Health Evidence Review Commission's

Health Technology Assessment Subcommittee

September 24, 2012

Meridian Park Hospital
Community Health Education Center, Room 104
19300 SW 65th Avenue, Tualatin, OR 97062

AGENDA

HEALTH TECHNOLOGY ASSESSMENT SUBCOMMITTEE (HTAS)

Meridian Park Hospital Health
Education Center, Room 104
Tualatin, Oregon
September 24, 2012 from 1:00 pm - 4:00 pm

All agenda items are subject to change and times listed are approximate

Public comment on listed topics will be taken at the time that topic is discussed and may be limited depending on the number of individuals providing testimony

#	Time	Item	Presenter	Action Item
1	1:00 PM	Call to Order	Alissa Craft	
2	1:05 PM	Review of May minutes	Alissa Craft	X
3	1:10 PM	Review Public Comment 1) Vertebroplasty, Sacroplasty, and Kyphoplasty 2) Viscosupplementation for osteoarthritis of the knee 3) Continuous glucose monitoring in Type II diabetes 4) MRI for breast cancer diagnosis 5) Diagnosis of sleep apnea in adults 6) Treatment of sleep apnea in adults	Alison Little	X
4	2:15 PM	Coverage Guidance Algorithm	Darren Coffman Alison Little Wally Shaffer	
5	2:45 PM	Review Draft Coverage Guidances 1) Self-monitoring of blood glucose 2) PET scans for breast cancer 3) Carotid endarterectomy	Wally Shaffer	X
6	3:45 PM	Confirm next meeting: Nov. 26th	Alissa Craft	
7	3:50 PM	General Public Comment		
8	4:00 PM	Adjournment	Alissa Craft	

MINUTES

Health Technology Assessment Subcommittee
Meridian Park Community Health Education Center
19300 SW 65th Avenue, Tualatin, OR
June 25, 2012, 9:00-12:00pm

Members Present: Alissa Craft, DO, MBA; Gerald Ahmann, MD; George Waldmann, MD (by phone)

Members Absent: Ed Toggert, MD; James MacKay, MD

Staff Present: Darren Coffman; Wally Shaffer, MD, MPH; Dave Lenar

Also Attending: Alison Little, MD (CEBP); Shannon Vandergriff (CEBP); Joanie Cosgrove (LHNW); Judy Fry, RN (ADA); Judy Summers, MS (JDRF); Susanna Reiner; Andrew Ahmann, MD (OHSU); Bill Struyk (Johnson and Johnson); Kenneth Ward, MD (OHSU); Michael Bolen (Medtronic); Debi Martin (JDRF); Denise Taray (DMAP); Gianna Mingo (Johnson and Johnson); Jessica Goodrich (ADA); Kate Skoglund (OHPR)

---

1. CALL TO ORDER

Alissa Craft called the meeting of the Health Technology Assessment Subcommittee (HTAS) to order at 9:00 am.

---

2. REVIEW OF MAY MINUTES

No changes were made to the March minutes.
Minutes approved 3-0.

---

3. REVIEW OF PUBLIC COMMENTS

A) Artificial Disc Replacement

Alison Little reviewed the public comments and the CEbP's recommended responses. Members discussed the issue of allowing a second surgery at a different level following a successful first surgery. Ahmann felt there should be some leeway to allow a second surgery after some time period, but there was no evidence to address what length of time may be appropriate.

No changes were made to the draft coverage guidance.

A motion was made to approve the draft coverage guidance as written and forward to HERC. **Motion approved 3-0.**

DRAFT

B) Lumbar Discography

Alison Little reviewed the public comments and the CEbP's recommended responses. There was minimal discussion.

No changes were made to the draft coverage guidance.

A motion was made to approve the draft coverage guidance as written and forward to HERC. **Motion approved 3-0.**

C) Hip Resurfacing

Alison Little reviewed additional evidence of the safety of hip resurfacing compared to total hip arthroplasty and metal ion concerns. Little then reviewed the public comments and the CEbP's recommended responses. Members still had concerns about metal ions and recognize that the evidence is limited since negative outcomes would not be seen in the data yet.

No changes were made to the draft coverage guidance.

A motion was made to approve the draft coverage guidance as written and forward to HERC. **Motion approved 2-1.**

---

4. REVIEW OF NEW DRAFT COVERAGE GUIDANCES

A. Treatment of sleep apnea in adults

Wally Shaffer presented the revised evidence summary for treatment of sleep apnea in adults and the new draft coverage guidance was discussed. There was minimal discussion among members.

Action:

No changes to the draft coverage guidance were made.

A motion was made to approve and seconded. **Motion approved 3-0.**

B. Self monitoring of blood glucose in Type 1 and Type 2 diabetes

Wally Shaffer presented the evidence summary for self monitoring of blood glucose in Type 1 and Type 2 diabetes and public comment was accepted before discussion. Following public comment, members discussed the need for more evidence concerning recommended testing amounts for patients using agents, including sulfonylurea, which may increase incidence of hypoglycemic episodes.

Action:

DRAFT

Before moving ahead with a recommended coverage guidance, members have asked for more information on self monitoring for diabetic patients taking sulfonylurea and other medications which may increase the risk of hypoglycemic episodes.

C. Continuous glucose monitoring in Type 1 diabetes

Wally Shaffer presented the revised evidence summary for continuous glucose monitoring in Type 1 diabetes and and public comment was accepted before discussion. The members felt that CGM could be very helpful, but found it difficult to expand the coverage guidance based on the present evidence. Members discussed the definition of "poorly controlled" to help add clarity to who could qualify for coverage. Even though HbA1c > 8% is used as the primary determinant of well controlled, frequent hypoglycemic episodes should also be considered and added language to clarify. In order to not limit coverage and allow plans leeway to add coverage, members changed the phrase "should only be covered for" to "should be covered for."

Action:

Revise the draft coverage guidance to "Real-time continuous glucose monitoring systems should be covered for Type 1 diabetes mellitus patients with a history of recurrent hypoglycemia or HbA1c > 8% for whom insulin pump management is being considered, initiated, or utilized. Retrospective continuous glucose monitoring systems should not be covered."

A motion was made to approve the amended draft coverage guidance and seconded. **Motion approved 3-0.**

---

5. PUBLIC COMMENT

Prior to ending discussion of the draft coverage guidance for self monitoring of blood glucose in Type 1 and Type 2 diabetes, the subcommittee received two public comments.

1) Dr. Andrew Ahmann from OHSU commented that monitoring of blood glucose is a difficult area to study. A diabetic patient with HbA1c under 7% and not taking any agents which cause hypoglycemia, such as sulfonylurea, is very different than a patient with the same HbA1c but is taking sulfonylurea. Study results may be biased because people who check less often already have better glucose control than those who check more often. He also states that getting only one value per week is useless from a clinical standpoint as it does not give much information.

2) Judy Fry, RN, representing the American Diabetes Association, commented that test strips are given in quantities and degrade over time so under a blood glucose testing regimen of only once per week, the test strips would begin to give inaccurate results before a new quantity of strips could be dispersed per the draft coverage guidance. She also commented that the amount a person tests their blood glucose is dependent on individual circumstances and should not be limited.

DRAFT

Prior to ending discussion of the draft coverage guidance for continuous monitoring of blood glucose in Type 1 daibetes, the subcommittee received five public comments.

1) Dr. Kenneth Ward, a diabetes specialist from OHSU, commented that there are two recent studies, STAR 3 and JDRF, which saw an average decrease in HbA1c of .5% and the JDRF study showed fewer severe hypoglycemic episodes using continuous glucose monitoring. The JDRF study showed benefits in patients using insulin pumps as well as those using daily insulin injections. He stated that CGM should not be limited only to those with poorly controlled blood glucose since even if patients are tightly controlled they still suffer hypoglycemic episodes and other problems.

2) Dr. Andrew Ahmann from OHSU commented that some of the devices used in the studies included in the Cochrane report are not currently used or available. Devices are rapidly changing so relying on evidence from older devices isn't very helpful. Dr. Ahmann also believes that CGM should not be limited to poorly controlled diabetecs.

3) Debra Martin, a board member for JDRF and mother of a diabetic child, comments that her daughter uses CGM combined with insulin pump to control blood glucose and it has worked very well as her daughter is at an age where many diabetic children have difficulty with blood glucose control.

4) Gianna Mingo commented that she has used CGM along with an insulin pump for many years and has allowed her to be more aware of blood glucoe control. Before using CGm she was often hospitalized, but has not needed hospitalization since and her HbA1c has decreased signifinantly after uses CGM.

5) Shannon Young, mother of a young daughter with diabetes, commented that CGM with insulin pump has greatly helped control her daughter's blood glucose. CGM devices provide a warning when blood glucose is low which has significantly reduced her daughter's nighttime hypoglycemic episodes. She also states that it has been educational for her daughter to learn which activities, foods,etc. have a large effect on blood glucose.

---

6. ADJOURNMENT

The meeting was adjourned at 11:35am. The next meeting is scheduled for September 24, 2012 from 1:00-4:00pm in Room 117B of the Meridian Park Hospital Community Health Education Center in Tualatin.

DRAFT

Review Public Comments

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: VERTEBROPLASTY, KYPHOPLASTY, SACROPLASTY

DATE: XX/XX/XXXX

HERC COVERAGE GUIDANCE

Vertebroplasty, kyphoplasty, and sacroplasty should not be covered for routine osteoporotic compression fractures.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

EVIDENCE SOURCE

Washington State Health Care Authority Health Technology Assessment Program. (2010). *Vertebroplasty, kyphoplasty and sacroplasty: Health technology assessment.* Olympia, WA: Health Technology Assessment Program. Retrieved from http://www.hta.hca.wa.gov/documents/vks_final_report.pdf

The summary of evidence in this document is derived directly from this evidence source, and portions are extracted verbatim.

DRAFT

SUMMARY OF EVIDENCE

Clinical Background

Vertebral compression fractures and sacral insufficiency fractures often result in considerable pain, loss of function, and decreased quality of life. Patients with osteopenic vertebral or sacral fractures are at greater risk of morbidity and mortality, yet operative intervention (e.g., fusion with instrumentation) may be problematic in this elderly population making less invasive methods more attractive.

Vertebroplasty, kyphoplasty and sacroplasty (collectively, percutaneous vertebral and sacral surgery) are surgical procedures used to treat spinal pain believed to be caused by fractures in the vertebra or sacrum. These are all cementoplasty techniques that are thought to relieve pain by stabilizing the fractured bone(s), but the mechanism of pain relief is not clear. Osteoporosis, vertebral metastasis and multiple myeloma are the most frequently reported indications for these procedures.

Vertebroplasty involves injection of bone cement into a partially collapsed vertebral body under computed tomography (CT) or fluoroscopic guidance. Kyphoplasty is a modification of vertebroplasty that expands the partially collapsed vertebral body with an inflatable balloon before the injection of bone cement. Sacroplasty is an extension of vertebroplasty, involving the injection of bone cement into the sacrum to repair sacral insufficiency fractures.

These surgical procedures are less invasive than other spinal surgical procedures, but more invasive than conservative medical therapy. Although a number of non-randomized studies have reported improvements in pain and functioning following these procedures, significant questions remain about their safety, efficacy and effectiveness, and cost effectiveness.

Evidence Review

Efficacy/Effectiveness

Vertebroplasty vs. sham surgery or conservative medical therapy

In two RCTs, vertebroplasty was no more effective than sham surgery in reducing pain or improving function or quality of life at one month and three months. In a large RCT comparing vertebroplasty with conservative medical therapy, vertebroplasty was more effective than conservative treatment in reducing self-reported pain intensity for follow-up points of up to one year. In two small RCTs, vertebroplasty and conservative medical therapy patients showed comparable improvement in pain, with inconsistent findings for functional outcomes. In four cohort studies (two prospective and two retrospective), vertebroplasty was more effective than conservative medical therapy in reducing pain up to six months, but pain levels were comparable for the two groups after one year. For a very limited set of functional outcomes, vertebroplasty led to earlier improvements than conservative medical therapy, followed by equivalent levels of functioning after six months to a year.

DRAFT

Kyphoplasty (KP) vs. conservative medical therapy

In one RCT, kyphoplasty was more effective than conservative medical therapy in reducing pain intensity for follow-up points up to one year. Pain was reduced more rapidly in kyphoplasty patients, and although the group differences were diminished by 12 months, they remained statistically significant. Kyphoplasty was also more effective than conservative medical therapy in improving functional outcomes over one year; again, group differences were diminished at 12 months but remained statistically significant. In two cohort studies (one prospective and one retrospective), kyphoplasty reduced pain more than conservative medical therapy for periods up to three years, and kyphoplasty improved a limited set of functional outcomes more than conservative medical therapy.

Vertebroplasty vs. kyphoplasty

One poor-quality RCT found that back pain scores improved equally for vertebroplasty and kyphoplasty patients over six months. Evidence from 12 cohort studies (six prospective and six retrospective) demonstrated that vertebroplasty and kyphoplasty led to comparable pain reduction at follow-up periods up to two years in 8 of 10 studies, and that vertebroplasty and kyphoplasty demonstrated comparable improvements at follow-up times up to two years in four of five studies.

Sacroplasty

No comparative studies were identified; case series suggest improvement in pain following sacroplasty.

Safety

Vertebroplasty and kyphoplasty

New fractures: In comparative studies, the rate of new fractures at any location following vertebroplasty, kyphoplasty, or conservative medical therapy was up to 25% at six months post-surgery, and up to 30% at 12 months, with no consistent pattern across studies in different rates for vertebroplasty, kyphoplasty, and conservative medical therapy. In cohort studies, from 22% to 66% of new fractures occurred in adjacent vertebrae, however, these rates are based on very small numbers. A systematic review concluded that the proportion of new fractures that were adjacent was higher for kyphoplasty (75%) than for vertebroplasty (52%). Systematic reviews of case series report slightly higher rates of new fractures at any location for vertebroplasty (16-21%) than for kyphoplasty (7-17%).

Cement leakage: Rates of asymptomatic cement leakage are up to 80% for vertebroplasty and 50% for kyphoplasty. Comparative studies and systematic reviews (consisting largely of case series) suggest that cement leakage is greater in vertebroplasty than in kyphoplasty; however, symptomatic leaks are rare.

Pulmonary cement embolism (PCE): One RCT reported a PCE rate for vertebroplasty of 26%, with all cases asymptomatic. Systematic reviews of case series report pooled PCE rates from 0.1% to 1.7%, with insufficient information to compare rates for vertebroplasty and kyphoplasty.

DRAFT

Mortality (data from systematic reviews primarily of case series): Rates in prospective studies of 2.1% for vertebroplasty and 0.6% for retrospective studies. Overall mortality for kyphoplasty ranged from 2.3% to 3.2% in 2 different reviews. Perioperative mortality was 0.01%.

Sacroplasty
Across four case series, rate of cement leakage was 20.5%.

[Evidence Source]

Overall Summary

Vertebroplasty is no more effective than sham surgery, and comparisons to conservative medical therapy are inconsistent. Vertebroplasty appears to have similar efficacy as kyphoplasty. No trials of kyphoplasty to sham surgery have been conducted, but kyphoplasty may be more effective than conservative medical therapy early on, although differences diminish by 12 months. There are no RCTs of sacroplasty. Mortality rates for vertebroplasty and kyphoplasty range from 0.6% to 3.2%, and both are associated with high rates of cement leakage.

PROCEDURE

Vertebroplasty
Kyphoplasty
Sacroplasty

DIAGNOSES

Vertebral compression fracture
Sacral insufficiency fracture

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
733.13	Pathologic fracture of vertebrae
805.00	Closed fracture of cervical vertebra, unspecified level
805.01	Closed fracture of first cervical vertebra
805.02	Closed fracture of second cervical vertebra
805.03	Closed fracture of third cervical vertebra
805.04	Closed fracture of fourth cervical vertebra
805.05	Closed fracture of fifth cervical vertebra
805.06	Closed fracture of sixth cervical vertebra
805.07	Closed fracture of seventh cervical vertebra
805.08	Closed fracture of multiple cervical vertebrae
805.2	Closed fracture of dorsal [thoracic] vertebra without mention of spinal cord injury
805.4	Closed fracture of lumbar vertebra without mention of spinal cord injury

DRAFT

CODES	DESCRIPTION
805.6	Closed fracture of sacrum and coccyx without mention of spinal cord injury
805.8	Closed fracture of unspecified vertebral column without mention of spinal cord injury
ICD-9 Volume 3 (Procedure Codes)	
81.65	Percutaneous Vertebroplasty
81.66	Percutaneous Vertebral Augmentation
CPT Codes	
22520	Percutaneous vertebroplasty, 1 vertebral body, unilateral or bilateral injection; thoracic
22521	lumbar
+22522	each additional thoracic or lumbar vertebral body
22523	Percutaneous vertebral augmentation, including cavity creation (fracture reduction and bone biopsy included when performed) using mechanical device, 1 vertebral body, unilateral or bilateral cannulation (eg, kyphoplasty); thoracic
22524	lumbar
+22525	each additional thoracic or lumbar vertebral body
0200T	Percutaneous sacral augmentation (sacroplasty), unilateral injection(s), including the use of a balloon or mechanical device, when used, 1 or more needles
0201T	Percutaneous sacral augmentation (sacroplasty), bilateral injection(s), including the use of a balloon or mechanical device, when used, 2 or more needles
HCPCS Codes	
S2360	Percutaneous vertebroplasty, one vertebral body, unilateral or bilateral injection; cervical
S2361	Each additional cervical vertebral body

Note: Inclusion on this list does not guarantee coverage

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT

HERC Coverage Guidance – Vertebroplasty, Kyphoplasty, Sacroplasty
Disposition of Public Comments

General Comments

Stakeholder	#	Comment	Disposition
American Association of Orthopaedic Surgeons Washington, D.C	1	Thank you for the opportunity to comment on the draft guidance regarding vertebroplasty, kyphoplasty, and sacroplasty for routine osteoporotic compression fractures. The American Association of Orthopaedic Surgeons represents 98% of the orthopaedic surgeons practicing in the United States, 368 of who practice in Oregon. Orthopaedic surgeons are the preeminent physicians providing surgical treatment for musculoskeletal conditions and disease. I currently serve as the President of the AAOS and have practiced in Tualatin, Oregon for more than 30 years.	Thank you for taking the time to comment.
	2	The AAOS firmly supports the incorporation of evidence into clinical practice, and is actively involved in developing and promoting Evidence Based Clinical Practice Guidelines for a number of musculoskeletal conditions, including The Treatment of Symptomatic Osteoporotic Spinal Compression fractures (http://www.aaos.org/research/guidelines/SCFguideline.pdf), for which the corresponding Summary of Recommendations is attached.	Thank you for providing this reference. The HTAS appreciates the AAOS' interest in producing evidence-based practice guidelines, and is impressed by the rigor of your development process.
	3	Through the AAOS' rigorously researched evidence-based clinical practice guideline development process, the AAOS has determined that the three procedures addressed in your draft coverage guidance are distinct from each other and deserving of similarly distinct treatment in terms of coverage guidance. Recommendation 8 of the AAOS clinical practice guideline recommends "against vertebroplasty for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact" (Grade of Recommendation: A). The Oregon Draft Coverage Guidance is consistent with this recommendation.	The HTAS agrees.
	4	However, Recommendation 9 of the AAOS clinical practice guideline states that "kyphoplasty is an option for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact" (Grade of Recommendation: C). The Oregon Draft Coverage Guidance is inconsistent with this recommendation.	The AAOS guideline relied on 5 studies, 4 of which were included in the WA HTA review, while an updated publication of the fifth trial was included in the WA HTA. Two compared kyphoplasty to conservative treatment and 3 compared it to vertebroplasty. The 2 trials that used conservative treatment as the comparator found clinically important differences only at 1 week and 1 month in one trial, and "possibly clinically important improvement" in the other. Two of the 3 trials that used vertebroplasty as the comparator found no difference between groups, while the third found differences in

DRAFT

Stakeholder	#	Comment	Disposition
			favor of kyphoplasty only at 2 years. Because of the inconsistent results noted here, the AOSS downgraded the strength of their recommendation from moderate to weak, so that kyphoplasty could be an "option."
	5	The AAOS clinical practice guideline for The Treatment of Symptomatic Osteoporotic Spinal Compression Fractures does not address sacroplasty. The treatment of vertebral compression fractures by either kyphoplasty or vertebroplasty should be considered completely separately from sacroplasty for sacral insufficiency fractures, as these are distinct anatomical and pathologic conditions.	The HTAS appreciates this distinction but has chosen to address all three procedures in one guidance to reflect the scope of the evidence source. Although they are included in the same Coverage Guidance, each procedure is evaluated and recommendations are made separately.
	6	Given the distinctions between the three procedures and their evidence-based clinical practice guideline recommendations, the AAOS urges the HERC to consider amending its coverage guidance to be consistent with evidence-based clinical practice guidelines. This would mean amending the coverage guidance to read: "Vertebroplasty should not be covered for routine osteoporotic compression fractures. Kyphoplasty should be covered for routine osteoporotic compression fractures." Thank you for your consideration of these amendments.	The HTAS understands the rationale presented but does not believe the evidence pertaining to kyphoplasty is sufficiently strong to recommend coverage of the procedure. *For HTAS discussion*
Medtronic, Inc. Memphis, TN	7	We appreciate this opportunity to submit comments on the Health Technology Assessment Subcommittee's (HTAS) Draft Coverage Guidance for Vertebroplasty, Kyphoplasty and Sacroplasty. As you are aware, Medtronic's Spinal and Biologics division manufactures products that treat a variety of disorders of the spine. These products are utilized by spinal and orthopedic surgeons to treat patients with acute symptomatic vertebral compression fractures that are known to significantly impair quality of life and increase risk of death. We are very interested in ensuring that the coverage guidance for Kyphoplasty reflects the latest clinical evidence and standard of care.	Thank you for your comment and for providing the studies referred to in your comments.
	8	Thank you for the consideration of our previous comments submitted April 16, 2012. We applaud the HTAS decision to provide expanded coverage from the initial draft for balloon kyphoplasty (BKP), including coverage for all cancer indications and for non-routine osteoporotic compression fractures. We believe the clinical evidence clearly supports this determination. **Additionally, we believe that the evidence supports an even broader coverage determination and application for osteoporosis cases.** Recent evidence has emerged since the Washington Health Technology Assessment Program (WA HTAP) conducted their review that supports a broadened positive coverage determination. In addition, it is worth noting that the major commercial payers in Oregon, plus a Medicare Local Coverage Decision (LCD) for the Oregon region,	The HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies.

DRAFT

Stakeholder	#	Comment	Disposition
		provide for a broader coverage of BKP. We ask the HTAS to adopt coverage guidance in keeping with the clinical indications of the LCD to expand coverage for patients with osteoporosis.	
	9	First, we submit the following as additional support of the HTAS positive coverage determination for BKP for all cancer indications. The growing body of evidence, including one randomized-controlled trial and two recent systematic reviews, demonstrates the relative superior safety and effectiveness of BKP compared to non-surgical management in the treatment of eligible vertebral compression fractures (VCFs) in patients with multiple myeloma or spinal metastases from primary tumors (Berenson 2011, Bouza 2009, Aghayev 2011). In addition, the National Institute for Health and Clinical Excellence (NICE, 2008) guidelines recommend cemental augmentation procedures for VCFs in cancer patients.	The search dates of the Bouza SR are included in the WA HTA review. The Aghayev review is narrative, not systematic. The Berenson RCT compared kyphoplasty to medical management in patients with malignancy, N=134, unblinded and funded by industry. Found significant decrease in pain in the KP group at 1 month. General NICE guidance for VP and KP due Dec 2012.
	10	Second, we appreciate and understand the HTAS evidence source as the WA HTAP, however, the Washington review was conducted in 2010 and relevant evidence has since emerged and should be considered as part of the HERC review. Discussion at the HTAS meeting on April 23, 2012 led to restrictions on coverage of osteoporosis cases partially because it was determined there were no long-term results regarding effectiveness. **However, studies are now available associating BKP with long-term effectiveness, increased life expectancy, and cost-effectiveness.** The final coverage guidance should reflect the latest clinical evidence and be expanded to include coverage for additional osteoporosis cases. The following randomized, controlled trials indicate that BKP has been shown to provide clinically and statistically greater pain relief, restoration of mobility, and quality of life than non-surgical management (Boonen 2011, Berenson 2011). Please see our previous correspondence where we included more detailed explanations of the studies; the studies are also attached for your review	See Comment #9 concerning Berenson. Boonen is an unblinded RCT, N=300, funded by industry. Found improved SF-36 scores averaged across 24 months compared to non-surgical management, as well as pain and function scores at 1,3,6 and 12 mos. 23% drop out rate. Excluded fractures associated with malignancy or acute trauma.
	11	The following recent retrospective analysis of Medicare data indicates that BKP has been associated with an increased life expectancy compared to non-surgical management (Edidin OI 2012). In another analysis of Medicare patients published this year, BKP was determined cost-effective compared with non-surgical management (Edidin CEA 2012). Both of these studies showing the advantages of BKP should be considered as part of the HERC review.	These are both retrospective database studies that use a model for estimating life expectancy, not actual data, as well as claims data to identify vertebral fractures and their treatment. Both are highly susceptible to bias.
	12	Lastly, as further support for our assertion that the coverage for BKP ought to be extended for additional osteoporosis cases, we submit the results of our review of the coverage polices of the top ten commercial carriers in Oregon (the majority of which were updated in 2011, after the WA HTAP review). Eight of the ten carriers publish their policies and all of them have positive coverage policies for BKP for osteoporosis cases. Judging from information gathered from provider bulletins, it is likely the remaining two do as well. **Additionally, the Medicare LCD is positive for all indications for BKP.**	The HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies. Medicare LCD language confirmed. Entire

DRAFT

Stakeholder	#	Comment	Disposition
		Following are the indications for the Medicare LCD: For Both Percutaneous Vertebroplasty and Percutaneous Vertebral Augmentation: One indication – painful compression fracture, regardless of etiology, described below. Clearly demonstrated vertebral compression fracture, with severe pain, refractory to conservative treatment and referable specifically to that site – non-specific documentation of "lower back pain" or similar language will not support payment. … Neither Percutaneous Vertebroplasty nor Percutaneous Vertebral Augmentation is indicated for treatment of lesions of the sacrum or coccyx. NAS will not allow payment for any such treatment until and unless either becomes listed as a covered indication in FDA labeling AND literature supports and describes appropriate criteria for such use. The CPT Category III codes, 0200T and 0201T, are non-covered. See: http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=32032&ContrId=243&ver=11&ContrVer=1&CntrctrSelected=243*1&Cntrctr=243&name=Noridian+Administrative+Services%2c+LLC+(02301%2c+MAC+-+Part+A)&LCntrctr=243*1%7c244*1&bc=AgACAAIAAAAA& To reduce confusion for surgeons and patients, we encourage the HTAS to adopt a final coverage guidance for BKP in keeping with the indications provided in the LCD.	policy is lengthy and included as a separate document.
	13	In summary, we applaud the work of the HTAS thus far on the draft coverage for BKP for all cancer indications and for non-routine osteoporotic compression fractures. However, it is our belief that the recent and emerging clinical evidence supports a broader application of coverage for BKP for other osteoporosis cases. It associates BKP with long-term positive outcomes, increased life expectancy and cost-effectiveness. We hope the HTAS will choose to follow the existing commercial policies and the indications of the LCD for the state of Oregon; they are supported by the new data showing positive results and long-term effectiveness for BKP in osteoporosis cases. Thank you again for your consideration of our comments and the attached studies.	The provided studies do not substantially alter the conclusions of the WA HTA evidence report. *For HTAS discussion*
DePuy Spine Raynham, MA	14	DePuy Spine Inc. is grateful for the opportunity to provide Oregon's Health Evidence Review Commission (HERC) with comments on its draft non-coverage policy for vertebroplasty, kyphoplasty, and sacroplasty for treatment of routine osteoporotic vertebral compression fractures (VCFs). We encourage the HERC to take into account the body of evidence for these treatment options, as well as feedback from the full spectrum of treating physicians (e.g., internists, interventional radiologists, pain specialists, and surgeons) and patients to ensure that its coverage policy fosters appropriate access to evidence-based treatment for VCFs. Below we provide rationale for HERC's continued coverage of vertebroplasty and kyphoplasty for a	Thank you for your comment.

