfaction; impact on opioid use; and return to work, were either not measured at all, or not measured or reported using consistent, validated instruments.
- 3.2. The committee agreed that epidural Steroid Injections were the most highly studied. The committee focused on evidence related to lumbar back pain (with and without radiculopathy) and then cervical/thoracic pain.
- 3.3. The committee agreed that for epidural injections for lumbar pain without radiculopathy, the evidence that injections are effective is unproven, based on low to moderate quality evidence of no benefit when compared either to placebo, physical therapy, trigger point injection, discectomy or dry needling based on eight randomized trials for various indications that showed no benefit in pain or function, nor opioid use or quality of life for those trials that measured it.
- 3.4. The committee agreed that the evidence showed that epidural injections for lumbar pain with sciatica or radiculopathy is more effective than conservative management based on seven of seventeen studies that showed benefit over placebo or comparator interventions, while acknowledging the overall evidence is low and some is mixed. The committee agreed that higher weight should be placed on more recent studies to assure that more modern techniques (guided) were used and evaluated.
- From the Chou Systematic review, seventeen total trials (seven were considered to be higher-quality trials) were identified; seven reported positive results; seven reported no benefit or negative results; and three were unclear. Three lower quality RCTs published after the SR were also included; with two reporting negative results and one reporting positive results. Regarding the more recent RCTs, two reported on pain (both negative at twelve months, although one was positive at six months) and three on function (mixed results, one positive, one mixed, and one negative).
  - Of the studies using more modern techniques including Ng, Reu, and Karpinnin reported improvement in pain (including leg pain) and ODI scores.
- 3.5. The committee agreed that the evidence of effectiveness of epidural injections for cervical pain is unproven based on low evidence of mixed benefit from three included trials. The committee agreed that higher weight should be placed on more recent studies to assure that more modern techniques were used and evaluated. For neck pain with radiculitis two studies showed no benefit in terms of pain, function, or opioid use at both three and twelve months or on employment at twelve; but one study showed superior results in pain, analgesic use, and employment at one week and twelve.
- 3.6. The committee agreed that effectiveness of facet joint injections is unproven based on low quality evidence from five studies that reported no benefit as well as three systematic reviews with mixed results where two lower quality systematic reviews reported no benefit, while one low quality systematic review reported short term benefit. The two placebo controlled studies, one of higher quality, reported no clinically significant response at three months, but a statistically significant response at six months. The committee discussed the

issue of whether fluoroguidance was used in the primary two trials from 1991 and 1989 as it was not reported and this is now a standard of care. The committee agreed with the evidence reviews' question about the biological rationale for the injection working at 6 months, but not at 3 months and the note that the intervention group received co-interventions (physical therapy). Due to the questions about the technique and results, the committee agreed that the evidence was insufficient (not confirmatory of no benefit) on effectiveness of facet joint injections.

- 3.7. The committee agreed that effectiveness of sacroiliac joint injections overall is unproven based on low evidence, but one small, higher quality trial showed that patients without spondyloarthropathy showed benefit at one month in improved VAS scores, which would be consistent with expectations of a peripheral joint.
- 3.8. The committee agreed that intradiscal injections overall is unproven based on moderate evidence of no benefit; the data from three RCTs included in the systematic review were most compelling (two from 2004 and one from 1992) on 316 patients showing negative results on pain and function at both two weeks and one to two years.
- 3.9. The evidence on effectiveness of medial branch blocks is unproven based on overall very low quality evidence, with one study that showed no benefit at 3, 12, or 24 months in pain scores; individuals achieving more than 50% pain relief; improvement in ODI scores; or changes in opioid use.

#### **4. Evidence about the technology's special populations, patient characteristics and adjunct treatment**

The committee agreed that no compelling evidence exists to differentiate sub groups or special populations.

- 4.1. The committee agreed that it would be important to know whether any sub-population, technique, patient or other characteristics impacts the effect of spinal injections. Except for the presence of radiculopathy, current studies reviewing procedure approach or patient characteristics were low quality, but generally found no benefit of spinal injections. The committee agreed with the evidence based report that there is inadequate evidence to identify characteristics that either enhance or reduce the efficacy of spinal injections such as approach of epidural steroid injection; diagnosis; or pre-injection pain intensity or duration, type of steroid, sex, age, or MRI findings.