DRAFT

Stakeholder	#	Comment	Disposition
		carefully selected subset of patients with acute VCFs who fail to respond, or who are intolerant of, non-invasive management (NIM).	
	15	**Patients with debilitating symptoms despite an adequate trial of non-invasive management have few treatment options to reduce pain and hasten return to normal function after acute VCF.** Few treatment options are available for patients suffering from painful VCFs that are unresponsive to non-invasive management (e.g., bed rest, physical therapy, analgesia, and bracing). As a result, patients may endure months of severe pain, restricted mobility, poor quality of life (QoL), and/or depression.[1] Patients with VCFs are confined to bed nine times more often than those without VCFs, increasing their risk of further VCFs and suboptimal recovery.[2] The impact of VCFs on QoL has been estimated to be similar to that attributable to chronic obstructive pulmonary disease.[3]	HTAS understands the significant impact of VCFs on patients.
	16	**The two sham-controlled studies published in the NEJM fail to provide evidence about the role of vertebroplasty for a carefully selected subgroup of patients with acute VCFs.** Randomized controlled clinical trials (RCTs) that compared vertebroplasty to a simulated procedure (sham) highlight the challenges of conducting adequately powered RCTs of vertebroplasty, including barriers to recruitment and the need for careful patient selection.[4, 5] Subsequent to the publication of these studies in the New England Journal of Medicine (NEJM), position statements by national medical societies identified severe limitations that pose challenges to interpretation of these studies.[6, 7] Among these, high non-participation rates, the inclusion of patients with chronic fractures, measurement of "overall pain" rather than back pain, significant crossover from NIM, potential analgesic effect from peri-facet injection, as well as limited statistical power warrant particular concern. Further, the studies' investigators did not require clinical correlation of fracture level/imaging with physical examination (percussion, palpation, motion testing), which is particularly important for verification of symptomatic VCFs in elderly patients. Taken together, these issues limit the generalizability and validity of the studies for real-world clinical management of VCFs. In order to address these limitations and generate new evidence for a relevant sub-population of patients with VCFs, investigators currently are recruiting patients to participate in VERTOS IV, which will compare vertebroplasty to sham procedure among patients with radiographically confirmed acute VCFs (≤ 6 weeks of pain).[8]	While there may be issues related to generalizability of the two sham controlled trials, they offer the best evidence regarding effectiveness. See also response to comment #27
	17	**Two published, randomized studies were powered to evaluate the safety and efficacy of kyphoplasty and vertebroplasty relative to NIM for the subset of patients with acute VCFs.** Prospective, randomized controlled studies that compared either vertebroplasty or kyphoplasty to NIM have shown these treatments to provide benefits in the way of improved pain relief and/or function relative to non-surgical management for well-defined population of patients with acute, non-malignant VCFs. In the randomized Fracture Reduction Evaluation (FREE) study, statistically significant improvements	The citations listed were published before the date of the WA HTA report (Aug 2010). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded

DRAFT

Stakeholder	#	Comment	Disposition
		in pain and function were sustained at 12 months for patients receiving kyphoplasty versus NIM.[9] In VERTOS II, a prospective multicenter RCT with 202 patients with acute VCFs, vertebroplasty provided statistically significant improvements in pain relief versus NIM at 12 months post-procedure (VAS 2.2 vs. 3.8; p = 0.014).[10] The incidence of new fractures was similar in both groups at the one-year follow-up time point (p = 0.28), and there were no serious complications or adverse events. Unlike the studies of vertebroplasty versus sham procedures, these two studies provide direct evidence for a well-defined population of patients suffering from acute VCFs (i.e., fractures ≤ 3 months of age), but cannot rule out response bias that may have occurred due to lack of blinding.	based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	18	**Professional guidelines on the appropriateness of vertebroplasty and kyphoplasty are varied and informed by distinct evidence.** Two professional guidelines were published *prior to availability* of the aforementioned VERTOS II study, which established the relative efficacy of vertebroplasty compared with NIM for acute VCFs. The American Academy of Orthopaedic Surgeons (AAOS) in 2010 released guidelines that vertebroplasty should not be considered for treatment of VCFs, a decision heavily influenced by the aforementioned sham-controlled studies.[11] In contrast, Appropriateness Criteria® published by the American College of Radiology (ACR) in 2010 indicate that both vertebroplasty and kyphoplasty may be appropriate for carefully selected patients after a failed trial of conservative measures or due to intolerance to conservative management.[12] The following vignettes within the ACR's Appropriateness Criteria® describe patients who may be considered for vertebroplasty or kyphoplasty after failure, or intolerance of, narcotics or non-steroidal anti-inflammatory drugs (NSAIDS): *"75-year-old woman with a documented old T9 compression fracture and 1-3-week old painful compression fracture of T12 without history of trauma. Patient has a history of gastric ulcer-related NSAIDs 2 years ago. Patient lives alone, is active, and the new fracture is impeding her independence. The older T9 fracture healed within 4-5 weeks."* *"80-year-old woman with a documented old T9 compression fracture treated by a percutaneous vertebroplasty 4 months ago. Now complains of a 5-week-old painful compression fracture of T12 without history of trauma. Patient is chronically constipated with history of cathartic abuse. Patient lives alone, is active, and the new fracture is impeding her independence."*	While the AAOS literature search was completed prior to the publication of VERTOS II, the WA HTA report was not, and VERTOS II was included in that review.
	19	**The HERC's coverage decision should be informed by the full body of literature, including new clinical studies published since completion of Washington State Healthcare Authority's systematic review.** The Washington State Healthcare Authority's coverage decision was based on an analysis dated November 4, 2010, suggesting that an updated systematic review of the literature is warranted. For example, two prospective, randomized studies comparing vertebroplasty to NIM for patients with acute (≤ 3 months)	Thank you for providing this reference. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes.

Stakeholder	#	Comment	Disposition
		and chronic (> 3 months) non-neoplastic VCFs were not yet published at the time of the Washington State HTA, and should be included in the HERC's review.[13, 14] Farrokhi et al. (2011) randomized patients to receive either vertebroplasty (n = 40) or NIM (n = 42).[13] Pain relief in the vertebroplasty group was significantly greater than that in the NIM group at 1 week, 2 months and 6 months (p<0.05), demonstrating an immediate and sustained benefit from vertebroplasty. Pain relief was maintained for the 36-month study duration, though between-group differences were not statistically significant beyond 12 months. Improvements in disability as measured by the Oswestry Disability Index (ODI) were statistically greater at all time points (1 week to 36 months) for patients in the vertebroplasty group relative to those in the NIM group. The incidence of new vertebral fractures was statistically higher among patients in the NIM arm relative to those in the vertebroplasty arm (13.3% versus 2.2%, p < 0.01). One patient who received vertebroplasty experienced cement leakage that resulted in lower-extremity pain and weakness subsequently alleviated with spinal decompression surgery.	
	20	In a single-center study in Spain, Blasco and colleagues randomized 125 patients to receive either vertebroplasty or NIM.[14] Patients in both treatment arms experienced reduced pain at all time points through 12-month follow up, though those in the vertebroplasty arm experienced superior improvement at the 2-month time point (p = 0.035). Significant improvement from baseline function, as measured by the Quality of Life Questionnaire of the European Foundation for Osteoporosis [Qualeffo-41] was observed at all time points for patients in the vertebroplasty arm and only at the 6-month time point for patients who received NIM. Vertebroplasty was associated with a significantly increased incidence of vertebral fractures (odds ratio [OR], 2.78; 95% confidence interval [CI], 1.02–7.62). Cement leakage occurred in 49% of vertebroplasty procedures, though these were not associated with immediate clinical sequelae.	Thank you for providing this reference. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes.
	21	A recently completed meta-analysis completed by Papanastassiou et al. (2012) sought to determine if differences in safety or efficacy exist between balloon kyphoplasty, vertebroplasty, and NIM for the treatment of VCFs.[15] A total of 27 studies were included, 9 of which compared vertebroplasty to NIM, 12 of which compared balloon kyphoplasty to vertebroplasty, and 6 of which compared balloon kyphoplasty to NIM. Key findings from that study are as follows: • Pain reduction for both kyphoplasty (-5.07/10 points) and vertebroplasty (-4.55/10) was statistically superior (p < 0.01) to that for NIM (-2.17/10), while no difference was found between kyphoplasty and vertebroplasty (p = 0.35). • Subsequent fractures occurred more frequently in the NIM group (22 %) compared with vertebroplasty (11 %, p = 0.04) and kyphoplasty (11 %, p = 0.01). • Patients with baseline fracture age less than 7 weeks experienced greater pain reduction (approximately 5.0 to 7.0 points) than those with VCFs treated later (approximately 2.3 to 4.5 points).	Based on this MA, KP appears to have similar efficacy to VP. Since VP does not have evidence of effectiveness compared to sham, one could conclude that KP similarly offers no benefit compared to sham.

DRAFT

Stakeholder	#	Comment	Disposition
		• Improvements QoL, as measured by the SF-36 Physical Component Summary (PCS) were superior for kyphoplasty versus vertebroplasty (p = 0.04), though the study's authors note that these differences should be interpreted with caution due to a limited number of studies and heterogeneity of pooled results.	
	22	**The HERC should seek to minimize variation to patient access to vertebroplasty and kyphoplasty in the state of Oregon and, like other public and private payers in the state, preserve access for the subset of refractory patients most likely to benefit from these procedures.** In 2011, Noridian Administrative Services (NAS), the Medicare Administrative Contractor (MAC) for Oregon and nine other states, released a coverage policy that provides access to vertebroplasty and kyphoplasty for a limited subgroup of patients suffering from acute VCF.[16] The following are among key coverage criteria in this policy, as informed by the full-body of literature and extensive public comment: • Vertebral compression fracture (VCF), with severe pain, refractory to conservative treatment and referable specifically to that site; • Patient's pain is documented to be severe (e.g., 7 or greater on 0 to 10 Visual Analog Scale [VAS]); • Fracture has been acceptably confirmed by plain film x-ray or by MRI, and results correlate unequivocally with the patient's pain; and • Fracture has been present for 4 months or less.	The HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies. Limitations listed by the commenter confirmed in the LCD. *For HTAS discussion*
	23	DePuy Spine supports access to vertebroplasty and kyphoplasty for patients who are refractory to conservative medical management and who have met other professional society criteria. We encourage HERC's final coverage position to thoughtfully reflect the body of literature in its totality, including professional society treatment guidelines, Medicare and commercial payer policies, and not least the perspectives of patients in the state of Oregon.	HTAS does not find that the evidence supports the effectiveness of either of these procedures.
North American Spine Society Burr Ridge, IL	24	The North American Spine Society would like to take this opportunity to comment on the recently proposed draft coverage guidance from Oregon Health Evidence Review Commission (HERC) to revise their current coverage guidance for vertebral augmentation for osteoporotic compression and sacral fractures. NASS is a multispecialty medical organization dedicated to fostering the highest quality, evidence-based, ethical spine care.	Thank you for this information and for taking the time to comment. In the future, please provide full citations for studies referenced in your comments.
	25	In reviewing the draft coverage guidance, we recognize that HERC has modified the Washington State Health Care Authority Health Technology Assessment (HTA) for Vertebroplasty, Kyphoplasty and Sacroplasty that was published in 2010. NASS has provided comments previously on Vertebroplasty, Kyphoplasty and Sacroplasty to Washington State HTA on February 18, 2011 and Noridian on May 27, 2011.	Thank you for this information.
	26	NASS believes there should be several distinctions made when considering kyphoplasty, vertebroplasty	The HTAS appreciates this distinction but

DRAFT

Stakeholder	#	Comment	Disposition
		and sacroplasty. The treatment of vertebral compression fractures by either kyphoplasty or vertebroplasty should be considered completely separately from sacroplasty for sacral insufficiency fractures. These are distinct anatomical and pathologic conditions. It is also imperative to distinguish cement augmentation procedures for neoplasm either primary or metastatic as a distinct and separate entity from osteoporotic compression fractures.	has chosen to address all three procedures in one guidance to reflect the scope of the evidence source. Although they are included in the same Coverage Guidance, each procedure is evaluated and recommendations are made separately.
	27	Within the comment letters to Washington State HTA and Noridian, we discussed the relevance of data published subsequent to the two New England Journal of Medicine (NEJM) articles (i.e. Kallmes et al, Buchbinder et al). NASS disagrees with the distinction in coverage policy between vertebroplasty and kyphoplasty. We certainly appreciate the decision to limit coverage of vertebroplasty based on the recent randomized controlled trials by Buchbinder et al and Kallmes et al published in the New England Journal of Medicine. However, these studies have legitimate weaknesses, particularly in the acuity of the fractures. NASS has published a systematic response to these two studies recently and appreciate the investigators' responses to our critique. Most notably, the two studies do not provide irrefutable evidence that vertebroplasty would not result in better outcomes compared to a sham procedure in truly acute fractures (i.e. 3 months old or less).	Citations not provided, but retrieved. Stated weaknesses include: • inclusion criteria included medical therapy for at least 4 weeks, resulting in a study of "healed fractures" • small enrollment (30-36% of eligible patients), limiting subgroup analysis • exclusion of patients with pathologic fractures • sham local anaesthetic injection is not an appropriate control • difference in cross over rates Authors responded to all of these weaknesses. It is not clear why the commenter makes the assumption that these two trials do not address acute fractures. In the Kallmes trial, patients could have pain for up to a year, but 38-44% had pain for 1-13 weeks, and for fractures of an uncertain age, marrow edema was required. In the Buchbinder trial, marrow edema was also required, and 32% of patients had pain duration less than 6 weeks.
	28	Second, the treatment effects in the NEJM studies about vertebroplasty were comparable to those found in the randomized controlled trials about kyphoplasty. Considering the inherent similarity of the two procedures, NASS believes that the same coverage rationale for kyphoplasty should be applied to vertebroplasty. The strongest support for this statement is the fact that kyphoplasty has been directly	HTAS agrees that the inherent similarity of KP and VP allows similar coverage decisions to be made. However, since VP does not have evidence of effectiveness compared

DRAFT

Stakeholder	#	Comment	Disposition
		compared to non-operative treatment in a randomized trial, while vertebroplasty was not compared to non-operative treatment in the NEJM trials. Thus, there is a lack of evidence of the comparative effectiveness of the non-operative treatment prescribed in the current draft policy versus vertebroplasty. Previous prospective, nonrandomized evidence (Alvarez et al, 2006) suggests that vertebroplasty has advantages when performed within 6 weeks from fracture.	to sham, which is a study type that is less susceptible to bias, HTAS concludes that KP also does not have evidence of effectiveness. In addition, the Kallmes and Buchbinder trials are supported by the findings of an open randomized trial that did not show any benefit of vertebroplasty over usual care at 3 months (Rousing 2009). See comment #52 for description of study.
	29	More recently, the study published by Klazen et al (Lancet, 2010), a randomized prospective study comparing vertebroplasty to non-operative treatment, demonstrated significantly better results with the former. Inherent in its design, this study was not blinded, and thus can be critiqued in this regard in comparison to the blinded, sham experiments published in the NEJM. Relevant to the current discussion, this study augments the current knowledge about the efficacy/effectiveness of vertebroplasty for osteoporotic compression fractures.	This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes.
	30	1. By using a non-operative treatment comparator, the study is more of a "real world" comparison of the two commonly used treatments, instead of the sham procedure used in the NEJM articles that included an anesthetic injection that may have some therapeutic effect.	Pain is an outcome that is highly subjective and susceptible to placebo effect. Use of a sham procedure is essential in this circumstance to identify true effect.
	31	2. The initial enrollment process detailed that 229 patients who could have been included in the study had spontaneous resolution of their pain and thus dropped out. This reinforces previously known knowledge about the favorable natural history of most patients with acute osteoporotic compression fractures.	This supports the rationale of the Kallmes and Buchbinder trials to require 4 weeks of medical therapy before enrollment.
	32	3. The inclusion criteria were much more stringent and specific than those used in the two NEJM studies, specifically that patients had a "visual analogue scale [pain] score of 5 or more; bone oedema of vertebral fracture on MRI; focal tenderness at fracture level…" prior to entry.	The significance of this fact, as it pertains to this evidence, is not clear.
	33	4. Fractures, on average, were more acute in the Klazen et al study compared to the NEJM studies.	The significance of this fact, as it pertains to this evidence, is not clear.
	34	At the NASS 26th Annual Meeting, November 2011 in Chicago IL, there were presentations showing both better hospital discharge outcomes and better survivorship in patients treated with vertebral cement augmentation. Edidin et al (Spine Journal 2011) looked at life expectancy following diagnosis of a vertebral compression fracture. The study utilized the Medicare database and looked at 100 percent of national inpatient and outpatient claims data from 2005–2008 for patients with a newly diagnosed vertebral compression fracture (VCF) identified using ICD-9-CM diagnosis codes. Using CPT-4 and ICD-9-CM	Both of these are retrospective database studies that are highly susceptible to bias. Gerling citation not provided.

DRAFT

Stakeholder	#	Comment	Disposition
		procedure codes, patients were stratified into operated (kyphoplasty or vertebroplasty) and non-operated patients. Of the 858,978 patients with a newly diagnosed VCF were identified, including 119,253 kyphoplasty patients (13.9 percent) and 63,693 vertebroplasty patients (7.4 percent). Across all gender-age groups, the median life expectancy predicted by the parametric Weibull model was 2.2 to 7.3 years greater for operated than non-operated patients. Although in abstract form in The Spine Journal the results were published in the Journal of Bone and Mineral Research, 2011 Jul;26(7):1617-26. Gerling et al (Spine, 2011) in their review of Cement Augmentation of Refractory Osteoporotic Vertebral Compression Fractures came to similar conclusions. They reviewed a university hospital database to identify all participants treated with primary diagnosis of osteoporotic vertebral compression fracture between 1993 and 2006. They identified 46 patients treated with cement augmentation and 129 matched controls meeting inclusion criteria. Patients not differ with respect to age, sex, and comorbidities. "A significant survival advantage was found after cement augmentation compared with controls (P < 0.001; log rank), regardless of co-morbidities, age, or the number of fractures diagnosed at the start date (P = 0.565)." They concluded cement augmentation of refractory osteoporotic vertebral compression fracture improves survival for up to 2 years when compared with conservative pain management with bed rest, narcotics, and extension bracing, regardless of age, sex, and number of fractures or co morbidities.	
	35	Zambini et al (Spine Journal 2011) looked at hospital outcomes of both osteoporotic and neoplastic vertebral compression fracture treatment with kyphoplasty and vertebroplasty in the United States. The study utilized a national healthcare database, Nationwide Inpatient Sample (NIS), which is an annual survey of approximately 1,000 hospitals, containing data from 20 percent of all inpatient hospitalizations in the U.S. In a nationwide estimate of 86,810 neoplastic (74.7 percent emergent, 25.3 percent elective) and 370,933 non-neoplastic (77.5 percent emergent, 22.5 percent elective) patients were identified. Among the neoplastic group, 71.8 percent of elective and 23.0 percent of emergent patients underwent kyphoplasty, while for the non-neoplastic group, 69.4 percent of elective and 17.5 percent of emergent patients underwent kyphoplasty. The corresponding percent of patients that underwent vertebroplasty was 10.4 percent, 11.0 percent, 9.6 percent, and 9.0 percent, respectively. The remaining patients underwent non surgical management (NSM). After adjusting for all covariates, compared with NSM patients, kyphoplasty and vertebroplasty patients had significantly higher likelihood of routine discharge (P > 0.001) and lower risk of discharge to skilled nursing facility (P > 0.001). Compared with NSM patients, kyphoplasty and vertebroplasty patients also had lower risk of in-hospital mortality, pressure ulcer, pneumonia, and infection (P > 0.029), but had higher risk of complication of surgical procedure or medical care (P > 0.001). They concluded kyphoplasty and vertebroplasty patients have a higher likelihood of better in-hospital outcomes than NSM patients. These results while only currently in abstract form are compelling and NASS will continue to follow and review the final publication.	Database studies are considered a low level of evidence and highly susceptible to bias. Citation not provided.
	36	Considering the findings of the Lancet study, comparing them to those of the NEJM studies, in addition to	HTAS disagrees that the evidence supports

DRAFT

Stakeholder	#	Comment	Disposition
		previously published, non-industry sponsored prospective comparative data (Alvarez et al, 2006), a number of points become apparent. 1. Vertebral augmentation can be considered in patients with pain that persists beyond six weeks despite non-operative care. This is supported by previous data that has demonstrated spontaneous pain relief in the majority of patients in the acute setting in this approximate time interval.	this recommendation.
	37	2. Vertebral augmentation via vertebroplasty or kyphoplasty should not be routinely considered in patients with fractures that are older than 3 months. This is supported by the findings of the two NEJM studies that failed to show that vertebroplasty was better than placebo in patients who mostly had fractures that were older than 3 months.	The NEJM studies also showed no effect on the 32-44% of patients who had fractures less than 3 months old.
	38	3. Within the appropriate time interval (6 weeks to 3 months from the onset of fracture), vertebral augmentation should be considered only if the patient has an MRI (or bone scan) that demonstrates bone edema within the fractured vertebral body and that this level corresponds to the site of pain upon physical examination (i.e. via percussing or palpating the patient's spinous processes). This can be confirmed with a plain radiograph with an opaque marker placed at the point of maximal tenderness.	The Buchbinder trial required evidence of marrow edema in all participants, and the Kallmes trial required it for any fracture of uncertain age. Even so, there was no evidence of efficacy of VP.
	39	4. Vertebral augmentation prior to six weeks should be considered only in those patients who are admitted to a hospital for management of pain associated with an osteoporotic compression fracture, are bed-bound secondary to pain, have failed to respond to non-operative inpatient care, and have satisfied the details outlined in criteria 3 (above). This is particularly true for patients with chemically-induced osteoporosis from medications such as corticosteroids or those with malignancy in whom bed rest could result in hypercalcemia.	The evidence does not support differential treatment based on the subgroups described by the commenter.
	40	5. We do not feel that a unilateral non-coverage determination is appropriate. NASS believes it would be far better to enforce appropriateness criteria to coverage of this procedure.	*For HTAS discussion*
	41	6. NASS currently agrees with a non-coverage policy for sacroplasty until further evidence is published.	Thank you for your comment.
	42	7. We strongly feel that vertebral cement augmentation for the treatment of pathological fractures (i.e. metastatic lesions, multiple myeloma) should be covered as a medically necessary procedure. The coverage policy should distinguish between vertebral cement augmentation for osteoporotic compression fractures, which should follow the above described appropriateness criteria, and pathological fractures, which should not, by nature of the disease, have a restricted time period of appropriate use. NASS hopes that you consider the above appropriate use criteria in development of a finalized policy for vertebral augmentation.	HTAS did not include guidance on treatment of pathologic fractures due to limitations of the evidence base.
Oregon Association of Orthopaedists,	43	The following comments are submitted on behalf of the Oregon Association of Orthopaedists, Inc., whose members practice throughout the state of Oregon. Additionally, I have practiced as a spine specialist in Oregon since 1988.	Thank you for this information and for taking the time to comment.

DRAFT

Stakeholder	#	Comment	Disposition
Inc. Portland, OR		We want to endorse the recommendation submitted by the North American Spine Society (NASS) that your guidance should reflect the distinctions between kyphoplasty, vertebroplasty and sacroplasty.	
	44	We concur with the NASS' clinical practice guideline recommending kyphoplasty or vertebroplasty treatment for patients who present with an osteoporotic spinal compression fracture with 6 weeks to 3 months of symptoms. This procedure is only indicated before 6 weeks if the patient is incapacitated and essentially at bed rest with the pain. There should also be MRI imaging showing acute changes with correlating clinical signs and symptoms and no neurologic deficit. For these patients, kyphoplasty and vertebroplasty can significantly relieve pain and restore mobility. The NASS May 22, 2012 letter clearly summarized an accurate review of the literature supporting this position. The Washington State Health Care Authority HTAA 2010 policy is based on a less rigorous critique of the literature.	The NASS letter does not represent a thorough review of the literature, since no systematic search was done. It is not clear why the commenter believes that the WA HTA policy, which was based on a systematic review of the literature, is less rigorous.
	45	Your draft guidance does not distinguish between vertebroplasty and kyphoplasty. We concur with NASS' recommendation that your coverage guidance be amended to read: "Vertebroplasty and Kyphoplasty should be covered for routine osteoporotic compression fractures." The treatment of vertebral compression fractures by kyphoplasty or vertebroplasty is separate from sacroplasty for sacral insufficiency fractures. Thank you for your consideration of our comments.	HTAS does not believe the evidence for VP and KP is sufficiently strong to recommend coverage. HTAS appreciates the distinction between procedures but has chosen to address all three procedures in one guidance to reflect the scope of the evidence source. Although they are included in the same Coverage Guidance, each procedure is evaluated and recommendations are made separately.
Society of Interventional Radiology Fairfax, VA	46	The Society of Interventional Radiology (SIR) appreciates the opportunity to present our opinion on the above-referenced topic. The Society of Interventional Radiology (SIR) is a professional medical association that represents 5,000 members who are practicing in the specialty of vascular and interventional radiology. The Society is dedicated to improving public health through pioneering advances in minimally invasive, image-guided therapy. Our members are at the forefront of new and minimally invasive therapies to treat an array of diseases and conditions without surgery. Interventional radiology treatments have become first-line care for a wide variety of conditions and patients, including osteoporosis patients with spinal fractures, peripheral arterial disease, deep vein thrombosis, uterine fibroids, cancer and stroke patients.	Thank you for this information and for taking the time to comment. In the future, please provide full citations for studies referenced in your comments. (No citations were provided)
	47	The draft guidance of the Health Evidence Review Commission has indicated that vertebroplasty, kyphoplasty, and sacroplasty should not be covered for routine osteoporotic compression fractures. Although the HERC has made a clinical distinction between vertebroplasty and kyphoplasty, it is our opinion that for purposes of analysis, it is appropriate to consider these two procedures collectively. The	HTAS agrees that because of similarity of VP and KP procedures, considering the procedures together is reasonable. Since as the commenter states, "patient outcomes

DRAFT

Stakeholder	#	Comment	Disposition
		clinical decision-making to diagnosis a vertebral compression fracture (VCF) is identical prior to either procedure, and patient outcomes for both procedures are similar. Therefore, in our analysis of the trials below, we will be considering kyphoplasty in addition to vertebroplasty together as treatment for osteoporotic vertebral fractures. In terms of sacroplasty, the SIR is actively working to coordinate research on this procedure, and although we are encouraged by the anecdotal reports, we concur that it should not be considered for routine fractures.	for both procedures are similar", and because the best evidence indicates the VP is not effective for osteoporotic VCFs, neither procedure should be covered.
	48	Within the past three years, results from five randomized controlled trials of percutaneous vertebral augmentation (PVA) vs. medical or sham therapy have been reported. The two largest trials totaling 502 patients reported better outcomes for patients treated with PVA vs. conservative medical therapy. Two smaller trials totaling 209 patients reported no improvement in outcomes vs. sham therapy. The smallest trial including 49 patients reported better outcomes at one month for patients treated with PVA vs. conservative therapy, but no improvement in outcomes at three or twelve months. The inclusion criteria, primary outcome measures, and results of each trial are briefly summarized below.	Please see disposition for individual trial summaries listed below.
	49	***Trial Summaries:*** The *Fracture Reduction Evaluation (FREE*) trial enrolled 300 patients over a 34 months period. One thousand twelve hundred seventy-nine patients were assessed, of whom 614 met eligibility criteria and 300 (49%) were enrolled. Inclusion criteria included one to three VCF, at least one of which had edema demonstrated by MRI and >15% height loss, and fracture age < three months. Although patients with multiple myeloma or metastases were included; only two such patients were enrolled in each treatment arm, so that this was effectively a study of osteoporotic VCF. Kyphoplasties were performed upon 149 patients; the remaining 151 patients were treated with medical therapy. Follow up evaluation included both clinical and radiographic evaluations up to one year after treatment. The primary outcome measure was the change in the SF-36 physical component score from baseline at one month. The primary outcome measure was significantly greater for those patients treated with vertebral augmentation ($p<0.001$). Secondary outcome measures of back pain and disability showed consistently superior and statistically significant results for the vertebral augmentation group up to one year after treatment, with the exception of opiate use at 12 months, which was not significantly different between the two groups. This was an industry sponsored study. In the FREE study, pain and narcotic use were also among several secondary outcomes. Graph showing significant differences in narcotic use between intervention and control only at the 3 month assessment (no differences at 1 week, 1 month, 6 months and 1 year). Referenced as: *Ashraf, Unpublished Presentation, 2010*	Citation not provided. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes.
	50	The ***Investigational Vertebroplasty Safety and Efficacy Trial (INVEST***) trial by Kallmes, et al enrolled 131 patients over a 50 month period. The original enrollment target was 250 patients, which was revised	The assumption that if the original enrollment target had been met, the study

Stakeholder	#	Comment	Disposition
		downward. One thousand eight hundred thirteen patients were assessed, of whom 431 met eligibility criteria and 131 (30%) were enrolled. Inclusion criteria included one to three VCF and fracture age of < twelve months. Patients with known malignancy were excluded. Patients with VCF of uncertain age could be enrolled if an MRI showed edema or a bone scan showed hyperactive uptake. Vertebroplasties were performed upon 68 patients and sham procedures upon 63 patients. The sham procedure included superficial and deep injection of local anesthetics and mixing of cement within the operating room to simulate a vertebral augmentation procedure, as this was to be a blinded trial. Follow up consisted of interviews conducted in person at one and twelve months and by telephone at three and fourteen days and three months, and radiographs at twelve months. Physical reevaluation was not performed as part of the follow up protocol. The primary outcome measure was the change in the modified Roland-Morris Disability Questionnaire and average pain intensity at one month. The primary outcome measures were not significantly different between the two patient groups at one month. A secondary outcome measure was clinically meaningful improvement in pain at one month; 64% of patients receiving vertebral augmentation achieved this vs. 48% of controls (p=0.06). This outcome is particularly notable because the *p* value is so close to reaching statistical significance. Had the original enrollment target been met and with the same distributions of patient outcomes, this study would have shown statistically significant positive results for clinically meaningful pain improvement at one month for the vertebral augmentation arm. The SIR commented on this trial in detail in a letter to the *New England Journal of Medicine.*	would have shown statistically significant positive results cannot be supported. The commenter assumes that VP patients would have more favorable outcomes. Of note, study groups did not differ significantly on ANY primary or secondary outcomes, including pain and QOL. While there was indeed a trend seen in clinically meaningful pain improvement in the VP group, no such trend was seen in physical disability related to back pain outcome (P=0.99). This study had 80% power to detect important differences in the primary outcome measures (a 3 point difference between groups on the Roland-Morris Disability Questionnaire, or a 1.5 point difference on patient rating of back pain intensity on a scale of 1-10).
	51	The randomized trial of vertebroplasty for painful osteoporotic fractures reported by Buchbinder et al enrolled 78 patients over a 54 month period. Four hundred sixty eight patients were assessed, of whom 219 met eligibility criteria and 78 (36%) were enrolled. Inclusion criteria included one or two VCF, fracture age of < twelve months, and MRI showing edema and/or a fracture line within the target vertebrae. Patients with known malignancy were excluded. Vertebroplasties were performed upon 38 patients and sham procedures upon 40 patients. The sham procedure was essentially the same as that used in the INVEST trial; this was also intended to be a blinded trial. Follow up consisted of mailed questionnaires at one week and one, three, and six months. As with the INVEST trial, physical reevaluation was not performed as part of the follow up protocol. The primary outcome measure was the score for overall pain over the course of the previous week at three months. The investigators reported that overall pain was not significantly different between patients undergoing vertebral augmentation and control subjects at any of the measured time points. This study was partially supported by industry.	Thank you for providing this study detail. Please provide citation in the future.
	52	Rousing et al reported upon forty-nine patient treated with vertebroplasty or conservative therapy for osteoporotic VCF over a period of 84 months. The numbers of patients screened and assessed were not reported, so that the percentage of eligible patients enrolled remains unknown. Inclusion criteria included one to three VCF and fracture age < eight weeks. If more than one fracture was present, either edema on MRI or hyperactive uptake on a bone scan was used to determine which fractures were subacute. Forty	The outcome for which a significant effect was found (pain at 1 month) was not prespecified, and was not published in the original paper. Not clear if this is unpublished information, since no citation

DRAFT

Stakeholder	#	Comment	Disposition
		patients were enrolled with pain of < two weeks duration. Patients with known malignancy were excluded. Vertebroplasties were performed upon 25 patients; the remaining 24 patients were treated with medical therapy. Follow up evaluation included both clinical and radiographic up to one year after treatment. The primary outcome measures were pain relief at three and twelve months as measured by the visual analog score (VAS). The investigators reported no statistically significant differences between the vertebral augmentation patients and the controls for pain or various functional measurements at three or twelve months. Supplementary analysis of pain at one month post treatment was, however, significantly different between the two groups; the mean VAS for the vertebral augmentation group (3.5) was significantly less than that for the controls (6.4) (p<0.01).	provided. Of note, there was a significant increased risk of new VCFs in the intervention group (RR=2.9).
	53	***VERTOS II*** On August 10, 2010, the results of the VERTOS II open-label randomized control trial were published online in *The Lancet.* VERTOS II provides markedly different results from Kallmes and Buchbinder. The VERTOS II trial enrolled 202 patients over a 31 month period. Nine hundred thirty-four patients were screened, of whom 431 met eligibility criteria and 202 (47%) were enrolled. Inclusion criteria included one to three VCF, >15% vertebral height loss, bone edema on MRI, and fracture age of < six weeks. Patients with known malignancy were excluded. Vertebroplasties were performed upon 101 patients and the other 101 patients were treated with medical therapy. Follow up evaluation included both clinical and radiographic evaluations and patient questionnaires up to one year after treatment. The primary outcome measures were pain relief at one month and one year as measured by the visual analog score (VAS). Statistically significant improved pain relief was reported for patients treated with vertebral augmentation vs. controls at all measured time points from one day through one year. Secondary analyses included positive proof of cost-effectiveness for vertebral augmentation. This study was partially supported by industry.	Citation not provided. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes.
	54	In their findings, the VERTOS II authors note that vertebroplasty resulted in better pain relief after one, three, and six months and one year (P<0.001, P<0.001, P=0.025, and P=0.014, respectively) over conservative treatment. No serious complications or adverse events were reported. The incidence of new compression fractures was lower in the vertebroplasty group, although not significantly different from the conservative care (control) group.	Citation not provided. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes.
	55	The VERTOS II study additionally notes that vertebroplasty appears to be a cost effective treatment. The "adjusted trial-based incremental cost-effectiveness ratio for vertebroplasty, as compared to conservative treatment, was €22,685 per QALY gained." While we concur that many VCFs heal on their own through conservative treatment, the long term costs of conservative care, pain narcotics, risks of deep vein thrombosis, pressure sores, and often the need for skilled nursing (or extensive family care) are all potential consequences of conservative care.	Since evidence of effectiveness has not been established, it is inappropriate to calculate an ICER.

DRAFT

Stakeholder	#	Comment	Disposition
	56	***Analysis of the Trials*** Many controversial points were raised about the INVEST and Buchbinder et al trials that reported unexpectedly negative results. Whether a proper control arm for a vertebral augmentation study requires a sham procedure and whether such a sham procedure is ethical could be debated endlessly. Valid arguments can be made that either sham or medical treatment are acceptable and ethical controls. Whether appropriate follow up absolutely necessitates a physical examination might also be argued without resolution. The fragility of the statistics resulting from the INVEST trial's reduced enrollment has also been questioned. Debate continues about the alleged disparities between the patients enrolled into the INVEST, Buchbinder et al and Rousing et al trials vs. "real world" patients. None of these issues has any remaining significance now that data from all five trials has been published. Controversy and conflicting results permeate all aspects of medicine. One must focus upon both the quality and the quantity of evidence.	HTAS disagrees that controversy and conflicting results permeate all aspects of medicine, but agrees that when results are conflicting, is it imperative to focus on both the quality and the quantity of the evidence.
	57	The principle limitation of the VERTOS II study is the lack of a sham control. However, this deserves closer scrutiny. We in the medical provider community would comment that it is extremely difficult to recruit patients to a sham controlled trial, and it may not be feasible to conduct a study of this type. Of note, in the Kallmes study, many US institutions would not endorse sham trials and many investigators remain wary of sham trials. In fact, in recent presentations, Dr. Kallmes has stopped using the term sham for patients that receive medial branch block and has used the term "control intervention."	The lack of a sham control results in serious susceptibility to bias in this trial. Both sham controlled trials had sufficient power to detect a difference, and because they were completed, would seem to contradict the statement that such trials are not feasible.
	58	Therefore, the VERTOS II study represents the highest quality of data regarding percutaneous vertebroplasty for symptomatic vertebral compression fractures. The strength of this study is the on-going positive benefit at the one year follow up period. In addition to long term pain relief, this study demonstrated very rapid pain relief. Short term pain outcome is vitally important in and of itself as patients with disabling acute pain are at significant risk of further complications and are not candidates for long term conservative therapy.	HTAS disagrees that VERTOS II is the highest quality data. This was an unblinded study, which any evidence-based text book would identify as a lower quality of evidence than a blinded trial.
	59	***Failed Conservative Treatment: What is the Threshold?*** In the treatment of an osteoporotic VCF, a common question that is confronted is how long should conservative medical management be employed before considering an interventional procedure? We would purport that assigning strict time limits to such a clinical decision would be problematic, and is best made on a case-by-case basis. The concept of a mandatory period of medical management prior to PVA did not originate within the medical literature. The first published reference regarding this appears to be within an FDA guidance document published in 2004, "Clinical Trial Considerations: Vertebral Augmentation Devices to Treat Spinal Insufficiency Fractures". The document states that trials should include "patients that (sic) have failed various, currently available conservative treatments, after a sufficient time period when fractures would be expected to heal, generally eight weeks, or more." This	Defining a period for conservative treatment is not needed for procedures that are not effective.

Stakeholder	#	Comment	Disposition
		document does not identify the author(s). The document has an expiration date of May 31, 2007, but has never been updated to our knowledge. Accordingly, it is imperative that the decision to treat a VCF patient with a procedure must be made based on the presentation of each patient. As Klazen and her co-authors have speculated on the appropriateness of a medical management time period, they have also noted that "waiting 6 months in all patients can cause unnecessary pain and lost days for work and normal activity, when treatment with vertebral augmentation can provide almost immediate pain relief."	
	60	Defining what constitutes failure of conservative medical therapy for patients with VCF must integrate the patient's pain level, their response to analgesics, and their functional status including the impact of the medical therapies employed. Pain is, of course, subjective and individual, so that a certain level on a scale such as the VAS would be inadequate. However, pain that prevents ambulation or physical therapy represents a rather simple and dependable measure of both "severe" pain and significant disability. In addition, prompt restoration of ambulatory status or return to best prior sub-ambulatory status is clinically important. Even in the absence of other pathology, prolonged bed rest of greater than 48 hours duration clearly represents a significant hazard to the patient. For patients who were non –ambulatory prior to their incident VCF, a significant reduction in prior physical functional status should be considered the equivalent of being rendered non-ambulatory.	Defining a period for conservative treatment is not needed for procedures that are not effective.
	61	***Summary:*** In sum, the two largest trials with the highest rates of patient enrollment and inclusion criteria generally viewed as being similar to typical "real world" patients have demonstrated benefits for vertebral augmentation persisting through one year post intervention. One of the smaller trials (Rousing et al) also demonstrated benefit from vertebral augmentation up to one month post intervention, but not beyond this point. The INVEST trial reported a very strong trend toward clinically meaningful improvement in pain for the vertebral augmentation group at one month. This finding narrowly missed achieving clinical significance despite the reduced number of patients enrolled vs. the original goal. Only the trial by Buchbinder et al failed to show that vertebral augmentation was beneficial at one month post intervention. A long-term (one year) benefit for vertebral augmentation was proven in the two largest trials; with total patient enrollment double that of the remaining three trials. Even if one were to accept the results from the INVEST and Buchbinder trials without question, a premise unacceptable to many physicians, the overall message remains clear. Therefore, after carefully weighing all of the available evidence, we must conclude that vertebral augmentation of osteoporotic VCF is very clearly beneficial in the short term and likely also in the long term, as well as being cost effective.	The two largest studies referred to by the commenter are unblinded, and of lower quality than the Kallmes and Buchbinder trials. HTAS disagrees that Buchbinder was the only trial to show lack of benefit at 1 month, since Kallmes found study groups did not differ significantly on ANY primary or secondary outcomes, including pain and QOL. It is not clear why unbiased physicians would have difficulty accepting the INVEST and Buchbinder trials, both published in the NEJM.
	62	Prolonged arbitrary time periods of medical management do not have a role in the current treatment of patients with VCF. It is clear from the available clinical data that early intervention for patients severely	HTAS disagrees that early intervention with VP produces better clinical outcomes, since

DRAFT

Stakeholder	#	Comment	Disposition
		affected by VCF produces better clinical outcomes and that this is also cost effective.	the available evidence does not support that conclusion.
	63	In sum, we would ask the HERC to carefully review all of the evidence, as well as to consider the professional opinions of physicians who are treating osteoporotic fracture patients every day. If denied access to spinal augmentation procedures, we believe that Oregonians would not have available to them a procedure that we believe should be part of a physician's treatment options. I thank the HERC for the opportunity present our views. If desired, several of our members in Oregon would be pleased to go into further details about our position.	Thank you for your comment. HTAS has reached a different conclusion after examining the available evidence. *For HTAS discussion*
Neurological Surgeon Portland, OR	64	The vertebroplasty/kyphoplasty topic is the most difficult of the three. The two randomized, controlled, blinded trials of vertebroplasty showed no advantage over sham surgery, but in fact, both groups were considerably better postoperatively. Therefore, some have interpreted the data not as showing that the procedure is ineffective, but showing that it works for reasons we do not understand. The Mayo Clinic is currently conducting further trials to try to determine why the sham surgery was so effective. There has also been much criticism of the methods of the studies. For example, the procedures were all done by radiologists, not spine surgeons, raising the question of whether the patients were properly screened for surgery, etc. Of course, criticizing and arguing against well done studies that show a result you do not want to see is sometimes inappropriate and must be viewed cautiously.	Thank you for this information, and for providing your perspective.
	65	My own practice is based on more than 8 years of experience with kyphoplasty. In over 100 procedures, I have found it to be about 80% effective in producing dramatic and rapid relief of pain. I have had a number of patients have 5 or more kyphoplasties over several years. I do not believe they would continue to undergo repeated procedures if the effect was not significant. Many patients have told me that they had to fail prolonged conservative management to get to their first kyphoplasty, so when they fractured another vertebra, they demanded immediate surgery without a waiting period, again indicating a strong belief in the effectiveness of the procedure. For patients hospitalized with unbearable pain, kyphoplasty has allowed mobilization and discharge, which must result in some cost savings over prolonged hospitalization or a nursing home. Many of these patients are in agony and without other effective treatment options.	Thank you for this information, and for providing your perspective.
	66	My own preference would be for the following: 1. Patients hospitalized because of unbearable pain from a new osteoporotic or malignant compression fracture and whose pain cannot be rapidly brought under control to the point of discharge to home should be allowed to have immediate kyphoplasty.	*For HTAS discussion*
	67	2. Patients with a new osteoporotic or malignant compression fracture who have failed 6-12 weeks of appropriate conservative management (pain medication, bracing, Miacalcin, TENS, PT, etc) with continuing need for potent narcotics, severe narcotic side effects (sedation, confusion, constipation, respiratory	*For HTAS discussion*

DRAFT

Stakeholder	#	Comment	Disposition
		suppression), and/or impaired mobility should be allowed to have an elective kyphoplasty. I realize that this is contrary to the draft recommendations, but I hope to allow some room for the procedure as some patients really do need more than medical management.	

DRAFT

Local Coverage Determination (LCD) for Vertebroplasty, Vertebral Augmentation; Percutaneous (L32032)

Contractor Information

Contractor Name	Contractor Number	Contractor Type
Noridian Administrative Services, LLC opens in new window	02301	MAC - Part A

Back to Top

LCD Information

Document Information

LCD ID Number
L32032

LCD Title
Vertebroplasty, Vertebral Augmentation; Percutaneous

Primary Geographic Jurisdiction opens in new window
Oregon

Contractor's Determination Number
A2011.01 R2

Oversight Region
Region X

AMA CPT/ADA CDT Copyright Statement
CPT only copyright 2002-2011 American Medical Association. All Rights Reserved. CPT is a registered trademark of the American Medical Association. Applicable FARS/DFARS Apply to Government Use. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. The Code on Dental Procedures and Nomenclature (Code) is published in Current Dental Terminology (CDT). Copyright © American Dental Association. All rights reserved. CDT and CDT-2010 are trademarks of the American Dental Association.

Original Determination Effective Date
For services performed on or after 09/06/2011

Original Determination Ending Date

Revision Effective Date
For services performed on or after 02/27/2012

Revision Ending Date

CMS National Coverage Policy

Title XVIII of the Social Security Act, Section 1862(a)(1)(A). This section allows coverage and payment for only those services that are considered to be reasonable and necessary.

Title XVIII of the Social Security Act, Section 1833(e). This section prohibits Medicare payment for any claim which lacks the necessary information to process the claim.

Indications and Limitations of Coverage and/or Medical Necessity

Medical record review has demonstrated widespread, fundamental errors in patient selection, technical performance of procedures, pre and post procedural assessment of patients and the common absence of follow-up of any kind – which initiated our coverage review and resulted in this LCD. Among our clinical concerns are the failure to attempt appropriate conservative management for a reasonable – or any - period of time; failure to inform patients of alternative treatments and potential complications of the injection procedures; treatment of an inappropriate number of levels; treatment during an active infection; treatment in the face of other unaddressed pain generators both spinal and in other body areas; treatment when other procedures are indicated or performed; failure to adequately follow patients for a reasonable period of time; and, a disturbing incidence of complications. These concerns resulted in an extensive literature review, consequent proposal to non-cover any vertebral augmentation procedure and, ultimately, resulted in this policy.

In the US, more than one quarter of the population age 50 years or older experience one vertebral fracture in their remaining lifetimes. Fractured vertebral bodies may produce intractable pain. Vertebral augmentation procedures are some of the invasive treatments that may be employed to address pain refractory to non-invasive therapeutic modalities. The percutaneous injection of medical cement or polymethylmethacrylate (PMM) into the vertebral body is believed to stabilize the fracture, and so reduce pain and improve activities of daily living.

Vertebral *compression fractures* due to osteoporosis represent significant morbidity to a large number of Medicare beneficiaries. It is estimated that perhaps 250,000 individuals out of some 700,000 who suffer from this condition annually fail to respond adequately to conservative, symptom-directed care. This population may represent candidates for vertebral stabilization procedures.

After an exhaustive analysis of the currently available literature and the comments of hundreds of providers on Vertebroplasty and Vertebral Augmentation procedures including kyphoplasty and with the assistance of representatives of eight specialty societies, NAS has determined that there is insufficient evidence on the surgical approaches to treatment of painful Vertebral Compression Fractures (VCFs) to differentiate among the procedures for purposes of this policy. No clear evidence demonstrates that one procedure is different from another in terms of short- or long-term efficacy, complications, mortality or any other parameter useful for differentiating coverage.

Percutaneous Vertebroplasty (PV):
First described in the literature in 1987 by two French neuroradiologists as a treatment for painful hemangiomas of the spine, Percutaneous Vertebroplasty, also known as PV or PVP, is a therapeutic, interventional radiologic procedure which consists of the injection of a material (usually polymethylmethacrylate) under imaging guidance (either fluoroscopy or CT) into a cervical, thoracic or lumbar vertebral body lesion for the relief of pain and the strengthening of bone.

Several days prior to Vertebroplasty, radiography and/or computed tomography (CT) or MRI, consistent with the physician's judgment and absent contraindications may be performed to assess the extent of vertebral collapse, the location and extent of the lytic or degenerative process, the visibility and degree of involvement of the pedicles, the presence of cortical destruction or fracture and the presence of epidural or foraminal stenosis caused by tumor extension or bone fragment retropulsion.

NAS requires that medical record documentation support that the procedure is conducted in accordance with the clinical and procedural criteria established in the literature produced in recent years.

The most important clinical information – **information that must be unequivocally documented in the medical record** – is that one or more vertebral compression fractures are present and that the patient’s pain is predominantly, if not solely, related to the demonstrated fracture(s). The fracture can be acceptably confirmed by plain film x-ray or by MRI, depending on the clinical circumstances. In situations where the patient’s history does not clearly document the age of the compression fracture, MRI may be useful if vertebral augmentation is considered.

Percutaneous Vertebral Augmentation:
This procedure is similar to Percutaneous Vertebroplasty in that stabilization of the collapsed vertebra is accomplished by the injection of methylmethacrylate cement into the body of the vertebra. The primary difference in the case of Vertebral Augmentation is that the fracture itself is at least partially reduced by expanding the intrabody space by the use of an appropriate, literature-supported, FDA-approved vertebral augmentation device. Once the compression is reduced to an acceptable degree, the bone cement is then injected. In this way, some of the bony deformity and resulting kyphosis may be reduced.

The FDA-labeled description of Percutaneous Vertebral Augmentation defines it as entailing a percutaneous approach, and NAS has valued it accordingly.

Indications and Limitations:

For Both Percutaneous Vertebroplasty and Percutaneous Vertebral Augmentation: One indication – painful compression fracture, regardless of etiology, described below.