#### **5. Is it cost-effective?**

The committee concludes that no compelling evidence exists with respect to spinal injections being cost-effective and thus the cost effectiveness of all spinal injections are unproven.

- 5.1. The committee agreed that insufficient evidence exists to conclude that epidural steroid injections are cost effective based on data from two economic analyses.
- 5.2. The committee agreed that no evidence was reported for facet injections, medial branch blocks, sacroiliac joint injections or Intradiscal injections for any type of cervical injection.

#### **Committee Decision**

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and agency and state utilization information.

- The committee concluded that the current evidence on Spinal Injections demonstrates that there is sufficient evidence to cover with conditions the use of therapeutic Epidural injections in the lumbar or cervical-thoracic spine for chronic pain.

- The committee concluded that the current evidence on Spinal Injections demonstrates that there is sufficient evidence to cover with conditions therapeutic Sacroiliac joint injections for chronic pain.
- The committee concluded that the current evidence on Spinal Injections demonstrates that there is insufficient evidence to cover the other therapeutic spinal injections: Facet joint injections; medial branch block injections; and Intradiscal injections.

The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. Based on these findings, the committee voted to cover with conditions lumbar epidural injections. Based on these findings, the committee voted to cover with conditions cervical-thoracic epidural injections. Based on these findings, the committee voted to not cover medial branch blocks. Based on these findings, the committee voted to not cover Intradiscal injections. Based on these findings, the committee voted to not cover facet injections. Based on these findings, the committee voted to cover with conditions Sacroiliac joint injections.

### **Spinal Injections Coverage Vote**

The clinical committee utilized their decision tool to first gauge committee judgment on the status of the evidence in the three primary areas of safety, efficacy, and cost.

Spinal Injections Evidentiary Votes:

**Is there sufficient evidence under some or all situations that lumbar epidural injections are:**

|                       | <b>Unproven<br/>(no)</b> | <b>Equivalent<br/>(yes)</b> | <b>Less<br/>(yes)</b> | <b>More<br/>(yes)</b> |
|-----------------------|--------------------------|-----------------------------|-----------------------|-----------------------|
| <b>Effective</b>      | <b>2</b>                 | <b>0</b>                    | <b>0</b>              | <b>9</b>              |
| <b>Safe</b>           | <b>1</b>                 | <b>8</b>                    | <b>1</b>              | <b>1</b>              |
| <b>Cost-effective</b> | <b>10</b>                | <b>0</b>                    | <b>1</b>              | <b>0</b>              |

**Is there sufficient evidence under some or all situations that cervical-thoracic epidural injections are:**

|                       | <b>Unproven<br/>(no)</b> | <b>Equivalent<br/>(yes)</b> | <b>Less<br/>(yes)</b> | <b>More<br/>(yes)</b> |
|-----------------------|--------------------------|-----------------------------|-----------------------|-----------------------|
| <b>Effective</b>      | <b>10</b>                | <b>1</b>                    | <b>0</b>              | <b>0</b>              |
| <b>Safe</b>           | <b>9</b>                 | <b>1</b>                    | <b>1</b>              | <b>0</b>              |
| <b>Cost-effective</b> | <b>11</b>                | <b>0</b>                    | <b>0</b>              | <b>0</b>              |

Is there sufficient evidence under some or all situations that medial branch block (cervical + lumbar) injections are:

|                       | <b>Unproven<br/>(no)</b> | <b>Equivalent<br/>(yes)</b> | <b>Less<br/>(yes)</b> | <b>More<br/>(yes)</b> |
|-----------------------|--------------------------|-----------------------------|-----------------------|-----------------------|
| <b>Effective</b>      | <b>10</b>                | <b>1</b>                    | 0                     | 0                     |
| <b>Safe</b>           | <b>11</b>                | 0                           | 0                     | 0                     |
| <b>Cost-effective</b> | <b>11</b>                | 0                           | 0                     | 0                     |