- Clearly demonstrated vertebral compression fracture, with severe pain, refractory to conservative treatment and referable specifically to that site – non-specific documentation of “lower back pain” or similar language will not support payment.

- So long as the LCD-specified vertebral compression fracture is documented and so long as there is literature support for Vertebroplasty or Vertebral Augmentation for compression fractures caused by that condition, NAS will consider treatment eligible for payment if all LCD requirements are met.

- Assuming all of the below criteria are fulfilled, the **only** circumstance in which these procedures will be considered by NAS to be medically reasonable and necessary occurs when there is a painful compression fracture (e.g., pain level &gt 7 on VAS 1-10) which is refractory to non-invasive pain intervention(s) applied for reasonable time periods and only when interference with basic activities of daily life (ADLs) is present and documented, and then ***only*** *after a documented comprehensive pain evaluation and examination.*

- This comprehensive pain assessment and consequent pain management treatment plan must address all pain generators affecting the patient's painful state and physical function. The plan must begin with the least invasive approaches that address all or most of the pain generators. For example, a patient with multiple painful bony metastases and a compression fracture may be served best with an implantable pump for analgesia. On the other hand, a surgical stabilization procedure may be more appropriate in a patient with multiple compression fractures in the thoracic spine.

- Complete assessment of the patient by the provider (or provider group with interval assessment by the proceduralist) who performs the procedure is an **absolute requirement**. The History and Physical exam must be present in the medical record prior to performance of the procedure. Likewise, the record must contain a **detailed** operative procedure narrative report. A "boilerplate" or other non-specific "canned" report will not fulfill this requirement.

- The medical record must clearly document preoperatively that the patient is neurologically intact relative to the vertebral levels of proposed treatment. (See reference to this in the "Absolute Contraindications" section below.

- Critical clinical information – **information that must be unequivocally documented in the medical record** – is that one or more painful vertebral compression fractures are present and that the patient's pain is *predominantly*, if not solely, related to the demonstrated fracture(s). Any patient currently significantly symptomatic from other spinal pathology requires treatment prior to performance of vertebroplasty or vertebral augmentation procedures.

- The fracture can be acceptably confirmed by plain film x-ray or by MRI, depending on the clinical circumstances. In situations where the patient's history does not clearly document the age of the compression fracture, MRI may be useful if vertebral augmentation is considered.

- The medical record **must** document that appropriate imaging has been performed preoperatively and that the findings of the imaging performed correlate unequivocally with the patient's pain.

- NAS requires medical record documentation that the procedure is conducted in accordance with the clinical and procedural criteria established in the literature produced in recent years.

- Each and every such procedure must be performed with utilization of CT or fluoroscopic, **real-time** imaging guidance during the procedure, with retained images of final trocar placement as well as retained images of the vertebral body at the end of the procedure.

- Coverage for any procedure is limited to no more than three (3) vertebral levels on any date of service. Payable levels are only within the range of T5-L-5 (L4/L5, not L5/S1).

- Based on literature review and review of numerous claims for both Percutaneous Vertebroplasty and Percutaneous Vertebral Augmentation procedures, NAS will **NOT** allow payment for these procedures when performed immediately following acute compression fractures or diagnosis of them. No such procedures will be allowed payment when the procedure is performed in the Emergency Department or immediately following the beneficiary's presentation to the ED. Conservative management, even for a short period of time, includes *appropriate* dosage of *appropriate* analgesic medication for the patient's entire pain condition, not one component of it, such as compression fracture as noted above.

- NAS recognizes that prolonged delay of either treatment pending response to medical management may not be always in the patient's best interest. In those instances where the provider believes it to be medically reasonable and necessary to proceed to treatment within a brief time after the vertebral collapse has occurred, the provider **must** clearly and legibly document the rationale for this decision in the medical record. For example, adequate pain control impairs basic ADLs or is associated with respiratory compromise.

- The medical record **must** document that reasonable follow-up of the patient is arranged for by the operating provider for at least one year if operating provider is not anticipating personally providing this follow-up. The name and contact information of the following provider must be present in the patient's medical record.

- The medical record **must** contain evidence of follow-up assessment of the patient at one week, one month and three months postoperatively. Telephone follow-up with documentation of outcomes is acceptable. Alternatively, the three month follow-up may be waived if the medical record documents communication between the treating physician and the primary or referring physician, which includes discussion of patient's procedure, response, prognosis and necessary follow-up. The medical record **must** contain patient comfort/activity/pain scores for each of those follow-ups.

- **Neither Percutaneous Vertebroplasty nor Percutaneous Vertebral Augmentation is indicated for treatment of lesions of the sacrum or coccyx. NAS will not allow payment for any such treatment until and unless either becomes listed as a covered indication in FDA labeling AND literature supports and describes appropriate criteria for such use. The CPT Category III codes, 0200T and 0201T, are non-covered.**

Contraindications for both Percutaneous Vertebroplasty and Percutaneous Vertebral Augmentation:

Absolute Contraindications:

- Symptomatic foraminal stenosis or other spinal degenerative disease, or facet arthropathy, or other significant coexistent spinal or bony pain generators require treatment before an intervention. Following adequate address of all other pain generators, residual disabling pain localized to the compression fracture may allow payment for vertebroplasty or vertebral augmentation procedures.

- Bone fragment retropulsion.

- Absence of a confirmed fracture. The medical record must support that the fracture has been present no more than 4 months;

- Symptoms that cannot be related to a fracture;

- Neither Percutaneous Vertebroplasty nor Percutaneous vertebral Augmentation will be separately paid when combined with any open spine procedure;

- Unstable fracture or requirement for stabilization procedure in same or adjacent spinal region;

- Radicular symptoms without evidence of adequate pain management and address of the underlying pathology;

- Asymptomatic vertebral compression fracture;

- Active osteomyelitis whether fungal, bacterial or mycobacterial, or any other active infection, including urinary tract infection (UTI);

- Presence of painful metastases to areas other than the spine, spinal cord compression, primary bone and osteoblastic tumors, solitary plasmacytomas;

- Uncorrected coagulation disorders;

- Known allergy to any of the materials used in these procedures;

- Presence of any other condition described as a contraindication in the FDA labeling.

- The medical record does not indicate appropriate attempts at conservative medical management, including (either singly or in combination), bed rest, bracing, and local or systemic analgesics (e.g., narcotic and/or non-narcotic drugs) has been tried and failed, except as noted above.

- The service does not follow the guidelines of NAS; and/or

- Prophylactic treatment for osteoporosis of the spine or for chronic back pain of long-standing duration, even if associated with old compression fractures. Prophylactic procedures will be denied.

Provision and billing for the services of an assistant surgeon are not considered reasonable and necessary for either Percutaneous Vertebroplasty or Percutaneous Vertebral Augmentation and are not payable.

Bone biopsy done at the same level as Vertebral Augmentation is part of the primary procedure and will **not** be separately payable. This point is also noted in the current CPT description of codes 22523, 22524, 22525.

Though this policy refers only to "polymethylmethacrylate" and "methylmethacrylate," NAS will consider an otherwise-covered procedure to be payable when utilizing any other material FDA-approved for that purpose.

Preoperative diagnostic imaging studies are not the subject of this policy, but are the subjects of other NAS policies.

Payment for Vertebroplasty (procedure codes 22520, 22521, 22522) and Vertebral Augmentation (22523, 22524, 22525) are all-inclusive for the entire procedure (i.e., including injection, intraosseous venography, etc.). See CPT Coding Guidelines for instructions for billing and coding of fluoroscopic and CT guidance.

Absent clear medical record documentation to the contrary, these procedures are not performed on an inpatient basis and do not, in and of themselves, ever require inpatient admission.

All the requirements, restrictions and other provisions of this LCD apply to the vertebroplasty and vertebral augmentation procedures regardless of setting, inpatient (81.65 and 81.66) or outpatient.

Compliance with the provisions in this policy is subject to monitoring by post payment data analysis and subsequent medical review.

Coverage under the 2011 NAS Vertebroplasty, Vertebral Augmentation LCD will be maintained for a maximum of three years from its effective date under current literature support. NAS presumes and requires that during that time better outcomes data will be collected, analyzed and reported. If such data warrants expansion or narrowing of coverage of either or both of these surgical approaches, NAS will so modify this LCD at the end of that 3-year period. If such data is not forthcoming during that time so as to give rational literature support for these procedures, NAS anticipates at that time considering converting this LCD to one of **total** non-coverage of these procedures.

Back to Top

Coding Information

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

011x Hospital Inpatient (Including Medicare Part A)
012x Hospital Inpatient (Medicare Part B only)
013x Hospital Outpatient
022x Skilled Nursing - Inpatient (Medicare Part B only)
023x Skilled Nursing - Outpatient
071x Clinic - Rural Health
077x Clinic - Federally Qualified Health Center (FQHC)
085x Critical Access Hospital

Revenue Codes:

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory; unless specified in the policy services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

032X Radiology - Diagnostic - General Classification
033X Radiology - Therapeutic and/or Chemotherapy Administration - General Classification
036X Operating Room Services - General Classification
040X Other Imaging Services - General Classification
045X Emergency Room - General Classification
049X Ambulatory Surgical Care - General Classification
050X Outpatient Services - General Classification
051X Clinic - General Classification
076X Specialty Services - General Classification
096X Professional Fees - General Classification

CPT/HCPCS Codes
The following procedure codes may be covered when the appropriate two diagnoses codes (one from Group 1 and one from group 2) appear on the claim. All the requirements, restrictions and other provisions of this LCD apply to the vertebroplasty and vertebral augmentation procedures regardless of setting, inpatient (81.65 and 81.66) or outpatient.

22520 PERCUTANEOUS VERTEBROPLASTY (BONE BIOPSY INCLUDED WHEN PERFORMED), 1 VERTEBRAL BODY, UNILATERAL OR BILATERAL INJECTION; THORACIC
22521 PERCUTANEOUS VERTEBROPLASTY (BONE BIOPSY INCLUDED WHEN PERFORMED), 1 VERTEBRAL BODY, UNILATERAL OR BILATERAL INJECTION; LUMBAR
22522

	PERCUTANEOUS VERTEBROPLASTY (BONE BIOPSY INCLUDED WHEN PERFORMED), 1 VERTEBRAL BODY, UNILATERAL OR BILATERAL INJECTION; EACH ADDITIONAL THORACIC OR LUMBAR VERTEBRAL BODY (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
22523	PERCUTANEOUS VERTEBRAL AUGMENTATION, INCLUDING CAVITY CREATION (FRACTURE REDUCTION AND BONE BIOPSY INCLUDED WHEN PERFORMED) USING MECHANICAL DEVICE, 1 VERTEBRAL BODY, UNILATERAL OR BILATERAL CANNULATION (EG, KYPHOPLASTY); THORACIC
22524	PERCUTANEOUS VERTEBRAL AUGMENTATION, INCLUDING CAVITY CREATION (FRACTURE REDUCTION AND BONE BIOPSY INCLUDED WHEN PERFORMED) USING MECHANICAL DEVICE, 1 VERTEBRAL BODY, UNILATERAL OR BILATERAL CANNULATION (EG, KYPHOPLASTY); LUMBAR
22525	PERCUTANEOUS VERTEBRAL AUGMENTATION, INCLUDING CAVITY CREATION (FRACTURE REDUCTION AND BONE BIOPSY INCLUDED WHEN PERFORMED) USING MECHANICAL DEVICE, 1 VERTEBRAL BODY, UNILATERAL OR BILATERAL CANNULATION (EG, KYPHOPLASTY); EACH ADDITIONAL THORACIC OR LUMBAR VERTEBRAL BODY (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
72291	RADIOLOGICAL SUPERVISION AND INTERPRETATION, PERCUTANEOUS VERTEBROPLASTY, VERTEBRAL AUGMENTATION, OR SACRAL AUGMENTATION (SACROPLASTY), INCLUDING CAVITY CREATION, PER VERTEBRAL BODY OR SACRUM; UNDER FLUOROSCOPIC GUIDANCE
72292	RADIOLOGICAL SUPERVISION AND INTERPRETATION, PERCUTANEOUS VERTEBROPLASTY, VERTEBRAL AUGMENTATION, OR SACRAL AUGMENTATION (SACROPLASTY), INCLUDING CAVITY CREATION, PER VERTEBRAL BODY OR SACRUM; UNDER CT GUIDANCE

The following procedure codes are non-covered, regardless of diagnosis.

0200T	PERCUTANEOUS SACRAL AUGMENTATION (SACROPLASTY), UNILATERAL INJECTION(S), INCLUDING THE USE OF A BALLOON OR MECHANICAL DEVICE, WHEN USED, 1 OR MORE NEEDLES
0201T	PERCUTANEOUS SACRAL AUGMENTATION (SACROPLASTY), BILATERAL INJECTIONS, INCLUDING THE USE OF A BALLOON OR MECHANICAL DEVICE, WHEN USED, 2 OR MORE NEEDLES

ICD-9 Codes that Support Medical Necessity
Note: Diagnosis codes are based on the current ICD-9-CM codes that are effective at the time of LCD publication. Any updates to ICD-9-CM codes will be reviewed by NAS, and coverage should not be presumed until the results of such review have been published/posted.

Two codes are required to describe the medical necessity of the procedure: one for the compression fracture and one to indicate pain. These are the **only** covered ICD-9-CM codes that support medical necessity:

Group 1: Compression fracture

733.13	PATHOLOGICAL FRACTURE OF VERTEBRAE
805.2	CLOSED FRACTURE OF DORSAL (THORACIC) VERTEBRA WITHOUT SPINAL CORD INJURY
805.4	CLOSED FRACTURE OF LUMBAR VERTEBRA WITHOUT SPINAL CORD INJURY

Group 2: Pain, thoracic or lumbar spine:

724.1	PAIN IN THORACIC SPINE
724.2	LUMBAGO
724.5	BACKACHE UNSPECIFIED

Diagnoses that Support Medical Necessity
All ICD-9-CM codes listed in this policy under ICD-9-CM Codes that Support Medical Necessity above.
ICD-9 Codes that DO NOT Support Medical Necessity
All diagnoses **not** listed in this policy under ICD-9-CM Codes that Support Medical Necessity above.

ICD-9 Codes that DO NOT Support Medical Necessity Asterisk Explanation

Diagnoses that DO NOT Support Medical Necessity
All diagnoses **not** listed in this policy under ICD-9-CM Codes that Support Medical Necessity above
Back to Top

General Information

Documentations Requirements
All the documentation requirements described in the Indications section of this LCD must be met.

Documentation must validate the medical reasonableness and necessity of the procedure.

Documentation must be made available to NAS upon request. Lack of appropriate documentation will result in non-coverage of this procedure.

The HCPCS/CPT code(s) may be subject to Correct Coding Initiative (CCI) edits. This policy does not take precedence over CCI edits. Please refer to the CCI for correct coding guidelines and specific applicable code combinations prior to billing Medicare.

When the documentation does not meet the criteria for the service rendered or the documentation does not establish the medical necessity for the services, such services will be denied as not reasonable and necessary under Section 1862(a)(1) of the Social Security Act.

When requesting an *individual consideration* through the written redetermination (formerly appeal) process, providers must include all relevant medical records and literature that supports the request. At a minimum two (2) Phase II studies (human feasibility studies suggesting efficacy, pilots) or one (1) Phase III study (primary evidence of safety and efficacy, pivotal) must be submitted for the Medical Director's review.

Appendices

Utilization Guidelines

Sources of Information and Basis for Decision

Gray DT, Hollingworth W, Onwudiwe N, Jarvik JG. Costs and state-specific rates of thoracic and lumbar vertebroplasty, 2001-2005. *Spine (Phila Pa 1976) 2008;33*:1905-12.

Nussbaum DA, Gailloud P, Murphy K. A review of complications associated with vertebroplasty and kyphoplasty as reported to the Food and Drug Administration medical device related web site. *J Vasc Interv Radiol 2004;15*:1185-92.

Jensen ME, Evans AJ, Mathis JM, Kallmes DF, Cloft HJ, Dion JE. Percutaneous polymethylmethacrylate vertebroplasty in the treatment of osteoporotic vertebral body compression fractures: technical aspects. *AJNR Am J Neuroradiol 1997;18*:1897-904.

McDonald RJ, Gray LA, Cloft HJ, Thielen KR, Kallmes DF. The effect of operator variability and experience in vertebroplasty outcomes. *Radiology 2009;253*:478-85.

Baerlocher MO, Munk PL, Liu DM, et al. Clinical utility of vertebroplasty: need for better evidence. *Radiology 2010;255*:669-74.

Cooper C, Atkinson EJ, O'Fallon WM, Melton LJ, 3rd. Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985-1989. *J Bone Miner Res 1992;7*:221-7.

Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int 2006;17*:1726-33.

EPOS group. Incidence of vertebral fracture in Europe: results from the European Prospective Osteoporosis Study (EPOS). *J Bone Miner Res 2002;17*:716–24.

Ross PD. Clinical consequences of vertebral fractures. *Am J Med 1997;103*:30S-42S; discussion S-3S.

Ettinger B, Black DM, Nevitt MC, et al. Contribution of vertebral deformities to chronic back pain and disability. The Study of Osteoporotic Fractures Research Group. *J Bone Miner Res 1992;7*:449-56.

Silverman SL. The clinical consequences of vertebral compression fracture. *Bone 1992;13* Suppl 2:S27-31.

Lindsay R, Silverman SL, Cooper C, et al. Risk of new vertebral fracture in the year following a fracture. *Jama 2001;285*:320-3.

Black DM, Arden NK, Palermo L, Pearson J, Cummings SR. Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. Study of Osteoporotic Fractures Research Group. *J Bone Miner Res 1999;14*:821-8.

Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA, 3rd, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner Res 2000;15*:721-39.

Cauley JA, Thompson DE, Ensrud KC, Scott JC, Black D. Risk of mortality following clinical fractures. *Osteoporos Int 2000;11*:556-61.

Kado DM, Browner WS, Palermo L, Nevitt MC, Genant HK, Cummings SR. Vertebral fractures and mortality in older women: a prospective study. Study of Osteoporotic Fractures Research Group. *Arch Intern Med 1999;159*:1215-20.

Lieberman IH, Dudeney S, Reinhardt MK, Bell G. Initial outcome and efficacy of "kyphoplasty" in the treatment of painful osteoporotic vertebral compression fractures. *Spine (Phila Pa 1976) 2001;26*:1631-8. WA HTA: Vertebroplasty, Kyphoplasty and Sacroplasty Final Report (1142010) Page 119 of 126 WA Health Technology Assessment – HTA

Leroux JL, Denat B, Thomas E, Blotman F, Bonnel F. Sacral insufficiency fractures presenting as acute low-back pain. Biomechanical aspects. *Spine (Phila Pa 1976) 1993;18*:2502-6.

Smith DK, Dix JE. Percutaneous sacroplasty: long-axis injection technique. *AJR Am J Roentgenol 2006;186*:1252-5.

Binaghi S, Guntern D, Schnyder P, Theumann N. A new, easy, fast, and safe method for CT-guided sacroplasty. *Eur Radiol 2006;16*:2875-8.

Brook AL, Mirsky DM, Bello JA. Computerized tomography guided sacroplasty: a practical treatment for sacral insufficiency fracture: case report. *Spine (Phila Pa 1976) 2005;30*:E450-4.

Lin JT, Lane JM. Sacral stress fractures. *J Womens Health (Larchmt) 2003;12*:879-88.

Bayley E, Srinivas S, Boszczyk BM. Clinical outcomes of sacroplasty in sacral insufficiency fractures: a review of the literature. Eur Spine J 2009;18:1266-71.

Weber M, Hasler P, Gerber H. Insufficiency fractures of the sacrum. Twenty cases and review of the literature. *Spine (Phila Pa 1976) 1993;18*:2507-12.

Babayev M, Lachmann E, Nagler W. The controversy surrounding sacral insufficiency fractures: to ambulate or not to ambulate? *Am J Phys Med Rehabil 2000;79*:404-9.

Lin J, Lachmann E, Nagler W. Sacral insufficiency fractures: a report of two cases and a review of the literature. *J Womens Health Gend Based Med 2001;10*:699-705.

Costa L, Badia X, Chow E, Lipton A, Wardley A. Impact of skeletal complications on patients' quality of life, mobility, and functional independence. *Support Care Cancer 2008;16*:879-89.

Fourney DR, Schomer DF, Nader R, et al. Percutaneous vertebroplasty and kyphoplasty for painful vertebral body fractures in cancer patients. *J Neurosurg 2003;98*:21-30.

Galibert P, Deramond H, Rosat P, Le Gars D. [Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty]. *Neurochirurgie 1987;33*:166-8.

Amar AP, Larsen DW, Esnaashari N, Albuquerque FC, Lavine SD, Teitelbaum GP. Percutaneous transpedicular polymethylmethacrylate vertebroplasty for the treatment of spinal compression fractures. *Neurosurgery 2001;49*:1105-14; discussion 14-5.

Mark D. Percutaneous Vertebroplasty or Kyphoplasty for Vertebral Fractures Caused by Osteoporosis or Malignancy. In: BCBS Tec Assessment Program, ed.; 2008:1-38.

Martin JB, Wetzel SG, Seium Y, et al. Percutaneous vertebroplasty in metastatic disease: transpedicular access and treatment of lysed pedicles initial experience. *Radiology 2003;229*:593-7.

Kim AK, Jensen ME, Dion JE, Schweickert PA, Kaufmann TJ, Kallmes DF. Unilateral transpedicular percutaneous vertebroplasty: initial experience. *Radiology 2002;222*:737-41.

Bouza C, Lopez T, Magro A, Navalpotro L, Amate JM. Efficacy and safety of balloon kyphoplasty in the treatment of vertebral compression fractures: a systematic review. *Eur Spine J 2006;15*:1050-67.

Garfin SR, Yuan HA, Reiley MA. New technologies in spine: kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures. *Spine (Phila Pa 1976) 2001;26*:1511-5.

Lee MJ, Dumonski M, Cahill P, Stanley T, Park D, Singh K. Percutaneous treatment of vertebral compression fractures: a meta-analysis of complications. *Spine (Phila Pa 1976)2009;34*:1228-32. WA HTA: Vertebroplasty, Kyphoplasty and Sacroplasty Final Report (1142010) Page 120 of 126 WA Health Technology Assessment – HTA

Lieberman IH, Phillips FM, Togawa D, et al. Vertebral augmentation and the limits of interpreting complications reported in the food and drug administration manufacturer and user facility device experience database. *J Vasc Interv Radiol 2004;15*:1193-6.

Dehdashti AR, Martin JB, Jean B, Rufenacht DA. PMMA cementoplasty in symptomatic metastatic lesions of the S1 vertebral body. *Cardiovasc Intervent Radiol 2000;23*:235-7.

Garant M. Sacroplasty: a new treatment for sacral insufficiency fracture. *J Vasc Interv Radiol 2002;13*:1265-7.

Krueger A, Bliemel C, Zettl R, Ruchholtz S. Management of pulmonary cement embolism after percutaneous vertebroplasty and kyphoplasty: a systematic review of the literature. *Eur Spine J 2009;18*:1257-65.

Lee IJ, Choi AL, Yie MY, et al. CT evaluation of local leakage of bone cement after percutaneous kyphoplasty and vertebroplasty. *Acta Radiol 2010;51*:649-54.

Bohner M, Gasser B, Baroud G, Heini P. Theoretical and experimental model to describe the injection of a polymethylmethacrylate cement into a porous structure. *Biomaterials 2003;24*:2721-30.

Padovani B, Kasriel O, Brunner P, Peretti-Viton P. Pulmonary embolism caused by acrylic cement: a rare complication of percutaneous vertebroplasty. *AJNR Am J Neuroradiol 1999;20*:375-7.

Laredo JD, Hamze B. Complications of percutaneous vertebroplasty and their prevention. *Skeletal Radiol 2004;33*:493-505.

Freitag M, Gottschalk A, Schuster M, Wenk W, Wiesner L, Standl TG. Pulmonary embolism caused by polymethylmethacrylate during percutaneous vertebroplasty in orthopaedic surgery. *Acta Anaesthesiol Scand 2006;50*:248-51.

Jang JS, Lee SH, Jung SK. Pulmonary embolism of polymethylmethacrylate after percutaneous vertebroplasty: a report of three cases. *Spine (Phila Pa 1976) 2002;27*:E416-8.

Tozzi P, Abdelmoumene Y, Corno AF, Gersbach PA, Hoogewoud HM, von Segesser LK. Management of pulmonary embolism during acrylic vertebroplasty. *Ann Thorac Surg 2002;74*:1706-8.

Tanigawa N, Komemushi A, Kariya S, et al. Relationship between cement distribution pattern and new compression fracture after percutaneous vertebroplasty. *AJR Am J Roentgenol 2007;189*:W348-52.

Fribourg D, Tang C, Sra P, Delamarter R, Bae H. Incidence of subsequent vertebral fracture after kyphoplasty. *Spine (Phila Pa 1976)2004;29*:2270-6; discussion 7.

Mary E. Jensen M, J. Kevin McGraw, John F. Cardella, Joshua A. Hirsch. Position Statement on Percutaneous Vertebral Augmentation: A Consensus Statement Developed by the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology, American Association of Neurological Surgeons/Congress of Neurological Surgeons, and American Society of Spine Radiology. *Journal of Vascular and Interventional Radiology July 2009;(Vol.20, Issue 7, Supplement,* pages S326-S331).

Uhthoff HK, Jaworski ZF. Bone loss in response to long-term immobilisation. *J Bone Joint Surg Br 1978;60-B*:420-9.

Convertino VA, Bloomfield SA, Greenleaf JE. An overview of the issues: physiological effects of bed rest and restricted physical activity. *Med Sci Sports Exerc 1997;29*:187-90.

Taillandier J, Langue F, Alemanni M, Taillandier-Heriche E. Mortality and functional outcomes of pelvic insufficiency fractures in older patients. *Joint Bone Spine 2003;70*:287-9. WA HTA: Vertebroplasty, Kyphoplasty and Sacroplasty Final Report (1142010) Page 121 of 126 WA Health Technology Assessment – HTA

Masala S, Ciarrapico AM, Konda D, Vinicola V, Mammucari M, Simonetti G. Costeffectiveness of percutaneous vertebroplasty in osteoporotic vertebral fractures. *Eur Spine J 2008;17*:1242-50.

Cahill KS, Chi JH, Day A, Claus EB. Prevalence, complications, and hospital charges associated with use of bone-morphogenetic proteins in spinal fusion procedures. *JAMA 2009;302*:58-66.

Institute for Clinical Systems Improvement (ICSI). Assessment and Management of Chronic Pain. In. Bloomington, MN: *National Guideline Clearinghouse (NGC); 2008*:84.

National Collaborating Centre for Cancer. Metastatic Spinal Cord Compression. Diagnosis and Management of Adults at Risk of and with Metastatic Spinal Cord Compression. In: *(NICE)NIfHaCE, ed.; 2008*:39.

Interventional Procedures Programme. Interventional Procedure Guidance (IPG) for Vertebroplasty and Balloon Kyphoplasty. In: *National Institute for Health and Clinical Excellence; 2007*.

California Technology Assessment Forum (CTAF). Vertebroplasty as a Treatment for Osteoporotic Compression Fractures. In; 2010:1-16.

Belinson S. Percutaneous Vertebroplasty or Kyphoplasty for Vertebral Fractures Caused by Osteoporosis: Kaiser Foundation Health Plan and Southern California Permanente Group; 2010 April, 2010.

Kallmes DF, Comstock BA, Heagerty PJ, et al. A randomized trial of vertebroplasty for osteoporotic spinal fractures. *N Engl J Med 2009 Aug 6; 361(6)*:569-79.

Klazen CA, Lohle PN, de Vries J, et al. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. *Lancet. 2010 Sep 25;376(9746)*:1085-92. Epub 2010 Aug 9.

Venmans A, Klazen CA, Lohle PN, et al. Percutaneous Vertebroplasty and Pulmonary Cement Embolism: Results from VERTOS II. *AJNR Am J Neuroradiol.*

Venmans A, Klazen CA, van Rooij WJ, de Vries J, Mali WP, Lohle PN. Postprocedural CT for perivertebral cement leakage in percutaneous vertebroplasty is not necessary-results from VERTOS II. *Neuroradiology 2010*.

Klazen CA, Venmans A, de Vries J, et al. Percutaneous Vertebroplasty Is Not a Risk Factor for New Osteoporotic Compression Fractures: Results from VERTOS II. *AJNR Am J Neuroradiol.*

Oxford Centre for Evidence-based Medicine Levels of Evidence. 2009. (Accessed 9/27/10, at http://www.cebm.net/?o=1025.)

Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *BMJ 2004;328*:1490.

West S, King V, Carey TS, et al. Systems to Rate the Strength Of Scientific Evidence. Rockville, MD: Agency for Healthcare Research and Quality; 2002.

Bouza C, Lopez-Cuadrado T, Cediel P, Saz-Parkinson Z, Amate JM. Balloon kyphoplasty in malignant spinal fractures: a systematic review and meta-analysis. *BMC Palliat Care 2009;8*:12.

Eck JC, Nachtigall D, Humphreys SC, Hodges SD. Comparison of vertebroplasty and balloon kyphoplasty for treatment of vertebral compression fractures: a meta-analysis of the literature. *Spine J 2008;8*:488-97.

Mendel E, Bourekas E, Gerszten P, Golan JD. Percutaneous techniques in the treatment of spine tumors: what are the diagnostic and therapeutic indications and outcomes? *Spine (Phila Pa 1976) 2009;34*:S93-100. WA HTA: Vertebroplasty, Kyphoplasty and Sacroplasty Final Report (1142010) Page 122 of 126 WA Health Technology Assessment – HTA

Taylor RS, Fritzell P, Taylor RJ. Balloon kyphoplasty in the management of vertebral compression fractures: an updated systematic review and meta-analysis. *Eur Spine J 2007;16*:1085-100.

Mudano AS, Bian J, Cope JU, et al. Vertebroplasty and kyphoplasty are associated with an increased risk of secondary vertebral compression fractures: a population-based cohort study. *Osteoporos Int 2009;20*:819-26.

Zampini JM, White AP, McGuire KJ. Comparison of 5766 Vertebral Compression Fractures Treated With or Without Kyphoplasty. *Clin Orthop Relat Res 2010.*

Lange LL, Jacox A. Using large data bases in nursing and health policy research. *J Prof Nurs 1993;9*:204.

Baron JA, Weiderpass E. An introduction to epidemiological research with medical databases. *Ann Epidemiol 2000;10*:200-4.

Connell FA, Diehr P, Hart LG. The use of large data bases in health care studies. *Annu Rev Public Health 1987;8*:51-74.

Flood AB. Peaks and pits of using large data bases to measure quality of care. *Int J Technol Assess Health Care 1990;6*:253-62.

Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med 2009;361*:557-68.

Hrobjartsson A, Gotzsche PC. Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment. *N Engl J Med 2001;344*:1594-602.

Hrobjartsson A, Gotzsche PC. Is the placebo powerless? Update of a systematic review with 52 new randomized trials comparing placebo with no treatment. *J Intern Med 2004;256*:91-100.

Vase L, Riley JL, 3rd, Price DD. A comparison of placebo effects in clinical analgesic trials versus studies of placebo analgesia. *Pain 2002;99*:443-52.

Jarvik JG, Deyo RA. Cementing the evidence: time for a randomized trial of vertebroplasty. *AJNR Am J Neuroradiol 2000;21*:1373-4.

Kallmes DF, Comstock BA, Gray LA, et al. Baseline pain and disability in the Investigational Vertebroplasty Efficacy and Safety Trial. *AJNR Am J Neuroradiol 2009;30*:1203-5.

Grotle M, Brox JI, Vollestad NK. Concurrent comparison of responsiveness in pain and functional status measurements used for patients with low back pain. *Spine (Phila Pa 1976) 2004;29*:E492-501.

Rousing R, Hansen KL, Andersen MO, Jespersen SM, Thomsen K, Lauritsen JM. Twelvemonths follow-up in forty-nine patients with acute/semiacute osteoporotic vertebral fractures treated conservatively or with percutaneous vertebroplasty: a clinical randomized study. *Spine (Phila Pa 1976) 2010;35*:478-82.

Voormolen MH, Mali WP, Lohle PN, et al. Percutaneous vertebroplasty compared with optimal pain medication treatment: short-term clinical outcome of patients with subacute or chronic painful osteoporotic vertebral compression fractures. The VERTOS study. *AJNR Am J Neuroradiol 2007;28*:555-60.

Wardlaw D, Cummings SR, Van Meirhaeghe J, et al. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. *Lancet 2009 Mar 21;373(9668)*:1016-24.

Mathis JM, Ortiz AO, Zoarski GH. Vertebroplasty versus kyphoplasty: a comparison and contrast. *AJNR Am J Neuroradiol 2004;25*:840-5. WA HTA: Vertebroplasty, Kyphoplasty and Sacroplasty Final Report (1142010) Page 123 of 126 WA Health Technology Assessment – HTA

Liu JT, Liao WJ, Tan WC, et al. Balloon kyphoplasty versus vertebroplasty for treatment of osteoporotic vertebral compression fracture: a prospective, comparative, and randomized clinical study. *Osteoporos Int 2010;21*:359-64.

Alvarez L, Alcaraz M, Perez-Higueras A, et al. Percutaneous vertebroplasty: functional improvement in patients with osteoporotic compression fractures. *Spine (Phila Pa 1976) 2006;31*:1113-8.

Diamond TH, Bryant C, Browne L, Clark WA. Clinical outcomes after acute osteoporotic vertebral fractures: a 2-year non-randomised trial comparing percutaneous vertebroplasty with conservative therapy. *Med J Aust 2006;184*:113-7.

Ehteshami Rad A, Gray LA, Kallmes DF. Incident Vertebral Fractures in Patients not Undergoing Vertebroplasty.*J Vasc Interv Radiol 2010.*

Nakano M, Hirano N, Ishihara H, Kawaguchi Y, Watanabe H, Matsuura K. Calcium phosphate cement-based vertebroplasty compared with conservative treatment for osteoporotic compression fractures: a matched case-control study. *J Neurosurg Spine 2006;4*:110-7.

Kasperk C, Grafe IA, Schmitt S, et al. Three-year outcomes after kyphoplasty in patients with osteoporosis with painful vertebral fractures. *J Vasc Interv Radiol 2010 May;21(5)*:701-9.

An KC, Kang S, Choi JS, Seo JH. The clinical and radiological availability of percutaneous balloon kyphoplasty as a treatment for osteoporotic burst fractures. *Asian Spine J 2008;2*:9-14.

Ming JH, Zhou JL, Zhou PH, Zhou JP. Comparison of therapeutic effect between percutaneous kyphoplasty and pedicle screw system on vertebral compression fracture. *Chin J Traumatol 2007;10*:40-3.

De Negri P, Tirri T, Paternoster G, Modano P. Treatment of painful osteoporotic or traumatic vertebral compression fractures by percutaneous vertebral augmentation procedures: a nonrandomized comparison between vertebroplasty and kyphoplasty. *Clin J Pain 2007;23*:425-30.

Grohs JG, Matzner M, Trieb K, Krepler P. Minimal invasive stabilization of osteoporotic vertebral fractures: a prospective nonrandomized comparison of vertebroplasty and balloon kyphoplasty. *J Spinal Disord Tech 2005;18*:238-42.

Lovi A, Teli M, Ortolina A, Costa F, Fornari M, Brayda-Bruno M. Vertebroplasty and kyphoplasty: complementary techniques for the treatment of painful osteoporotic vertebral compression fractures. A prospective non-randomised study on 154 patients. *Eur Spine J 2009;18 Suppl 1*:95-101.

Röllinghoff M, Siewe J, Zarghooni K, et al. Effectiveness, security and height restoration on fresh compression fractures a comparative prospective study of vertebroplasty and kyphoplasty. *Minim Invasive Neurosurg 2009;52*:233-7.

Santiago FR, Abela AP, Alvarez LG, Osuna RM, Garcia MD. Pain and functional outcome after vertebroplasty and kyphoplasty. A comparative study. *Eur J Radiol 2010.*

Schofer MD, Efe T, Timmesfeld N, Kortmann HR, Quante M. Comparison of kyphoplasty and vertebroplasty in the treatment of fresh vertebral compression fractures. *Arch Orthop Trauma Surg 2009;129*:1391-9.

Frankel BM, Monroe T, Wang C. Percutaneous vertebral augmentation: an elevation in adjacent-level fracture risk in kyphoplasty as compared with vertebroplasty. *Spine J 2007;7*:575-82.

Hiwatashi A, Westesson PL, Yoshiura T, et al. Kyphoplasty and vertebroplasty produce the same degree of height restoration. *AJNR Am J Neuroradiol 2009;30*:669-73. WA HTA: Vertebroplasty, Kyphoplasty and Sacroplasty Final Report (1142010) Page 124 of 126 WA Health Technology Assessment – HTA

Köse KC, Cebesoy O, Akan B, Altinel L, Dincer D, Yazar T. Functional results of vertebral augmentation techniques in pathological vertebral fractures of myelomatous patients. *J Natl Med Assoc 2006;98*:1654-8.

Zhou JL, Liu SQ, Ming JH, Peng H, Qiu B. Comparison of therapeutic effect between percutaneous vertebroplasty and kyphoplasty on vertebral compression fracture. *Chin J Traumatol 2008;11*:42-4.

Chapman JR, Hanson BP, Dettori JR, Norvell DC. Spine outcomes measures and instruments. Dübendorf, Switzerland: *AOSpine International; 2007.*

Hawthorne G, Osborne R. Population norms and meaningful differences for the Assessment of Quality of Life (AQoL) measure. *Aust N Z J Public Health 2005;29*:136-42.

O'Neill TW, Cooper C, Cannata JB, et al. Reproducibility of a questionnaire on risk factors for osteoporosis in a multicentre prevalence survey: the European Vertebral Osteoporosis Study. *Int J Epidemiol 1994;23*:559-65.

Million R, Hall W, Nilsen KH, Baker RD, Jayson MI. Assessment of the progress of the back-pain patient 1981 Volvo Award in Clinical Science. *Spine (Phila Pa 1976) 1982;7*:204-12.

Patrick DL, Deyo RA, Atlas SJ, Singer DE, Chapin A, Keller RB. Assessing health-related quality of life in patients with sciatica. *Spine (Phila Pa 1976) 1995;20*:1899-908; discussion 909.

Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain 2008;9*:105-21.

Ostelo RW, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine (Phila Pa 1976) 2008;33*:90-4.

Strub WM, Hoffmann M, Ernst RJ, Bulas RV. Sacroplasty by CT and fluoroscopic guidance: is the procedure right for your patient? *AJNR Am J Neuroradiol 2007;28*:38-41.

Frey ME, Depalma MJ, Cifu DX, Bhagia SM, Carne W, Daitch JS. Percutaneous sacroplasty for osteoporotic sacral insufficiency fractures: a prospective, multicenter, observational pilot study. *Spine J 2008;8*:367-73.

Anselmetti GC, Manca A, Ortega C, Grignani G, Debernardi F, Regge D. Treatment of extraspinal painful bone metastases with percutaneous cementoplasty: a prospective study of 50 patients. *Cardiovasc Intervent Radiol 2008;31*:1165-73.

Basile A, Tsetis D, Cavalli M, et al. Sacroplasty for Local or Massive Localization of Multiple Myeloma. *Cardiovasc Intervent Radiol 2009*.

Georgy BA. Interventional techniques in managing persistent pain after vertebral augmentation procedures: a retrospective evaluation. *Pain Physician 2007;10*:673-6.

Whitlow CT, Mussat-Whitlow BJ, Mattern CW, Baker MD, Morris PP. Sacroplasty versus vertebroplasty: comparable clinical outcomes for the treatment of fracture-related pain. *AJNR Am J Neuroradiol 2007;28*:1266-70.

Butler CL, Given CA, 2nd, Michel SJ, Tibbs PA. Percutaneous sacroplasty for the treatment of sacral insufficiency fractures. *AJR Am J Roentgenol 2005;184*:1956-9.

Kamel EM, Binaghi S, Guntern D, Mouhsine E, Schnyder P, Theumann N. Outcome of long-axis percutaneous sacroplasty for the treatment of sacral insufficiency fractures. *Eur Radiol 2009 Dec; 19(12)* :3002-7.

Kang SE, Lee JW, Kim JH, Park KW, Yeom JS, Kang HS. Percutaneous sacroplasty with the use of C-arm flat-panel detector CT: technical feasibility and clinical outcome. *Skeletal Radiol 2010.* WA HTA: Vertebroplasty, Kyphoplasty and Sacroplasty Final Report (1142010) Page 125 of 126 WA Health Technology Assessment – HTA

Fourney DR. Vertebroplasty versus kyphoplasty in the cancer setting: rethinking the relative indications. *Support Cancer Ther 2005 Oct 1;3(1)*:26-7.

Bono CM, Heggeness M, Mick C, Resnick D, Watters IWC. North American Spine Society. Newly released vertebroplasty randomized controlled trials: a tale of two trials. *Spine J. Mar;10(3)*:238-40.

Ström O, Leonard C, Marsh D, Cooper C. Cost-effectiveness of balloon kyphoplasty in patients with symptomatic vertebral compression fractures in a UK setting. *Osteoporos Int 2010 Sep;21(9)*:1599-608.Epub 2009 Nov 19.

Garfin SR, Yuan HA, Reiley MA. New technologies in spine: kyphoplasty and Vertebroplasty for the treatment of painful osteoporotic compression fractures. *Spine 2001; 26(14)*:1511-5.

Martin JB, Jean B, Sugiu K, et al. Vertebroplasty: clinical experience and follow-up results. *Bone 1999 Aug; 25(2 suppl)*:11S-15S.

Ratliff J, Nguyen T, Heiss J, Root and spinal cord compression from methylmethacrylate Vertebroplasty. *Spine 2001; 26(13)*:E300-2.

Watts NB, Harris ST, Genant HK. Treatment of painful osteoporotic vertebral fractures with percutaneous Vertebroplasty or kyphoplasty. *Osteoporosis Int. 2001; 12(6)*:429-37.

Cortet B, Cotton A, Boutry N, et al. Percutaneous Vertebroplasty in the Treatment of Osteoporotic Vertebral Compression Fractures: An Open Prospective Study. *J Rheumatol. 1999 Oct; 26(1)*:2222-8.

Hardouin P, Grados F, Cotton A, et al. Should percutaneous Vertebroplasty be used to treat osteoporotic fractures? An update. *Joint Bone Spine 2001 May; 68(3)*:216.21.

Grados F, Depriester C, Cayrolle G, et al. Long-term observations of vertebral osteoporotic fractures treated by percutaneous Vertebroplasty. *Rheumatology 2000; Dec;39(12)*:1410-14.

Hardouin P, Fayada P, Leclet H, et al. Kyphoplasty. *Joint Bone Spine 2002 May; 69(3)*:256-61.

Lieberman IH, Dudeney S, Reinhardt MK, et al. Initial outcome and efficacy of kyphoplasty in the treatment of painful osteoporotic vertebral compression fractures. *Spine 2001; 26(14)*:1631-7.

Gold Deborah J, PhD, Silverman Stuart L, MD, FACP, FACR, "The Downward Spiral of Vertebral Osteoporosis: Consequences" Monograph, Remedica Communications, Inc., June 2003, Sponsored by Cedars-Sinai Medical Center, Los Angeles, CA.

Standard for the Performance of Percutaneous Vertebroplasty. American College of Radiology. Reston, Virginia. January 2001.

Jones JO, Bruel BM, Vattam SR, Management of painful vertebral hemangiomas with kyphoplasty; a report of two cases and a literative review. *Pain Physician. 2009 July-Aug;12(4)*: E297-303.

The role of vertebral augmentation in myeloma: International Myeloma Working Group Consensus Statement. MA Hussen *et al*, Leukemia, Volume 22, Number 8, August 2008.

Management of osteoporosis in postmenopausal women: 2010 position statement of the North American Menopause Society. *Menopause 2010 Jan-Feb;17(1)*:25-54; quiz 5-6.

Berenson JR, Pflugmacher R, Jarzem P, Zonder JA, Tillman JB, Ashraf T, et al. Final results of the first randomized trial comparing balloon kyphoplasty (BKP) to non-surgical management among cancer patients with vertebral compression fractures: marked improvement in back function, quality of life and pain in the BKP arm. *Blood 2009;114*:2873.

Pflugmacher R, Taylor R, Agarwal A, Melcher I, Disch A, Haas NP, et al. Balloon kyphoplasty in the treatment of metastatic disease of the spine: a 2-year prospective evaluation. *Eur Spine J 2008 Aug;17(8)*:1042-8.

Langdon J, Way A, Heaton S, Bernard J, Molloy S. Vertebral compression fractures—new clinical signs to aid diagnosis. *Ann R Coll Surg Engl 2010 Mar;92(2)*:163-6.

Oh GS, Kim HS, Ju CI, Kim SW, Lee SM, Shin H. Comparison of the results of balloon kyphoplasty performed at different times after injury. *J Korean Neurosurg Soc 2010 Mar;47(3)L*:199-202.

AAOS. The treatment of symptomatic osteoporotic spinal compression fractures: guideline and evidence report Sept. 24, 2010.
http://www.aaos.org/Research/guidelines/SCFguideline.pdf

Martin G. Radvany, MD, Kieran J. Murphy, MD FRCPC, Steven F. Millward, MD, et al. Research Reporting Standards for Percutaneous Vertebral Augmentation. *J Vasc Interv Radiol 2009; 20*:1279-1286.

Avram Allan Edidin, PhD; Kevin L. Ong, PhD; Edmund Lau, MS; Steven M. Kurtz, PhD Mortality Risk for Operated and Non-Operated Vertebral Fracture Patients in the Medicare Population. *JBMR(J Bone Miner Res. 2011 Feb 9. Doi: 10.1002/jbmr.353)*.

James Berenson, MD, Robert Pflugmacher, MD, Peter Jarzem, MD, Jeffrey Zonder, MD, Kenneth Schechtman, PhD, John B Tillman, PhD, Prof Leonard Bastian, MD, Talat Ashraf, MD, Prof Frank Vrionis, MD, for the Cancer Patient Fracture Evaluation (CAFÉ) Investigators. Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomized controlled trail. The Lancet Oncology, Volume 12, Issue 3, Pages 225-235, March 2011. Doi:10.1016/S1470-2045(11)70008-0.

Other Contractors' medical policies Advisory Committee Meeting Notes Advisory committee notes
This LCD was discussed at the Open Door Coverage Meetings held on February 17, 2011 and July 7, 2011.

This policy does not reflect the sole opinion of the contractor or Contractor Medical Director(s). Although the final decision rests with the contractor, this policy was developed in cooperation with the Carrier Advisory Committee(s) which include representatives from various interested medical specialty societies-the Part A Pain workgroup, and with significant input from eight specialty societies whose members have expertise in the management of back pain and/or in the use of the procedures addressed in this LCD.

The Section titled "Does the 'CPT 30% Rule' Apply?" needs clarification. This rule comes from the AMA (American Medical Association), the organization that holds the copyrights for all CPT codes. The rule states that if, in a given section (e.g., **surgery**) or subsection (e.g., surgery, **integumentary**) of the CPT Manual, more than 30% of the codes are listed in the LCD, then the short descriptors must be used rather than the long descriptors found in the CPT Manual.

This policy is subject to the reasonable and necessary guidelines and the limitation of liability provision.

Response to Provider Recommendations:

Comment: Several individuals and some specialty societies commented that the LCD was well-thought out and comprehensive.

Response: We appreciate the support and, in turn, thank the many practitioners and Specialty Societies that actively participated in the development of the LCD. The assistance is invaluable. Also, the comments and suggestions discussed below were excellent and helpful in refining this LCD. Thank you.

Comment: Many commenters stated that studies of these procedures are invalid, flawed and should not be taken into account. Further, some commenters believe that Specialty Society Guidelines are similarly flawed.

Response: We agree the literature is inconclusive, at best, and that Specialty Societies differ in their understanding of the utility of the procedures.

Comment: One commenter requested that we cover these procedures for any painful spinal compression fracture without regard to other factors including spinal instability, bone fragment retropulsion into the spinal canal, duration of fracture. The commenter contended that the evidence supports the position.

Response: The evidence is insufficient to support performance of the vertebral augmentation procedures in any population of patients. The LCD restricts coverage to the populations of patients least likely to be harmed form the procedures, most likely to benefit from the procedures, and most likely to produce outcomes favorable to coverage of the procedures in the future. Continued coverage depends on positive findings following re-analysis of both the peer-reviewed medical literature and outcomes three years after finalization of this LCD. With this in mind, the LCD requires physicians to document patient outcomes.

Comment: Two commenters recommended elimination of the requirement for a comprehensive pain evaluation since the vertebral augmentation procedures are needed to correct the vertebral compression fracture (VCF) itself.

Response: "Correction of compression fractures" (which may occur with some vertebral augmentation procedures) has not been demonstrated to affect patient outcomes and, in fact, appears to persist only in the short-term. Neither vertebroplasty nor the vertebral augmentation procedures prevent future fractures. On the contrary, there is concern that these procedures may contribute to the risk of future fractures.

Comment: Some commenters objected to requirement for a comprehensive pain evaluation prior to performance of procedures.

Response: Vertebroplasty and vertebral augmentation procedures are covered for the *treatment of pain,* which is both refractory to non-invasive therapies and significantly interfering with the activities of daily (ADLs) living, such that the patient requires assistance to perform an activity of daily living solely due to that pain. Comprehensive pain evaluation must occur prior to undertaking an interventional procedure in order to properly evaluate the potential for non-invasive treatments and/or more comprehensive treatments that relieve pain from all pain generators (e.g., facet and disc disease, multiple bony metastases).

Vertebroplasty and vertebral augmentation procedures are covered for the *treatment of pain,* refractory to non-invasive therapies and that significantly interferes with the activities of daily (ADLs) living, such that the patient requires assistance to perform an activity of daily living solely due to that pain. A comprehensive plan of care, developed prior to undertaking a plan of care for any one aspect of pain and/or disability, helps to avoid residual significant pain from other sources and the need for additional therapies. Medical records reviews (ours and those submitted to us by other reviewers) consistently demonstrate that the absence of such evaluation and comprehensive management results in significant ongoing pain – despite interventional procedures, additional medications and interventions, re-hospitalizations, and referrals to nursing facilities for ongoing debility in a substantial number of patients. In the case of the patient with adequately controlled or minimal or no pain prior to suffering vertebral compression fracture (VCF), the pain evaluation is appropriately focused on the VCF.

Comment: Several commenters and two Specialty Societies objected to the requirement for consultation with a pain management specialist for comprehensive pain evaluation prior to performance of interventional procedures.

Response: We concur with the objection and will clarify the wording in the LCD to eliminate this misunderstanding of our intention. For the purposes of this LCD, pain management specialists include those physicians without formal pain training whose experience allows them to perform and document a comprehensive patient pain evaluation and to develop and document a comprehensive plan of care. The plan of care must begin with the least invasive treatment strategy that addresses all significant pain generators and aspects of the pain and demonstrate expertise in pain management, including pharmaceutical whether delivered orally or by pain pump.

Comment: One commenter requested coverage for all procedures performed in the Emergency Room and other commenters requested consideration of ER coverage under specific circumstances.

Response: The Emergency Room is not the setting to perform a comprehensive assessment of a patient's pain or assess the response to non-invasive treatment, which may require monitoring for some hours. Patients presenting with severe pain and disability may be referred to Observation while sustained pain control is established and pain fully assessed. If pain is refractory to appropriate (and documented) interventions or treatment side-effects interfere with ADLs and discharge from Observation, invasive procedures may be undertaken to prevent hospitalization or institutionalization.

Comment: One Specialty Society requested coverage in the Emergency Room for treatment of VCF to avert deterioration and burst fractures.