Is there sufficient evidence under some or all situations that intradiscal injections are:

|                       | <b>Unproven<br/>(no)</b> | <b>Equivalent<br/>(yes)</b> | <b>Less<br/>(yes)</b> | <b>More<br/>(yes)</b> |
|-----------------------|--------------------------|-----------------------------|-----------------------|-----------------------|
| <b>Effective</b>      | <b>11</b>                | 0                           | 0                     | 0                     |
| <b>Safe</b>           | <b>11</b>                | 0                           | 0                     | 0                     |
| <b>Cost-effective</b> | <b>11</b>                | 0                           | 0                     | 0                     |

Is there sufficient evidence under some or all situations that facet injections are:

|                       | <b>Unproven<br/>(no)</b> | <b>Equivalent<br/>(yes)</b> | <b>Less<br/>(yes)</b> | <b>More<br/>(yes)</b> |
|-----------------------|--------------------------|-----------------------------|-----------------------|-----------------------|
| <b>Effective</b>      | <b>11</b>                | 0                           | 0                     | 0                     |
| <b>Safe</b>           | <b>11</b>                | 0                           | 0                     | 0                     |
| <b>Cost-effective</b> | <b>11</b>                | 0                           | 0                     | 0                     |

Is there sufficient evidence under some or all situations that sacroiliac joint injections are:

|                       | <b>Unproven<br/>(no)</b> | <b>Equivalent<br/>(yes)</b> | <b>Less<br/>(yes)</b> | <b>More<br/>(yes)</b> |
|-----------------------|--------------------------|-----------------------------|-----------------------|-----------------------|
| <b>Effective</b>      | <b>9</b>                 | 0                           | 0                     | <b>2</b>              |
| <b>Safe</b>           | <b>11</b>                | 0                           | 0                     | 0                     |
| <b>Cost-effective</b> | <b>11</b>                | 0                           | 0                     | 0                     |

Spinal Injections Vote: Based on the evidence provided and the information and comments presented, the committee moved to a vote on coverage.

| <b>HTCC COMMITTEE COVERAGE DETERMINATION VOTE</b> |                    |                                |   |
|---|--------------------|--------------------------------|---|
|   | <b>Not covered</b> | <b>Covered Unconditionally</b> | <b>Covered Under Certain Conditions</b> |
| <b>Lumbar Epidural Injection</b>                  | <b>1</b>           | <b>0</b>                       | <b>10</b>                               |
| <b>Cervical-thoracic Epidural Injection</b>       | <b>3</b>           | <b>0</b>                       | <b>8</b>                                |
| <b>Medial Branch Block Injections</b>             | <b>11</b>          | <b>0</b>                       | <b>0</b>                                |
| <b>Sacroiliac Joint Injections</b>                | <b>1</b>           | <b>3</b>                       | <b>7</b>                                |
| <b>Intradiscal Injections</b>                     | <b>10</b>          | <b>0</b>                       | <b>1</b>                                |
| <b>Facet Injections</b>                           | <b>9</b>           | <b>1</b>                       | <b>1</b>                                |

- *Action:* The committee chair directed HTA staff to prepare a Findings and Decision document on Spinal Injections reflective of the majority vote.
- *Limitations of Coverage:* Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, therapeutic Epidural Injections in the lumbar or cervical-thoracic spine is a covered benefit when all of the following conditions are met:
  1. For treatment of radicular pain
  2. With fluoroscopic guidance or CT guidance
  3. After failure of conservative therapy
  4. No more than two without clinically meaningful improvement in pain and function
  5. Maximum of 3 in 6 months
- *Limitations of Coverage:* Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, therapeutic Sacroiliac Joint Injections for chronic pain is a covered benefit when all of the following conditions are met:
  1. With Fluoroscopic guidance or CT guidance
  2. After failure of conservative therapy
  3. No more than one without clinically meaningful improvement in pain and function, under agency review

The committee reviewed the Clinical guidelines and Medicare decision. The Centers for Medicare and Medicaid Services have no published national coverage determinations (NCD) for any spinal injections. Therefore, the committee's coverage determinations are consistent with the clinical guidelines.