Response: Though the vast majority of VCFs do not result in neurological compromise and patients with VCFs do not require or receive invasive treatment, the commenter makes an argument to treat all patients with VCFs with some kind of invasive procedure since deterioration may occur at any time, including months and years after a fracture. We have seen no information that specifies any population of patients with VCFs likely to deteriorate or predictive factors for deterioration. Further, there is no clear evidence that vertebroplasty of vertebral augmentation procedures prevent deterioration or are the treatment of choice for fractures that may deteriorate. Coverage of treatment in the ED for this indication will be denied.

Comment: Some commenters requested coverage of the procedures regardless of the age (duration) of the fracture or presence of other painful disease including painful bony metastases at other unrelated spinal or other sites.

Response: Following a comprehensive pain evaluation, maximized treatment and plan that demonstrates the absence of other or additional non-invasive treatment possibilities; the documentation of persistent and debilitating pain (interferes with ADLs) localized to the site of the VCF; and MRI-defined fracture cleft or edema; treatment with vertebroplasty or kyphoplasty may be covered for fractures present greater than 3 months. No payment will be made for these procedures in the presence of painful bony metastases to other sites unless and until the pain from all other sites has been adequately controlled; maximized treatment and plan that demonstrates the absence of other or additional non-invasive treatment possibilities; and documentation of persistent and debilitating pain (interferes with ADLs) localized to the site of the VCF.

Comment: Several commenters and specialty societies suggested shorter periods than one year for patient follow-up. One Society suggested that notification of the patient's primary physician of diagnosis and treatment be substituted for visits with the physician who performed the procedure.

Response: While information about longer-term outcomes is limited (few patients, single centers) and longer-term outcomes is necessary from an evidence perspective, we recognize the importance of minimizing the burden of non-patient safety requirements on providers. We will modify the LCD to require documented follow up with outcomes at one week, one month and three months after the procedure. Follow-up may be by telephone. Alternatively, documented notification of the patient's primary physician of the patient's evaluation and treatment may substitute for the three month follow-up.

Comment: One commenter suggested revision of LCD to indicate that one member of a team may perform comprehensive pain evaluation and another, performing an indicated interventional procedure, perform a focused interval pain and procedural assessment.

Response: This is appropriate but does not require LCD modification. The LCD does not preclude this common practice style.

Comment: Some commenters requested "retropulsion" to be removed as absolute contraindication to performance of the procedures discussed in the LCD.

Response: NAS recognizes the bowing or bulging that commonly occurs with compression fracture and imagers not uncommonly refer to minimal retropulsion. Further, there is one article with very small numbers, indicating that in some hands, canal compromise may not change post-procedure. Nonetheless, FDA approval and manufacturers recommendations exclude patients with significant retropulsion. Moreover, NAS has no ability to either determine the proper "hands" or restrict to same. The absolute contraindication remains as stated in the LCD: retropulsion of *bone fragment* into the canal.

Comment: On group of commenters requested removal of radiculopathy from the list of absolute contraindications. Many patients have chronic radiculopathy.

Response: NAS accepts this recommendation. Radiculopathy section will be clarified to indicate the circumstance(s) under which radiculopathy may not contraindicate these procedures. In the presence of a newer onset pain from a compression fracture, the existence of long-standing radiculopathy from another spinal site (another spinal level) will not, in and of itself, contraindicate vertebroplasty of vertebral augmentation procedures. NB: Any patient currently significantly symptomatic from other spinal pathology requires treatment prior to vertebroplasty or vertebral augmentation intervention.

Comment: One group of commenters requested acceptance of "failure of conservative treatment" to those patients who were not well-managed on pain medication and those who could not tolerate oral pain medication.

Response: We will neither emend the LCD to include these groups nor alter complex review of medical records to allow this definition of failure of medical management. Rather, we require expert pain assessment and management, which may include pain patches, pumps, mixed and other modalities as appropriate to the patient. If assessment and reasonable management fails, then more invasive procedures may be attempted as appropriate.

Comment: Some commenters remarked that VAS scales are not always the best measures of pain severity and asked for reconsideration of the requirement.

Response: We concur. LCD will be modified to include other recognized pain scales and/or evidence of impaired ADLs, such that independent living (without assistance in those without previous need of assistance) is precluded. Information on ADLs may be provided by a caregiver.

Comment: One provider requested a definition of "refractory" pain for "reasonable time periods" (under Pre-Procedural Documentation).

Response: Timeframe is relative to the treatment the patient receives. If a patient experiences severe intractable pain despite appropriate pharmacological or other management, then a vertebral augmentation or vertebroplasty procedure may be considered. This requires no LCD modification.

Comment: One commenter reported that the literature demonstrates patients managed with kyphoplasty are more likely to return home than nursing facility and suffer fewer complications.

Response: One paper with a low "n" does not constitute sufficient evidence of the hypothesis. On the other hand, medical records' reviews clearly show a large number of repeat procedures, persistent and exacerbated pain, and nursing home transfers in patients undergoing invasive procedures without a pain plan and, all too often, in patients without either a trial of conservative management and/or the indications for the procedures.

Comment: One commenter, citing the potential for abuse of narcotics and listing the potential side-effects of narcotics including acute alcoholism, advocated for immediate Kyphoplasty. The commenter believes "Medical management is contraindicated and/or not tolerated by substantial number of patients…"

Response: Noridian rejects this argument and reminds the commenter the vast majority of patients with compression fractures (and other painful conditions) respond to conservative non-invasive therapy. Moreover and unlike many other conditions, in most patients, the pain and disability associated with compression fractures resolve by three months time spontaneously.

Comment: One commenter requested coverage of kyphoplasty in any patient with painful compressions fractures regardless of duration of pain. This commenter based the suggestion on the absence of such a requirement in the Practice Guidelines of a number of specialty societies, including the AAOS.

Response: The absolute LCD requirement is actually for a reasonable trial of appropriate pain management following a comprehensive assessment of the patient's pain prior to any invasive intervention, not simply duration of pain.. The societies listed by the commenter assisted NAS in the development of the LCD and agreed with the recommendation. The AAOS, however, noting that the evidence of efficacy for kyphoplasty was weak, did not recommend kyphoplasty.

Comment: One commenter indicated that "kyphoplasty is not just a therapy that treats pain" but also disability and the mandatory period of pain management prior to the intervention should be removed.

Response: We hope that the redress of pain lessens disability but, in and of itself, the alleviation of pain is a sufficient goal of therapy. Pain management, not correction of the compression fracture or the underlying causes of the fracture, is the only indication for which there is some suggestive evidence of the efficacy of kyphoplasty and the only indication for coverage of the procedure.

This medical policy consolidates and replaces all previous policies and publications on this subject by NAS and its predecessors for Medicare A.

Start Date of Comment Period 05/06/2011

End Date of Comment Period 06/20/2011

Start Date of Notice Period 07/22/2011

Revision History Number R2

Revision History Explanation This draft LCD has been released to final. The comments, NAS responses and all updates are found on final LCD version.

The Responses to Provider Recommendation documentation has been added to the section "Advisory Committee Meeting Notes"

Due to provider comments the section "Indications and Limitations of Coverage and/or Medical Necessity" has been updated.

J3 A2011.01 R1
This LCD describes the requirements, restrictions and other provisions regardless of the settings.

The following language has been added to the sections "Limitations of Coverage and/or Medical Necessity" and the paragraph preceding "CPT/HCPCS Codes":

"All the requirements, restrictions and other provisions of this LCD apply to the vertebroplasty and vertebral augmentation procedures regardless of setting, inpatient (81.65 and 81.66) or outpatient."

11/21/2011 - For the following CPT/HCPCS codes either the short description and/or the long description was changed. Depending on which description is used in this LCD, there may not be any change in how the code displays in the document:
22520 descriptor was changed in Group 1
22521 descriptor was changed in Group 1
22522 descriptor was changed in Group 1

A2011.01 R2
02/27/2012: The following states and contractor numbers were added to the LCD: Alaska MAC A (Contract #02101); Idaho MAC A (Contractor #02201); Oregon MAC A (Contract #02301); and Washington MAC A (Contract #02401).

Reason for Change Other

Related Documents
This LCD has no Related Documents.

LCD Attachments
There are no attachments for this LCD.

Back to Top

All Versions

Updated on 03/24/2012 with effective dates 02/27/2012 - N/A
Updated on 03/24/2012 with effective dates 02/27/2012 - N/A
Read the **LCD Disclaimer opens in new window**
Back to Top

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: VISCOSUPPLEMENTATION FOR OSTEOARTHRITIS OF THE KNEE

DATE: XX/XX/XXXX

HERC COVERAGE GUIDANCE

Viscosupplementation should not be covered for the treatment of pain associated with Osteoarthritis (OA) of the knee.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. In addition to an evidence-based guideline developed by the Evidence-based Guideline Subcommittee and a health technology assessment developed by the Heath Technology Assessment Subcommittee, coverage guidance may utilize an existing evidence report produced in the last 5 years by the Agency for Healthcare Research and Quality, the Medicaid Evidence-based Decisions Project or the Washington Health Technology Assessment Program.

EVIDENCE SOURCES

Hayes, Inc. (2010). *Hyaluronic Acid/Viscosupplementation.* Produced for the Medicaid Evidence-based Decisions Project and the Washington Health Technology Assessment Program. Portland, OR: Center for Evidence-based Policy, Oregon Health and Science University. Retrieved from http://www.hta.hca.wa.gov/documents/ha_final_report_042610.pdf

DRAFT

Hayes, Inc. (2010). *Viscosupplementation for osteoarthritis of the knee.* Produced for the Medicaid Evidence-based Decisions Project. Portland, OR: Center for Evidence-based Policy, Oregon Health and Science University. Retrieved from http://www.ohsu.edu/xd/research/centers-institutes/evidence-based-policy-center/med/index.cfm

Samson, D. J., Grant, M. D., Ratko, T. A., Bonnell, C. J., Ziegler, K. M., & Aronson, N. (2007). *Treatment of primary and secondary osteoarthritis of the knee.* AHRQ Evidence Report/Technology Assessment No. 157. AHRQ Publication No. 107-E012. Evidence Report/Technology Assessment, (157), 1-157.

The summary of evidence in this document is derived directly from these evidence sources, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Osteoarthritis (OA) is the most common form of chronic articular disease, affecting approximately 27 million adults in the United States. The most commonly affected joint is the knee, with prevalence estimates ranging from 12% to 16%. To date, there is no known cure for OA nor is there a disease-modifying agent. Optimal management generally requires a combination of both nonpharmacological and pharmacological therapies, and joint replacement surgery or a joint salvage procedure may be considered for selected patients with severe symptomatic OA who have not obtained adequate pain relief and functional improvement from medical therapy. Pharmacological therapy generally begins with acetaminophen, followed by nonsteroidal anti-inflammatory drugs (NSAIDs) if sufficient pain relief is not obtained. There is a small risk of systemic adverse effects with NSAIDs. Aspiration of fluid followed by intraarticular injection of a corticosteroid ameliorates pain in some patients, but duration of relief is usually limited to one to three weeks. Additionally, repeated intraarticular injections of corticosteroids have the potential to cause postinjection flare, infection, and progressive, long-term cartilage damage.

Recently, viscosupplementation with hyaluronan has been introduced as an alternative intraarticular injection therapy for OA. Hyaluronans are also known as sodium hyaluronate or hyaluronic acid (HA). Hyaluronic acid is a normal component of synovial fluid and cartilage. The viscous nature of the compound allows it to act as a joint lubricant, whereas its elasticity allows it to act as a shock absorber. Hyaluronic products are characterized by their molecular weight, which varies according to the source of the compound and method of preparation. Five HA products are currently marketed in the United States: Euflexxa® (Ferring), Hyalgan® (Sanofi-Aventis), Orthovisc® (Anika Therapeutics), Supartz® (Seikagaku Corporation), and Synvisc® (Genzyme). Synvisc is

a derivative of HA that consists of cross-linked polymers; the compound is referred to as Hylan G-F 20. Hyaluronate preparations have been approved by the Food and Drug Administration (FDA) for treatment of pain associated with OA of the knee in patients who have not had an adequate response to nonpharmacological, conservative treatment and simple analgesics. Recent systematic reviews have come to contradictory conclusions regarding the effectiveness of viscosupplementation, and national guidelines vary in their recommendations.

Evidence Review

There is consistent evidence demonstrating that viscosupplementation results in lower mean pain scores and improves mean function scores a few weeks after treatment. However, the magnitude of benefit may be too small to be clinically important. This evidence is derived from a quantitative synthesis of six meta-analyses performed by the Agency for Healthcare Research and Quality in 2007 which included 42 randomized placebo controlled trials and over 5000 patients (Samson 2007). The authors found that the average change in pain score, although consistent and statistically significant, was small, with weighted mean differences in the range of 1.0 to 22.5 on a 100 point visual acuity scale. While there is no definitive definition of clinical significance, several authors, including Sampson, consider a 20 to 40 point improvement on 100 point pain scales to be clinically significant. The authors also reviewed the five previously published study-level meta-analyses that came to a variety of conclusions regarding the efficacy of viscosupplementation. These ranged from negative to moderately positive to strongly positive. The authors of the Samson review considered only one meta-analysis to have reported data and analysis that fully supported the meta-analysis authors' conclusion. This was also the metaanalysis with a negative conclusion—that the *clinical* effectiveness of viscosupplementation has not been proven and that viscosupplementation may be associated with a higher risk of adverse events.

There is a much greater volume of evidence regarding impact on pain than on function, and many studies did not follow patients beyond three months. Therefore, the impact of viscosupplementation on eventual recovery of function is uncertain. Compared with intraarticular corticosteroid injection, viscosupplementation appears to confer longer-lasting benefit, but the evidence was considered low quality. For comparisons with other treatments, there was insufficient evidence to allow any conclusion. Adverse events occur at a frequency of approximately 2% in single courses of treatment and are primarily transient local reactions, although rare, serious reactions are possible. The rate of adverse events per patient has been shown to increase with repeat courses of treatment, but the only available data were for hylan (high-molecular weight HA).

Evidence pertaining to issues other than efficacy and safety is of low quality:

- Available evidence suggests that viscosupplementation may be as effective as NSAIDs (four RCTs) and results in fewer systemic adverse events (two RCTs); in

comparison with intraarticular corticosteroids, it has a delayed onset and longer lasting benefit (nine RCTs plus meta-analysis).

- Hylan may have a superior benefit compared with that of non–cross-linked HA, but the magnitude of difference is very uncertain and hylan poses a small increase in the risk of adverse events.
- To date, there is no evidence of a difference in benefit between low and medium molecular weight HA.
- Younger age may be associated with greater efficacy; evidence pertaining to effectiveness by other patient characteristics and history is lacking.

Overall Summary

While the evidence demonstrates that viscosupplementation results in lower mean pain scores and improved mean function scores a few weeks after treatment, the magnitude of benefit may be too small to be clinically important.

PROCEDURE

Viscosupplementation

DIAGNOSES

Osteoarthritis of the knee

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
715	Osteoarthrosis and allied disorders Note: Localized, in the subcategories below, includes bilateral involvement of the same site. Includes: arthritis or polyarthritis: degenerative hypertrophic degenerative joint disease osteoarthritis
715.16	Osteoarthrosis localized primary involving lower leg
715.26	Osteoarthrosis localized secondary involving lower leg
715.36	Osteoarthrosis localized not specified whether primary or secondary involving lower leg
715.96	Osteoarthrosis unspecified whether generalized or localized involving lower leg
717	Internal derangement of knee Includes: degeneration of articular cartilage or meniscus of knee; rupture, old of articular

DRAFT

CODES	DESCRIPTION
	cartilage or meniscus of knee; tear, old of articular cartilage or meniscus of knee
ICD-9 Volume 3 (procedure codes)	
81.92	Injection of therapeutic substance into joint or ligament as an ICD-9 procedure
ICD-10 Diagnosis Codes	
M15	Polyarthrosis Includes: arthrosis with mention of more than one site Excludes: bilateral involvement of single joint (M16-M19)
M15.0	Primary generalized (osteo)arthrosis
M15.3	Secondary multiple arthrosis
M15.4	Erosive (osteo)arthrosis
M15.8	Other polyarthrosis
M15.9	Polyarthrosis, unspecified
M17	Gonarthrosis (arthrosis of knee)
M17.0	Primary gonarthrosis, bilateral
M17.1	Other primary gonarthrosis
M17.2	Post-traumatic gonarthrosis, bilateral
M17.3	Other post-traumatic gonarthrosis
M17.4	Other secondary gonarthrosis, bilateral
M17.5	Other secondary gonarthrosis
M17.9	Gonarthrosis, unspecified
M19	Other arthrosis
CPT Codes applicable to viscosupplementation	
20610	Arthrocentesis, aspiration, and/or injection; major joint or bursa (e.g. shoulder, hip, knee joint)
CPT Codes applicable to total knee replacement (TKR)	
27440	Arthroplasty, knee tibial plateau
27441	Arthroplasty, knee tibial plateau; with debridement and partial synovectomy
27442	Arthroplasty, femoral condyles, or tibial plateau(s) knee
27443	Arthroplasty, femoral condyles, or tibial plateau(s) knee; with debridement and partial synovectomy
27445	Arthroplasty, knee, hinge prosthesis (e.g., Walldius type)
27446	Arthroplasty, knee condyle and plateau; medial or lateral compartment
27437	Arthroplasty, patella; without prosthesis
27438	Arthroplasty, patella; with prosthesis
27447	Arthroplasty, knee condyle and plateau; medial and lateral compartments with or without patella resurfacing (total knee arthroplasty)
HCPCS Level II Codes for viscosupplementation	
J7321	Hyaluronan or derivative, Hyalgan or Supartz, for intra-articular injection, per dose
J7323	Hyaluronan or derivative, Euflexxa, for intraarticular injection, per dose
J7324	Hyaluronan or derivative, Orthovisc, for intraarticular injection
J7325	Hyaluronan or derivative, Synvisc or Synvisc-One, for intraarticular injection, 1 mg

DRAFT

CODES	DESCRIPTION
HCPCS Level II Codes for intraarticular cortisone injection	
J0702	Injection betamethasone acetate 3 mg and betamethasone sodium phosphate, 3 mg
J0704	Injection, betamethasone sodium phosphate per 4 mg
J1020	Injection, methylprednisone acetate, 20 mg
J1030	Injection, methylprednisone acetate, 40 mg
J1040	Injection, methylprednisone acetate, 80 mg
J1094	Injection, dexamethasone acetate, 1 mg
J1100	Injection, dexamethasone sodium phosphate, 1 mg
J1700	Injection, hydrocortisone acetate, up to 25 mg
J1710	Injection, hydrocortisone sodium phosphate, up to 50 mg
J1720	Injection, hydrocortisone sodium succinate, up to 100 mg
J2650	Injection, prednisolone acetate, up to 1 mL
J2920	Injection methylprednisone sodium succinate up to 40 mg
J2930	Injection methylprednisone sodium succinate up to 125 mg
J3302	Injection triamcinolone diacetate, per 5 mg
J3303	Injection triamcinolone hexacetonide, per 5 mg

Note: Inclusion on this list does not guarantee coverage

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT

HERC Coverage Guidance – Viscosupplementation for Osteoarthritis of the Knee
Disposition of Public Comments

General Comments

Stakeholder	#	Comment	Disposition
Orthopedic Surgeon Boston, MA	1	As a practicing orthopedic surgeon and Chair of a former work group for the American Academy of Orthopedic Surgeons (AAOS) that developed the AAOS Guideline for the Treatment of Osteoarthritis of the Knee, I am very familiar with the literature surrounding the use of viscosupplementation for the treatment of osteoarthritis of the knee, the numerous meta-analyses of this literature, and the application of this evidence to the clinical practice of orthopedic surgery.	Thank you for taking the time to comment.
	2	I believe the Health Evidence Review Commission for the State of Oregon has reached the wrong conclusion for their coverage guidance for viscosupplementation in the treatment of osteoarthritis of the knee. Osteoarthritis of the knee has become epidemic in the United States due to high athletic activity, frequent knee injury, and the burgeoning problem that we have with obesity. We are limited in our treatment modalities for this condition. There are no disease modifying treatments and as a practicing physician I am deeply concerned that total knee arthroplasty (TKA) being done on relatively young, overweight patients, will lead to disastrous conclusion with multiple revisions, an astronomical burden of expense for the health care system, and is the wrong course.	HTAS is aware of the epidemic nature of obesity, and consequently, of OA of the knee and hip.
	3	While the literature concerning the use of HA products in the treatment of osteoarthritis of the knee is suboptimal, there are numerous reports outlining its benefit. The majority of insurers and many agencies, including the Washington Health Technology Assessment Clinical Committee, have recommended that viscosupplementation injections into the knee for osteoarthritis be covered with limitations. This is the appropriate recommendation. Clearly, viscosupplementation should not be the first line treatment for osteoarthritis of the knee, but needs to be covered for a limited population set. This population set should include those who have not had adequate response to non-pharmacologic conservative treatment and simple analgesics. It should also include those who are unable to take simple analgesics due to side effects or contraindications, such as hypertension or gastric ulcer disease. Limiting its use to two courses per year is reasonable. Repeated use of viscosupplementation should require documented evidence of the clinical benefit of prior courses of treatment.	HTAS agrees that the literature is suboptimal. *For HTAS discussion*
	4	As I have stated, I believe the Oregon Health Evidence Review Commission has reached the wrong conclusion in its recommendation for non-coverage of viscosupplementation for the treatment of osteoarthritis of the knee. I strongly recommend that the Commission reconsider their coverage guidance and would recommend that they adopt the recommendation of the Washington Health Technology Assessment Clinical Committee, which has been noted in your Draft Coverage Guidance. To leave your coverage guidance as you have proposed will likely lead to an increased use of narcotic analgesics and earlier use of total knee arthroplasty, both of which will be burdens on society for decades to come.	*For HTAS discussion*

DRAFT

Stakeholder	#	Comment	Disposition
Orthopedic Surgeon Portland, OR	5	I am writing to comment on your position regarding payment for viscosupplementation as a treatment for osteoarthritis of the knee that causes pain. This modality for pain control has been an essential part of my practice for alleviating patients' pain and helping them avoid total knee arthroplasty. In conjunction with the literature, which is summarized in the summary of evidence that you presented, my protocol for treating patients begins with non-pharmacologic, activity modification, nonsteroidal anti-inflammatories and then injections. Most patients that come to see a surgeon have already done nonsteroidals and activity modification and, thus, I most often start with a corticosteroid injection.	Thank you for sharing your experience with this treatment.
	6	As mentioned in your summary of evidence, I limit that injection to one injection because repeat injections can have harmful effects on the knee joint and can cause significant reactions for the patient. Once they have had a successful injection that eventually fails, my next step typically for these patients is viscosupplementation. And as mentioned in your summary of evidence, the patients tend to get a much longer period of relief from these injections versus corticosteroid injections. I do not repeat these injections more than twice a year and when the patient begins to have symptoms that are not alleviated for greater than six months with these injections or begin having severe limitation of motion, I do, at that point, suggest total knee arthroplasty. Most patients, however, with a treatment of viscosupplementation can avoid total knee arthroplasty for several years, and I think this is a significant benefit in terms of utilization of medical resources.	Thank you for sharing your experience with this treatment.
	7	I completely agree with the criteria of reserving viscosupplementation for patients who have not had an adequate response to non-pharmacological measures such as activity modification, as well as limiting them to two courses per year, with at least four months in between, and documented evidence of clinical benefit from a prior course of treatment, whether that be viscosupplementation or at least temporary relief from a corticosteroid injection that may or may not include local anesthetic.	*For HTAS discussion*
	8	To deny viscosupplementation to all patients with osteoarthritis I think would be doing a disservice to the medical community as well as the patients themselves and potentially cause an increase in cost utilization in terms of the increased usage of total knee arthroplasty as a treatment modality for osteoarthritis.	Thank you for your comment.
	9	In addition to the previously dictated letter regarding the viscosupplementation for patients with osteoarthritis, there is one particular patient population in which there has been a significant amount of literature that does show a positive effect of viscosupplementation in this particular patient group, which includes patients with symptomatic meniscal tears, post arthroscopy, having continued pain as a result of their concomitant osteoarthritis. Several studies show a positive effect that is lasting. In 2007, a study done in the Journal of Knee Surgery and Sports Traumatology and Arthroscopy, author Hempfling shows in a randomized controlled double blind study of 80 patients undergoing	This study was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate

DRAFT

Stakeholder	#	Comment	Disposition
		arthroscopic knee lavage, 40 patients were given hyaluronan 10 mL and 40 patients were given lavage. Both the control and study groups, the control group being the lavage and the study group being the hyaluronan, showed positive effects in three months. The treatment effect was maintained in the hyaluronan group for a year, as opposed to only three months in the lavage group.	individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	10	In 2008, Bert in the Journal of Arthroscopy and Related Surgery, reported on a prospective multi-center open label study on athletic patients with knee OA, who underwent knee arthroscopy for mechanical symptoms of meniscal pathology. On average, these patients were given Hylan G-F 20 treatments, initiation at an average of 3.4 months after arthroscopy, when they continued to have pain and decreased activity at baseline. At three and six months post injection, the Western Ontario and McMaster University Osteoarthritis Index and International Knee Documentation Committee scores significantly improved. At three months followup, the authors also reported improved activity levels. These were in patients who continued to have significant symptoms on average 3.4 months post knee meniscectomies secondary to the concomitant osteoarthritis.	This study was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	11	Again, in 2008, Huskin et al, in the Journal of Knee Surgery Sports Traumatology and Arthroscopy, also reported on an open label multi-center prospective study in patients who continued to have pain after arthroscopic meniscectomy with concomitant osteoarthritis, starting with injections at a mean time post surgery of 53 days, showing significant improvements in visual analog scale WOMAC scores, visual analog scale walking pain scores, physician global assessment and patient assessment.	This study was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.

DRAFT

Stakeholder	#	Comment	Disposition
	12	Thus in this population, patients who have mild osteoarthritis in conjunction with meniscal tears that are treated arthroscopically, there has been significant literature that shows an advantage of using viscosupplementation postoperatively in patients that continue to have pain. So, considering 90% of patients that have documented osteoarthritis will have meniscus tears seen on MRI scan, plus patients who have osteoarthritis that does not warrant total knee arthroplasty and have concomitant meniscal tears that are treated arthroscopically, have some relief, but then continue to have pain secondary to osteoarthritis, viscosupplementation is shown to have a benefit for them postoperatively when they continue to have pain.	Two of the three cited studies were not blinded or controlled. The population of the third study did not have meniscal tears.
	13	I think this patient population should be afforded the advantage of obtaining viscosupplementation to again attempt to reduce their pain and prevent them undergoing total knee arthroplasty.	Thank you for your comment.
Orthopedic Surgeon Beaverton, OR	14	I must comment in all earnestness regarding the apparent recommendation to discontinue viscosupplementation. This would be devastating to my patients with knee arthritis, who need it. These are: 1) Younger persons who have disabling arthritic knee pain and who are too young for total knee replacement. These people are unable to properly exercise because of their pain, so they gain weight, lose strength, become deconditioned (so they either fall and injure themselves, or require extensive and expensive physical therapy. They tend then to become diabetic, and you know the costs to health and society when that happens.) 2) Older individuals, who by reason of poor health, are unable to obtain a total knee replacement. They are doomed to suffer, until they die, with knee pain, without viscosupplements. It would be cruel to not provide patients such as these with viscosupplements. 3) Those who cannot afford a knee replacement either due to its expense or time away from productive work. Many fall into this category. 4) Unhealthy patients who are younger, eg those on renal dialysis, or type 1 diabetics, etc., ie high risk patients, where arthroplasy is too risky.	Thank you for sharing your experience with this treatment.
	15	I have been using viscosupplements for nearly 14 years, and, with only 2 exceptions, have not had untoward reactions. With Supartz over the last 6 years, I have had no inflammmatory reactions. It is thus VERY safe. It is also VERY effective, since my results are superb, ie 90+ % of my patients have sustained relief for 6-12 months, and pain typically improves by greater that 80-90%. Few failures occur, and these are typically those whose arthritis is milder, or those who have concomitant internal derangements, such as meniscus tear.	Thank you for sharing your experience with this treatment.
	16	Base on all the above, I strongly disagree with the results of your studies' conclusions, as they do not correlate to my own very extensive experience, on about 400 patients.	While anecdotal experience has a strong influence on individual opinion, it is inherently susceptible to bias. High quality RCTs are the best way to assess true treatment effects, and the evidence examined by HTAS is inconclusive.
	17	Viscosupplements are very cost effective compared to a knee replacement, which, without viscosupplements, would have to be done at a much earlier age, thus costing the insurer a lot now,	Thank you for your comment.

DRAFT

Stakeholder	#	Comment	Disposition
		when it could have been postponed, and then likely would have avoided the revision knee arthroplasy on the knee which could have waited. Postponing an arthroplasty in the proper patient is obviously in the best interests of patient and insurer alike. To discontinue viscosupplemets is assuredly penny wise and pound foolish.	
	18	I strongly object to discontinuation of viscosupplements for all the above reasons and implore you to avoid all the long term expenses and devastating orthopedic and medical consequences of a very wrong decision.	*For HTAS discussion*
Orthopedic Surgeon Tigard, OR	19	I have practiced general orthopedics in Oregon since 1991 and the use and application of viscosupplementation for patients with knee arthritis is an important medical treatment. I strongly request that it's use be continued as part of the available spectrum of treatments for the arthritic knee. Many patients are medically contraindicated to proceed with total knee arthroplasty because of medical problems or their youth. Taking away the option will have a negative effect on the health of those patients who need this treatment. Once cortisone is tried and found ineffective arthroscopy is not effective for arthritis pain alone and the only viable option short of a total knee replacement is viscosupplementation, which I have found effective throughout my years in practice. I urge you to continue to allow this treatment to be available for those in need.	Thank you for sharing your experience with the treatment.
Orthopedic Surgeon Corvallis, OR	20	I am an orthopaedic surgeon in practice in Corvallis. I see numerous patients each week that have definitely benefited from the use of viscosupplementation injections. I have seen an increase in mobility and decrease in pain level in those patients which can far outlast just a simple cortisone injection. Additionally, for those patients that can't undergo a knee replacement, these injections can be the only way to reduce their pain. I would emplore you to keep them as a treatment option for our patients.	Thank you for sharing your experience with the treatment.
Family Physician Milwaukie, OR	21	I am a family physician practicing in Milwaukie Oregon. I would like to express my extreme concern at the recent decision by this committee to restrict the use of HA into the knee for osteoarthritis. I have seen first hand the benefits of this protocol. I have had patients who I have given viscosupplementation get improved range of motion, strength, and overall function. This is at the savings of a total knee replacement. This will push patients to have more total knees at a cost of tens of thousands of dollars. There is clear evidence that this treatment works and should be a viable option for all patients. There was a recent review by a group in Washington similar to yours and it approved the treatment because of the overall preponderance of evidence showing that it improves mean pain scores and function scores. I emplore you to reconsider your position and approve this much needed treatment for the patients of Oregon.	Thank you for sharing your experience with the treatment. HTAS is aware of the different decision reached by the WA HTA clinical committee. *For HTAS discussion*
Arthritis Foundation (Great West	22	The Arthritis Foundation, Great West Region appreciates the opportunity to offer comments on the Health Evidence Review Commission draft coverage guidance for viscosupplementation for osteoarthritis of the knee. The Arthritis Foundation has participated in and supported the outcome of	Thank you for taking the time to comment.

DRAFT

Stakeholder	#	Comment	Disposition
Region) Seattle, WA		the Washington Health Technology Assessment Program (WA WHTAP) process referenced in the Health Technology Assessment Subcommittee (OR HTAS) draft, and it is with confusion and dismay that we read the proposal for non-coverage.	
	23	For people living with osteoarthritis, there are few options between pain management and joint replacement. Viscosupplementation offers hope for many in staving off joint replacement, and for those whose co-morbidities make surgery too risky, it may be the only option. Furthermore, the relief provided by this therapy may make it easier for people with knee OA to participate in physical activity, an important non-pharmacologic component to managing not only OA, but many other co-morbidities.	HTAS is aware of the limited treatment options available to patients with OA of the knee, but does not believe offering a treatment that does not provide any clinically meaningful improvement in pain is helpful.
	24	We understand that the same reports used as in the Washington determination and the Arthritis Foundation fails to understand how two evidence-based programs can rely on the same report and come to coverage decisions that are so different.	*For HTAS discussion*
	25	The WA HTAP Reimbursement determination found that "based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, Hyaluronic Acid / Viscosupplementation is a covered benefit for the treatment of pain associated with Osteoarthritis (OA) of the knee when all of the following conditions are met: • In patients who have not had an adequate response to non-pharmacological conservative treatment and simple analgesics; • Is limited to two courses per year with at least four months between courses; and • Documented evidence of clinical benefit from the prior course of treatment is required for subsequent treatment courses. The link to the full Washington HTA/HTCC report is: http://www.hta.hca.wa.gov/documents/findings_decision_ha_082010.pdf	HTAS is aware of the WA HTA decision.
	26	Given the decision for coverage with limitations in Washington, we ask that HERC make available a report detailing the evidence it relied upon to come to such a dissimilar decision using what appear to be the same evidence-based materials. We look forward to seeing a report, and strongly urge that the recommendation be changed to "coverage with limitations."	*For HTAS discussion*
Advocacy for the Improvement in Mobility (AIM) White Plains,	27	Advocacy for the Improvement in Mobility (AIM) is a non-profit corporation dedicated to ensuring patient access to appropriate, high quality musculoskeletal health care. We would like to comment on the recent Oregon HERC non-coverage decision for viscosupplementation for osteoarthritis of the knee. As noted in your analysis of the evidence concerning Hyaluronic (HA) supplementation, the Washington State Healthcare Authority has issued a limited coverage decision for this modality. We	Thank you for taking the time to comment. HTAS is aware of the WA HTA decision. Thank you for sharing the AAOS guideline recommendation. HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies.

DRAFT

Stakeholder	#	Comment	Disposition
NY		would agree with that decision based upon the Clinical Practice Guideline (CPG) issued by the American Academy of Orthopedic Surgeons (AAOS) on the treatment of osteoarthritis of the knee in 2008. The AAOS CPG recommendation 16 states: "We cannot recommend for or against the use of intra-articular hyaluronic acid for patients with mild to moderate symptomatic OA of the knee." Since the strength of recommendation is inconclusive and the treatment is recognized as safe we concur with Washington State and most private health care insurance carriers that HA treatments should be covered in the limited situations outlined by the HTA. In Oregon, the largest private payer, Regence Blue Cross Blue Shield of Oregon has a published medical coverage policy. National payers with Oregon beneficiaries such as Aetna and United Health Group also provide coverage. Attached are the Regence and Aetna coverage policies for viscosupplementation.	
	28	Medicare and most other private insurers do cover viscosupplementation in osteoarthritic patients with the appropriate symptoms and indications. To deny coverage to Medicaid patients for these procedures creates a potential treatment disparity for the poor and minority patients served by the Medicaid program. Clinical Practice Guidelines are necessary to help improve patient care and make treatment more consistent with the current state of medical knowledge. It is important to have experts examine guidelines to offer necessary insight concerning their relevance and veracity. Attached, please find three additional reference articles HERC might consider in finalizing coverage guidance. We would be happy to advise the HERC on further guidelines concerning musculoskeletal healthcare.	HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies, including Medicare. Only 2 articles attached. Moreland 2003 was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions. Goldberg 2010 is a narrative review only.
Director, Medical Affairs, Sanofi Biosurgery Cambridge,	29	OA of the knee is a chronic, progressive disease associated with a substantial public health burden both in terms of personal suffering and use of health care resources. Approximately 16% of adults age 45 years or older have symptomatic OA of the knee. The risk for developing the disease increases with advancing age, and currently 14.6 million Americans are estimated to have symptomatic OA of the knee. The painful symptoms and joint dysfunction associated with OA of the knee make it a leading cause of impaired mobility and disability. Patients with the disease experience significant	HTAS is aware of the burden of suffering of patients with OA.

DRAFT

Stakeholder	#	Comment	Disposition
MA		limitations of activity including difficulty walking, stooping, standing from a seated position, and climbing stairs. Patients with OA of the knee also have poorer social function and worsened health-related quality of life.	
	30	The cause of OA of the knee is complex and poorly understood. Degeneration of articular cartilage within the knee joint is accompanied by pathologic changes affecting the entire joint including the underlying bone. One pathologic change involves the reduction of the elastic and viscous qualities of the synovial fluid. The concentration and molecular weight of hyaluronic acid (the substance responsible for the viscoelastic qualities of this fluid) are decreased. One proposed mechanism of pain generation in OA is diminished elastoviscosity of the synovial fluid, which leads to reduced lubrication and protection of joint.	HTAS agrees that the pathogenesis of OA and the mechanism of pain generation are poorly understood.
	31	Currently, there is no treatment that can prevent or cure OA of the knee. Treatment goals include reducing joint pain and stiffness, maintaining and improving joint mobility, reducing physical disability and handicap, improving health-related quality of life, limiting the progression of joint damage, and educating patients about the disorder and its management. Treatment options include non-pharmacologic, pharmacologic, and intra-articular modalities. Many of these patients have risk factors precluding NSAIDs, and/or are not candidates for arthroscopy or total joint arthroplasty. The purpose of intra-articular therapy with viscosupplements is to help replace diseased synovial fluid that has lost its viscoelastic properties. The exact mechanism by which viscosupplements relieve OA pain of the knee is not fully known. Surgical interventions such as total knee replacement are a last resort for patients with severe symptoms who fail to respond to less invasive forms of therapy.	HTAS is aware of the treatment options available to patients with OA of the knee and their limited efficacy.
	32	Several reputable published meta-analyses and systematic reviews have concluded that this class of product is efficacious with a favorable risk-benefit profile. A recent Cochrane review affirmed the role of viscosupplements in treatment of OA of the knee, noting superior efficacy vs placebo, comparable efficacy vs NSAIDs, and longer-term benefits vs intra-articular steroids.As such, intra-articular HA has become a widely accepted treatment option and is included in several professional society guidelines including OARSI and ACR.	The Cochrane review is one of five meta-analyses that were included in the evidence source, with others reaching a different conclusion.
	33	We respect that Oregon HERC chose to commission an independent review of the most recent evidence. However, we wish to note that the Hayes report does not contain data from at least 4 recent publications that might provide more clarity to the questions you are trying to answer. Those publications are listed below.	The WA HTA report included 4 RCTs published after the date of the Hayes report.
	34	The Hayes report also excluded the Phase III (Synvisc-One) hylan G-F 20 single-injection trial called SOUND that led to the February, 2009 FDA approval of Synvisc-One. The SOUND trial was published online in March, 2009 and appeared in print earlier this year. It featured a 26-week, double-blinded, and placebo-controlled design, and was also intent-to-treat analyzed for both improvement and responders. These data withstood a full panel review by the FDA. The primary pain improvement	This study was published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included

DRAFT

Stakeholder	#	Comment	Disposition
		endpoint was reached, and, 71% of hylan G-F 20 patients experienced clinically meaningful pain reduction versus 53% of controls. The repeat treatment phase demonstrated that a second injection of hylan G-F 20 did not increase the frequency of adverse events. Synvisc-One can provide 6 months of analgesia with as little as one office visit.	or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	35	Trials have demonstrated the efficacy of hylan G-F 20 against treatment with intra-articular steroid, NSAIDs, and appropriate care.	HTAS agrees that there is some evidence of equivalency to other treatment modalities, but is unclear what is meant by "appropriate care."
	36	Determination of the magnitude of benefit in the Hayes report relied heavily on Effect Size. A published consensus statement from the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials, or IMMPACT group, urged considering improvements within treatment groups or patients in chronic pain trials, in addition to Effect Size, which is statistical in nature. IMMPACT considered pain reductions of 30% or more to be moderately clinically important. Mean pain was reduced 36% over 26 weeks in patients treated with Synvisc-One.	Citation not provided. Not clear which trial this is referring to. If referring to the SOUND trial, see comment #29
	37	There may have been valid evidence omitted for other products in the class as well. In general, while some may believe the efficacy data across the class to be inconsistent, viscosupplements have a safer systemic toxicity profile than NSAIDs/COX-2, and longer-lasting efficacy than an intra-articular corticosteroid. Adverse events are typically infrequent, local, mild to moderate, and generally consist of injection site reactions and knee pain or swelling. The GI, cardiovascular, and renal adverse events that can occur with NSAIDs/COX-2 do not happen with viscosupplements.	HTAS agrees that the efficacy data across this class of products is inconsistent.
	38	It would greatly benefit patients with OA knee pain who are not surgical candidates and are searching for treatment options with less harmful systemic side effects if they had continued access to viscosupplements. Sanofi will follow up with a review of the viscosupplement class in another letter. 1. Hochberg M, Altman R, April KT, Benkhalti M, Guyatt G, McGowan J et al. American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee. Arthritis Care & Res 2012;64(4):465-474. 2. Bannuru R, Natov N, Dasi U, Schmid C, McAlindon T. Therapeutic trajectory following intra-articular hyaluronic acid injection in knee osteoarthritis - meta-analysis. Osteoarthritis Cartilage. Jun 2011;19(6):611-619. 3. Chevalier X, Jerosch J, Goupille P, van Dijk N, Luyten FP, Scott DL, Bailleul F, Pavelka K. Single, intra-articular treatment with 6 mL of hylan G-F 20 in patients with symptomatic primary	Articles not attached. No additional letter submitted.

DRAFT

Stakeholder	#	Comment	Disposition
		osteoarthritis of the knee: A randomised, multi-centre, double-blind, placebo-controlled trial. Ann Rheum Dis 2010;69:113-119. 4. Zhang W, Nuki G, Moskowitz RW et al. OARSI recommendations for the management of hip and knee osteoarthritis Part III: changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage 2010;18:476-499.	
Zimmer, Inc. Minneapolis, MN	39	Zimmer appreciates this opportunity to comment on the draft guidance on viscosupplementation for osteoarthritis of the knee. We strongly encourage HERC to reconsider its proposal to not cover viscosupplementation for the treatment of pain associated with osteoarthritis (OA) of the knee. This treatment is one of only a handful of non-surgical treatments that reduces pain and may delay eventual arthroplasty. The additional benefit of minimal potential side effects makes this an important treatment alternative. We are greatly concerned that, if finalized, this non-coverage guidance reduces the viable therapy options to publicly insured Oregon residents.	Thank you for taking the time to comment.
	40	Zimmer recently introduced a new single injection viscosupplement for OA of the knee to the market called Gel-One® Cross-linked Hyaluronate, which was approved by the FDA. The following link provides an abstract of the published peer reviewed study showing the statistically significant benefit of this product (referenced as "Gel-200" in the publication) for patients who suffer from OA of the knee. http://www.sciencedirect.com/science/article/pii/S1063458412000374 * *Evidence Source: Strand, V., Baraf, H.S.B., Lavin, P.T., Lim, S., Hosokawa, H. *A multicenter, randomized controlled trial comparing a single intra-articular injection of Gel-200, a new cross-linked formulation of hyaluronic acid, to phosphate buffered saline for treatment of osteoarthritis of the knee.* Osteoartritis and Cartilage, volume 20, Issue 5, Pages 350-356, May 2012 The HERC draft cites the Sampson publication which considers a 20 to 40 point improvement on a 100 mm VAS scale to be a clinically significant therapy. The HERC draft implies that viscosupplementation studies do not show clinically significant improvements in pain sub-scores. However, in the study referenced above which was conducted for regulatory approval of the product, Gel-One (Gel-200) achieved an average improvement from baseline of 27.8 mm in WOMAC pain score, which amounts to a 39.3% improvement. (This is mentioned in the article as improvement from baseline exceeding 20mm) Studies for some other Hyaluronic Acid (HA) products, also conducted to support regulatory approval, have shown mean improvements of greater than 20 mm.	Strand 2011 is an RCT comparing Gel-200 to saline injection, N=379, primary outcome measure WOMAC pain score (VAS 100 mm) at week 13. Average baseline pain score was 69. While mean improvement from baseline may have been 28 mm in the Gel-200 group, the difference from the control group was at the greatest 8 mms (at 3 and 6 weeks). While the difference was statistically significant, this supports the conclusions of the evidence report that the effect is likely not clinically significant.
	41	The HERC draft concludes that because the RCTs for viscosupplementation did not focus on function and that the studies did not follow patients beyond 3 months, then there is insufficient evidence to understand the impact of viscosupplementation on the eventual recovery of function. However, it	HTAS understands that pain relief irrespective of functional improvement is an appropriate goal in this population.

DRAFT

Stakeholder	#	Comment	Disposition
		may be important to keep in mind that viscosupplementation is a therapy that is administered when other conservative therapies have failed. It is intended to relieve pain with minimal systemic or local side effects. It may delay eventual arthroplasty, but is not intended to be the final therapy in the continuum of care. Since most insurance coverage policies limit administration of HA injection treatments to once every six months, patients are likely to return for another course of treatment only if their pain was sufficiently relieved to experience some benefit over that six month period.	
	42	Zimmer would like to challenge HERC to justify why the committee has arrived at a different conclusion regarding coverage for viscosupplementation than that of the Washington state HTA clinical committee, which used the same clinical evidence. This therapy is widely covered by both private and public insurers. The HERC draft does not cite any unique or conclusive evidence that would contradict the rationale for coverage by virtually all payers across the country. Zimmer strongly encourages HERC to reconsider its non-coverage guidance proposal for viscosupplementation. Oregon residents will be denied a viable and widely used therapy alternative based on a rationale that is unique to HERC.	*For HTAS discussion*
DePuy Mitek, Inc. Raynham, MA	43	Thank you for the opportunity to provide comments on the Oregon HERC's recently developed draft coverage guidance entitled *Viscosupplemenation for Osteoarthritis of the Knee*. We strongly believe that the clinical evidence supports the listing of viscosupplementation with hyaluronic acid (HA) as a covered benefit for the treatment of pain associated with osteoarthritis (OA) of the knee. A summary of the clinical evidence supporting the use of viscosupplementation with HA in OA of the knee, and ORTHOVISC® specifically, is provided below.	Thank you for taking the time to comment.
	44	***Role in Therapy*** It is important that clinicians have access to the widest possible range of therapies for treatment of OA. Nonsurgical treatment options have limitations, NSAIDs cause cardiovascular and gastrointestinal complications. Intra-articular (IA) injections of corticosteroids often provide short term pain relief, but are known to potentially cause long-term cartilage damage. For patients who have not obtained sufficient pain relief from such therapies, joint replacement surgery may be considered, which is associated with morbidity and cost. HA is an intra-articular therapy for OA of the knee in patients who have not had an adequate response to conservative treatment or simple analgesics, who are seeking a longer duration of pain relief compared to IA steroid injections, and who may wish to delay or avoid surgery.	Thank you for your comment. The statement concerning corticosteroids causing long-term cartilage damage is not supported by the evidence.
	45	***Evidence Supporting Use of HA for OA of the Knee*** There is consistent evidence in the medical literature demonstrating that HA is safe and results in lower mean pain scores and improves mean function scores for up to six months. This evidence comes from four systematic reviews looking at the efficacy of HA (Bellamy 2006, Samson 2007, Hayes	All but Bannuru 2011 were included in the WA HTA evidence review.

DRAFT

Stakeholder	#	Comment	Disposition
		2010, Bannuru 2011), one comparing hylan with HA (Reichenbach 2007), and one comparing HA with corticosteroids (Bannuru 2009).	
	46	In the draft coverage guidance from Oregon's HERC, only two evidence sources are cited (Hayes in 2010 and Samson 2007 review). The 2006 Cochrane Review (Bellamy) and Hayes 2010 reviews had positive conclusions regarding the overall efficacy of HAs. The Cochrane report reviewed 76 trials, and is one of the most comprehensive reviews to date and examined multiple HA products for effects thru 52 weeks. In assessing the pooled effect size in comparison to placebo, the reduction in pain was significant and physical function also improved. HAs also demonstrated superior reduction in pain at 8 weeks over corticosteroids and continued to be significant up to 14 weeks.	Hayes 2010 is the WA HTA report, and includes Bellamy, Samson and 3 other SRs. In Bellamy, the mean effect measure difference at 8-12 weeks was 13mm VAS
	47	Samson et al reviewed 42 trials (N=5,843) which generally showed positive effects of HAs on pain and function scores compared to placebo. However, the authors cited considerable uncertainty of the results due to variable trial quality, potential publication bias, and unclear clinical significance of the changes reported. Nonetheless that the minimal clinically important threshold of 20 mm or 40 percent reduction in VAS pain from baseline proposed by Samson, has been successfully met by several of the large published HA studies.	While this threshold has been met for the HA group compared to baseline, when the mean difference from placebo injection is considered, it has not been met.
	48	Meta-analysis by Bannuru (2011) inferred that HAs are efficacious by 4 weeks, reaches peak effectiveness at 8 weeks and exerts a residual detectable effect at 24 weeks. The peak effect size (ES) for HAs of 0.46 is greater than published effects from other OA analgesics (acetaminophen ES = 0.13; NSAIDs ES = 0.29 COX-2 inhibitors ES = 0.44). An ES above 0.20 is considered to be clinically relevant on an individual patient basis in chronic pain conditions such as knee OA. This pooled analysis looking at post-administration trajectory of effect confirms that the magnitude of effect of HA exceeds a minimally clinically significant threshold.	Bannuru 2011 included 54 trials, 53 of which were funded or had involvement from industry. Authors calculated effect sizes using Bayesian random effects model.
	49	Hayes (2010) reported two studies with patients who improved ≥ 20 mm on a 100 mm scale where the results favored HA over placebo. Note that >20mm improvement was defined as clinically meaningful by the IMMPACT collaborative group. Overall, the different conclusions reached in the systematic reviews were due to differences in methodology (i.e., dissimilar sets of RCTs, differences in selection criteria).	Citations not provided. However, in the WA HTA report, there is mention on page 17 of 2 trials that report > 20 mm improvement, but both were compared to "conventional treatment", not placebo.
	50	We strongly encourage the Oregon HERC to *broaden* the evidence base to include the systematic reviews cited above, similar to the evidence-based approach recently published by Washington State HTA of Viscosupplemenations.	HTAS has utilized the WA HTA report as their evidence source.
	51	***Evidence Supporting the Use of ORTHOVISC® for OA of the Knee*** ORTHOVISC® is an effective treatment for reducing pain in patients with knee OA. Evidence from two clinical studies have shown significant improvements in mild to moderate pain for up to 6 months following treatment with three or four ORTHOVISC® injections (Brandt 2001, Neustadt 2005). It is	Both studies were published before the date of the WA HTA report (last search date Dec 2009). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies

Stakeholder	#	Comment	Disposition
		important to note that ORTHOVISC® gained FDA clearance on the basis of *responder rate*, rather than mean VAS pain score. Responder rate is defined as the percentage of patients that experience significant pain relief from a therapy, as opposed to the mean pain score experienced by the entire study population of responders and non- responders. Responder rate is a true indicator of patient benefit whereas mean population VAS scores tend to mask the effects on individual patients. Clinical data show that over 65.4% of patients responded to ORTHOVISC® and had significant, long term pain relief. ORTHOVISC® also has an excellent safety profile compared to the potential safety issues with NSAIDs and steroid injections.	are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	52	***HTAs and Guidelines*** A number of HTAs (i.e., Washington State Healthcare Authority, Veterans Administration), clinical guidelines (i.e., Osteoarthritis Research Society International) Medicare Administrative Contractor and health plan policies (i.e., Trailblazer, Regence Blue Cross Blue Shield Inc., United Health Group Inc.) have supported the use of viscosupplementation for OA of the knee. Most recently (2010), using some of the same source documents as cited in the *draft* Oregon coverage decision, the Washington State Health Care Authority committee concluded that there is sufficient evidence to cover viscosupplemenation with HAs for OA of the knee.	HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies. HTAS has utilized the WA HTA report as their evidence source, but reached different conclusions.
	53	In conclusion, we strongly believe that the clinical evidence cited above supports the listing of viscosupplementation with HAs, especially ORTHOVISC®, as a covered benefit for the treatment of pain associated with OA of the knee. If you have any questions about the information included in this letter or require additional information, please contact us.	*For HTAS discussion*
Bioventus, LLC Durham, NC	54	We are writing to respond to your May 21 decision to recommend non coverage of viscosupplements for patients with osteoarthritic knee pain. We appreciate the opportunity to provide commentary on this draft recommendation to the Health Evidence Review Commission (HERC) and respectfully request reconsideration of this decision. We understand Oregon State's concern around the cost of healthcare and the desire to find ways to reduce expenditures by seeking reductions in utilization of certain therapies. We believe, however, that the decision to discontinue access to viscosupplements will have the consequence of eliminating an important physician treatment tool, result in a reduction of the quality of care available to the residents of Oregon and may actually contribute to a rise in the cost of treating knee OA pain. We offer the following comments supporting this position.	Thank you for taking the time to comment.
	55	***Burden of Illness and Prevalence*** Osteoarthritis (OA) is a progressive disorder of the joints caused by gradual loss of cartilage. This manifests itself as pain, swelling and loss of function for the patient. Contributing factors include	The HTAS is aware of the natural history and burden of disease of OA of the knee.

Stakeholder	#	Comment	Disposition
		advancing age, trauma to the knee, and obesity. Arthritis is among the leading causes of disability in the US and osteoarthritis (OA) is the most common type of arthritis. Knee OA, is the most frequent form of lower extremity OA.	
	56	There are few options for treating knee OA and the associated pain before prior to expensive knee replacement. Typically patients will self-treat with OTC pain medications in the early stages of the disease before seeking help from a medical professional. Medical professionals have but a few conservative treatment options that include NSAIDs and corticosteroid injections to help maintain the patient before moving to the more radical and expensive option of total knee replacement (TKR). It is widely recognized that there is a gap in the OA treatment paradigm between conservative therapies and joint replacement that high-dose NSAID therapy and intra-articular corticosteroids cannot fill alone. Viscosupplements are needed to complete the knee OA treatment armamentarium.	The HTAS agrees that additional treatment options for OA of the knee are desirable, but providing an option that is not clinically significantly superior to placebo is not helpful.
	57	***Viscosupplementation*** Viscosupplementation provides an important FDA-approved treatment for patients with OA of the knee. It is the only available intra-articular analgesic for OA treatment, and the only device that is essentially free off systemic adverse events and drug interactions. It is a critically important option for patients with GI or CV comorbidities for whom chronic NSAID administration is contraindicated, and for patients who are not good candidates for (TKR). The safety and effectiveness of viscosupplements is not however, limited to this patient population.	HTAS disagrees that viscosupplementation is free of systemic AE. While most AE are minor and local, serious AE can occur, including sepsis of the joint, which clearly has systemic consequences.
	58	***Effectiveness of Viscosupplements*** A recently published Cochrane Systematic Review of viscosupplementation for the treatment of OA of the knee[3.] Identified 76 randomized controlled trials (RCTs) for analysis. This meta-analysis, supported the superiority of viscosupplement products over saline placebo, and concluded that the RCT literature provides evidence of efficacy. The analyses suggest that viscosupplements are comparable in efficacy to systemic forms of active (drug) intervention, with fewer systemic adverse events. The authors conclude that the analyses support the use of viscosupplement products in the treatment of knee OA.	The Cochrane review is one of five meta-analyses that were included in the evidence source, with others reaching a different conclusion.
	59	In virtually all clinical trials, regardless of patient type or inclusion criteria, patients treated with viscosupplements consistently demonstrated significant improvements in pain or function from baseline.	HTAS disagrees with this statement, as evidenced by the WA HTA review.
	60	***SUPARTZ Effectiveness*** The approval of SUPARTZ was based on five randomized, double-blind, saline-controlled multicenter trials, and an integrated analysis (n==1155) of thee primary patient data from these five RCTs.[4.] The SUPARTZ efficacy studies utilized a five-injection treatment regimen. In 2006 a label change was	Thank you for this information about your product.

DRAFT

Stakeholder	#	Comment	Disposition
		approved that modified the directions for use to include the statement "some patients may respond to 3 injections…….". [5.] This statement is based on several trials, one of which is included in the SUPARTZ labeling that compared 3-injection and 5-injection treatment regimens, and found the mean response comparable. Thus although FDA labeling allows physicians the flexibility of administering up to 5 SUPARTZ injections when required, although a 3-injection course of treatment with SUPARTZ has demonstrated effectiveness similar to products restricted to a 3-inj regimen. This flexibility allows physicians to decide when more than 3 injections are required.	
	61	***Safety of Viscosupplements*** Intra-articular viscosupplements are an extremely safe treatment for OA knee pain. Although on the US market since 1997, there has never been reported a patient fatality attributed to its' use. Moreover, because it is a locally acting device, has no known drug interactions, and is free of systemic side effects common to NSAIDs and intra-articular corticosteroid injections[7,8].	See comment #57.
	62	The primary adverse event associated with viscosupplements, are local reactions, which are usually transient and self-resolving. Examples include arthralgia, local joint pain and swelling, inflammation, injection site pain, and local erythema.	Thank you, the HTAS is aware of the AE profile of viscosupplementation.
	63	Overall IA-HA offers significant safety advantages over systemic OA treatments and corticosteroid injections	HTAS does not agree that viscosupplementation has a significantly different safety profile from intra-articular steroid injection.
	64	***SUPARTZ Safety Profile*** The safety of SUPARTZ was evaluated by an integrated analysis of the Intent-to-Treat (ITT) population from five, randomized, double-blind, saline-controlled multicenter trials. The most common adverse events occurring in SUPARTZ-treated patients were arthralgia, defined as joint pain with no evidence of inflammation, arthropathy/arthrosis/arthritis, defined as joint pain with evidence of inflammation, back pain, pain (non-specific), injection site reaction, headache, and injection site pain. There were no statistically significant differences in the incidence rates of these adverse events between thee saline control group and the SUPARTZ group.[4]	Thank you for this information.
	65	***Other Treatment Options*** NSAIDs Although NSAIDs are generally considered effective for OA pain, concerns about patient safety and high cost are important considerations. According to the AHRQ publication, *Managing Osteoarthritis*, nonsteroidal anti-inflammatory drugs were considered the medications of choice for osteoarthritis pain until research showed that they affect joint cartilage metabolism, have greater risk of toxicity than acetaminophen, can cause upper gastrointestinal bleeding, and may cause or aggravate peptic ulcer disease.[114] AHRQ research further showed that NSAIDs provided only a modest decrease in	HTAS is aware of the limitations and adverse events of NSAIDs.

DRAFT

Stakeholder	#	Comment	Disposition
		osteoarthritis pain and little improvement in function, and their association with ulcers, bleeding, and perforation caused a four- to five-fold increase in hospitalizations due to gastrointestinal complications. [14]	
	66	Corticosteroids Corticosteroids are not indicated for the treatment of pain whereas viscosupplements are specifically indicated to relieve pain associated with knee OA. A recent meta-analysis comparing intra-articular HA and corticosteroids concluded that although corticosteroids provide better short term relief, HA provides more sustained benefits (2-4 weeks compared to 3-6 months). [15] *Comments truncated, as word limit exceeded.*	See comment #48 regarding the Bannuru SR.
Patient/Citizen Aloha, OR	67	I am responding to the HERC DRAFTED coverage guidance that states Viscosupplementation should NOT be covered for the treatment of pain associated with Osteoarthritis (OA) of the knee. I served a vigorous career as a firefighter while maintaining an athletic lifestyle including basketball and tennis leagues. I began having pain in my knees 10 years ago and had to quit playing basketball. I tried taking ibuprophen, but the relief was always so temporary while having adverse reactions to it involving high protein in my kidnies. I continued tennis since it had less of a vertical impact on my knees. Within this last year the pain became so constant that I had to quit playing tennis as well. After multiple DR visitis I finally met with an Orthopedic surgeon and he performed a Bi-Lateral knee scope with debridement including meniscus and beginning stages of Osteoarthritis of both knees. 8-10 weeks following the surgery, I received a Synvisc 1 injection in each knee. I am still active and on my feet dayly. It has been approx 8 weeks since my injections and my pain has subsided progressively. I believe that the viscosupplement has played a vital and affective role in my pain relief and DO NOT agree with what you are proposing in not covering this procedure. I ask you, "What would be my alternative?" Should I have a $40K total knee to relieve my pain from Osteoarthritis? $80K for both knees? How about I continue conservative care such as a $160.00 knee injection in the recommended series by ALL of the viscosupplement companies. What you are suggesting in taking away conservative care COMPLETELY CONTRADICTS GOVERNOR KITZHABER and his conservative & preventative treatment initiative. Why on earth would you turn down an inexpensive knee injection when the alternative is a $40,000.00 option???	Thank you for taking the time to share your experience with this disease and treatment. HTAS is aware of the limited treatment options available to patients with OA of the knee, and is glad that you experienced a positive outcome. However, HTAS as a policy making body makes decisions based on the best available evidence, and does not believe offering a treatment that does not provide any clinically meaningful improvement in pain or function is helpful.
	68	I truly hope that you will give my agruement an honest evaluation and see that with my personal evidence of relief, and the costly alternative to the knee injection, you have made a grave error in drafting this NO COVERAGE GUIDANCE of viscosupplements. I invite your response either by email or phone call.	See comment #67.

DRAFT

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: CONTINUOUS GLUCOSE MONITORING IN DIABETES MELLITUS

DATE: XX/XX/XXXX

HERC COVERAGE GUIDANCE

Real-time continuous glucose monitoring systems should be covered for Type 1 diabetes mellitus patients with HbA1c levels greater than 8.0% or a history of recurrent hypoglycemia, for whom insulin pump management is being considered, initiated, or utilized.

Real-time continuous glucose monitoring systems should not be covered for Type 2 diabetes mellitus patients.

Retrospective continuous glucose monitoring systems should not be covered for either Type 1 or Type 2 diabetes mellitus.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

DRAFT

EVIDENCE SOURCES

Langendam M, Luijf YM, Hooft L, DeVries JH, Mudde AH, Scholten RJPM. (2012). Continuous glucose monitoring systems for type 1 diabetes mellitus. *Cochrane Database of Systematic Reviews*, Issue 1. Art. No.: CD008101. DOI: 10.1002/14651858.CD008101.pub2. Retrieved from http://summaries.cochrane.org/CD008101/continuous-glucose-monitoring-systems-for-type-1-diabetes-mellitus

Golden, S.H., Brown, T., Yeh, H.C., Maruthur, N., Ranasinghe, P., Berger, Z., et al. (2012). *Methods for Insulin Delivery and Glucose Monitoring: Comparative Effectiveness. Comparative Effectiveness Review No. 57.* (Prepared by Johns Hopkins University Evidence-based Practice Center under Contract No. 290-2007-10061-I.) AHRQ Publication No. 12-EHC036-EF. Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from www.effectivehealthcare.ahrq.gov/reports/final.cfm

The summary of evidence in this document is derived directly from these evidence sources, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Diabetes mellitus (DM) is a metabolic disorder resulting from a defect in insulin secretion, insulin action, or both. A consequence of this is chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism. Long-term complications of DM include retinopathy, nephropathy and neuropathy, and the risk of cardiovascular disease is increased. There are several types of diabetes. In type 1 DM the body is unable to produce insulin and therefore people with this type are treated with insulin. Type 1 DM accounts for 10% of cases, is typically seen at onset in children and young adults (less than 30 years), and is often referred to as insulin dependent diabetes.

Self-monitoring of blood glucose (SMBG) is an essential part of diabetes management and is used to optimize glycemic control. Regular testing of blood glucose levels allows patients with diabetes to adjust insulin dosage appropriately, and is typically done using a finger capillary blood sample and a blood glucose meter several times per day. Continuous glucose monitoring (CGM) systems measure interstitial fluid glucose levels to provide semi-continuous information about glucose levels, which may identify fluctuations that would not be identified with self-monitoring alone. Continuous glucose monitoring is considered to be particularly useful for children (to reduce the often very high number of finger punctures in this group), for patients with poorly controlled diabetes, for pregnant women in whom tight glucose control is essential with respect to the outcome of pregnancy and for patients with hypoglycemia unawareness (to prevent dangerous episodes of hypoglycemia). There are two types of CGM systems:

- those that measure the glucose concentration during a certain time span, storing the information in a monitor that can be downloaded later

- real-time systems that continuously provide the actual glucose concentration on a display.

Continuous glucose monitoring can be used continuously or intermittently (e.g., a couple of days per month or in intervals of three days). Evaluation of blood sugar control is generally done by monitoring changes in HbA1c. A clinically significant change in this value is generally considered to be 0.5%.

Evidence Review

Cochrane Review

Children

Four out of the five randomized controlled trials (RCT) that evaluated retrospective CGM systems found that HbA1c levels decreased in both the CGM and SMBG group during follow-up, while one found that HbA1c level did not change in the CGM group but decreased in the SMBG group. The mean difference between the CGM group and the SMBG group in change in HbA1c ranged from -0.5% to 0.1%, but was not statistically significant in any of the five RCTs.

Severe hypoglycemia was measured in four studies. The occurrence of events was very low, and there were no significant differences between groups. Ketoacidosis was measured in one study, but again, the number of events was very small. The one RCT that measured quality of life found no significant differences between CGM and SMBG.

All three studies that evaluated real-time systems found that the HbA1c levels in both the CGM and SMBG group declined during the study period. Three months after baseline the difference in change was statistically significant in favor of CGM (change in HbA1c -0.5% versus -0.2%). At six months and 12 months follow-up, however, the difference in change in HbA1c level was no longer significant. Another outcome examined was the proportion of patients who improved their HbA1c level by at least 0.5%, which is generally considered a change that is clinically significant. When evaluating that outcome, the proportion of patients who improved their HbA1c level by at least 0.5% was significantly larger in the CGM group at three months and at six months after baseline. The occurrence of severe hypoglycemia after six months of follow-up was somewhat lower in the CGM study arm, but the difference was not statistically significant. Ketoacidosis events did not occur at six months follow-up and rarely after 12 months follow-up. The two studies that examined quality of life found small differences that were not statistically significant.

Adolescents

The two studies that included adolescents both used real-time CGM systems. In both studies the HbA1c levels in the CGM and SMBG group declined during the study, but the differences were not statistically significant, and by six months follow-up, the differences were even less. The proportion of patients that had improved their HbA1c level by at least 0.5% was equal in both groups. Severe hypoglycemic and ketoacidotic events were infrequent, and there were no significant differences between the groups.

DRAFT

The outcomes of quality of life, patient satisfaction, diabetes complications, CGM-derived glucose control, death and costs were not measured in any of the studies in adolescents.

Adults

Change in HbA1c level was measured in two RCTs addressing retrospective CGM, neither of which found a significant difference in change between the study arms. The one study that reported severe hypoglycemia found no difference between groups.

Five studies evaluated real-time CGM systems, and found that the change in decrease in HbA1c varied between -0.1% and -1.1%, with this change being statistically significant in three of them. The same pattern was seen six and 12 months after baseline, although the number of studies was fewer. In one study, sensor usage of more than 60% was associated with HbA1c reduction, and a larger proportion of patients improved their HbA1c by at least 0.5% in the CGM group. (Compliance with protocol is generally considered to be sensor usage at least 70% of the time. Compliance varies significantly among studies, with some studies of adolescents having sensor usage as low as 30%.) One study measured HbA1c levels after 18 months follow-up and found the overall difference between groups was insignificant. Four studies measured the occurrence of severe hypoglycemia. At three months, the number of events was very low, and at six and 12 months, the risk of severe hypoglycemia was increased for CGM users, but the difference was not statistically significant. The number of ketoacidosis events was very small.

Two studies measured quality of life after six months and found the differences between the CGM and SMBG group were small and not statistically significant. Two studies investigated patient satisfaction, one after three months and one after six months follow-up, although for both, patients in the CGM group were using an insulin pump, while the SMBG used multiple daily injections of insulin. Patients in the CGM group scored significantly higher on overall satisfaction. The outcomes of diabetes complications, death and costs were not measured in any of the studies in adults.

Pregnant women with diabetes type

The only study on pregnant women with diabetes did not present the data for type 1 and type 2 diabetes separately, so it is not presented here.

Subgroup analysis

There were no studies that included patients with hypoglycemia unawareness. For studies that were limited to patients with poorly controlled diabetes (HbA1c greater than 8.0%), three were for retrospective CGM systems and four for real-time CGM. For the retrospective CGM systems, the evidence for improved glycemic control is conflicting. Significantly lower, as well as significantly higher HbA1c levels for the CGM group at the end of the study were found, and a third RCT showed no effect at all. For real-time CGM systems, there is limited evidence for improved glycemic control, with a statistically and clinically significant effect in two of the four RCTs. These two had the largest mean differences in the change in HbA1c of all studies that measured this outcome (-1.12% and -0.6%).

Meta-analysis including all age groups
There was a statistically significant larger decline in HbA1c level for real-time CGM users starting insulin pump therapy compared to patients using multiple daily injections of insulin and SMBG (mean difference in HbA1c level change from baseline -0.7%). For patients where only the CGM was a new device, the average decline in HbA1c level was also statistically significantly larger for CGM users compared to the SMBG users. However, the decline was much smaller than in the group with the sensor-augmented insulin pump: the average difference change in HbA1c was 0.2%.There were no statistically significant differences in the risk of severe hypoglycemia or ketoacidosis.

[Evidence Source]

AHRQ Review

Evidence was identified evaluating the comparative effectiveness of real-time CGM versus SMBG in individuals with type 1 diabetes only. Compared with SMBG, real-time CGM achieved a lower HbA1c, with a mean between-group difference of -0.30 percent. Slightly greater reductions occurred where sensor compliance was 60 percent or greater (mean difference of -0.36 percent). There was no difference in the rate of severe hypoglycemia or quality of life. The evidence for other outcomes was low or insufficient. For CGM that is used in combination with an insulin pump, CGM achieved a greater reduction in HbA1c compared to multiple daily injections of insulin with SMBG, with a mean between-group difference of -0.68 percent. There was no difference in the rate of hypoglycemia, but the CGM group had significantly less hyperglycemia. There were no studies of the comparative effectiveness of real-time CGM versus SMBG in individuals with type 2 diabetes.

[Evidence Source]

Overall Summary

Retrospective CGMs are not more efficacious for any outcome, in any age group. There is some evidence that real-time CGM is more effective at decreasing HbA1c in children, although this does not appear to be the case for adolescents. In adults, there is also some evidence that real-time CGM is more effective at decreasing HbA1c, although not all studies were statistically significant. The study with the longest period of follow up (18 months) found no differences. In addition, the amount of decrease in HbA1c may not be clinically significant (less than 0.5%), with two exceptions: studies that compared CGM plus insulin pump to multiple daily injections of insulin plus SMBG, and studies of poorly controlled diabetics (HbA1c > 8.0%). Two studies found no differences in quality of life, while two found increased patient satisfaction in the insulin pump plus CGM group (compared to multiple daily injections of insulin plus SMBG). There is no evidence of a difference between CGM and SMBG in the incidence of hypoglycemia or ketoacidosis. There is no evidence that addresses the effect of CGM on diabetic complications, costs or mortality.

PROCEDURE

Continuous Glucose Monitoring

DRAFT

DIAGNOSES

Type 1 Diabetes Mellitus

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
250.x1	Diabetes Mellitus, type 1, not stated as uncontrolled
250.x3	Diabetes Mellitus, type 1, uncontrolled
ICD-9 Volume 3 (Procedure Codes)	
None	
CPT Codes	
83036	Hemoglobin; glycosylated (A1C)
83037	Hemoglobin; glycosylated (A1C) by device cleared by FDA for home use
95250-1	Glucose monitoring by SQ device
97802- 97804	Medical nutrition therapy
98960-98962	Education and training for patient self-management by a qualified, nonphysician health care professional using a standardized curriculum, face-to-face, with the patient (could include caregiver/ family) each 30 minutes
99078	Physician educational services rendered to patients in a group setting (eg, prenatal, obesity, or diabetic instructions)
HCPCS Codes	
A4230-2	Insulin infusion pump supplies
A4233-6	Batteries for home blood glucose monitors
A4253	Blood Glucose test strips, box of 50
A4255	Platforms for home blood glucose monitor, 50/box
A4256	Calibrator solutions/chips
A4258	Spring-powered device for lancet, each
A4259	Lancets, per box of 100
A9274	External ambulatory insulin delivery system, disposable
A9276	Disposable sensor, CGM system
A9277	External transmitter, CGM system
A9278	External receiver, CGM system
E0607	Blood glucose monitor
E0784	Insulin infusion pump
E2100	Blood glucose monitor with voice synthesizer
E2101	Blood glucose monitor with integrated lancer
G0108-G0109	Diabetes outpatient self-management training services
G0270-G0271	Medical nutrition therapy; reassessment and subsequent intervention(s) following second referral in same year for change in diagnosis, medical condition or treatment regimen (including additional hours needed for renal disease)
S1030-1	Continuous non-invasive glucose monitoring device, purchase/rental
S9140	Diabetic management program, follow-up visit to non-MD provider
S9141	Diabetic management program, follow-up visit to MD provider

Note: Inclusion on this list does not guarantee coverage

DRAFT

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT

HERC Coverage Guidance – Continuous Glucose Monitoring in Type One Diabetes Mellitus
Disposition of Public Comments

General Comments

Stakeholder	#	Comment	Disposition
Medtronic Diabetes Northridge, CA	1	On behalf of Medtronic Diabetes, I am pleased to submit this response to the Oregon Health Evidence Review Commission and Health Technology Assessment Subcommittee with respect to the Draft Coverage Guidance on Continuous Glucose Monitoring. Medtronic appreciates the work Oregon HERC and HTAS has put forth this far to draft Coverage guidance for Continuous Glucose Monitoring.	Thank you for taking the time to comment.
	2	Based on the compelling and continually expanding data and trial results supporting the clinical value of CGM for patients with diabetes, we are in support of the draft guidance recommended at the June 25th meeting for Personal/Real-Time CGM. The guidance states that Personal/Real-Time CGM "should be covered for Type 1 diabetes mellitus patients with a history of recurrent hypoglycemia or HbA1c >8 for whom insulin pump management is being considered, initiated, or utilized.	Thank you for your comment.
	3	Medtronic however, does not agree with the recommendation on Retrospective (Professional) CGM. We do suggest that this device should be covered. Retrospective CGM provides Health Care Providers significant and meaningful insight to glucose patterns that otherwise would not be available. Health Care Providers utilize the data to help guide therapy, modify treatment regimens, and teach patients how food, activity, and personal involvement impacts their ability to better manage their disease. In addition, by not continuing to cover professional services (95250 and 95251) it would create disparity of care for the patients served in Oregon. All other payer entities in the state of Oregon including Medicare and all private/commercial payers including United Healthcare, Aetna, Cigna, Humana, Health Net, and Wellpoint/Anthem have coverage and payment for Retrospective CGM. We strongly urge HERC to continue to maintain coverage on line 10 of the Prioritized List of Services for Type 1 diabetes, and recommend that it be included for any insulin treated diabetes patient	The evidence source did not find a statistically significant difference in HbA1c levels or hypoglycemia in any trial that compared a retrospective CGM to control. The HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies.
	4	**Professional (Retrospective) CGM** **95250** Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording **95251** Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; interpretation and report	HTAS is aware of these CPT codes.
	5	Studies have shown that retrospective CGM detects glycemic excursions that were missed with SMBG and is particularly well suited to detecting asymptomatic hypoglycemia. CGM detected a longer duration of hypoglycemia than SMBG[1] and identified episodes of postprandial hyperglycemia[2, 3, 4] nocturnal hypoglycemia[5, 6, 7, 8] and asymptomatic hypoglycemia[9, 10] that were frequently not identified by SMBG. In a study of elderly individuals with well-controlled Type 2 diabetes, CGM captured 103 episodes of hypoglycemia in 20 patients over four 72-hour periods of monitoring and detected elevated postprandial glucose levels after 57% of meals.[11] None of the hypoglycemic episodes detected by CGM, many of which occurred at night, were recorded in patients' diaries. CGM is the best tool for detecting episodes of asymptomatic and nocturnal hypoglycemia, both of which	The citations listed were published before the date of the Cochrane review (last search date June 2011). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or

DRAFT

Stakeholder	#	Comment	Disposition
		tend to occur more frequently in patients who have hypoglycemia unawareness.[12]	excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	6	Studies document the following benefits of CGM: • CGM detects glycemic excursions missed with SMBG. Studies have shown that CGM detects glycemic excursions that were missed with SMBG and is particularly well suited to detecting asymptomatic hypoglycemia. CGM detected a longer duration of hypoglycemia than SMBG, [13] and identified episodes of postprandial hyperglycemia, [14, 15, 16] nocturnal hypoglycemia, [17, 18, 19, 20] and asymptomatic hypoglycemia[21, 22] that were frequently not identified by SMBG. CGM is the best tool for detecting episodes of asymptomatic and nocturnal hypoglycemia, both of which tend to occur more frequently in patients who have hypoglycemia unawareness.[23]	Assuming commenter is referring to retrospective CGM, see comment #5
	7	• CGM improves diabetes management. The identification of glycemic excursion patterns can be used to reduce the incidence of hyperglycemia and hypoglycemia by making changes to patients' diabetes management plans, including 1) altering the insulin-to-carbohydrate ratio, 2) altering the basal insulin regimen, 3) using glucose tablets instead of food or juice to treat hypoglycemia, 4) reducing the amount of supplemental insulin needed to correct elevated blood glucose values, and 5) changing patients' approaches to exercise. [24, 25]	Assuming commenter is referring to retrospective CGM, see comment #5
	8	• CGM improves diabetes outcomes. A substantial body of research has demonstrated that use of CGM by both adults and children can decrease A1C.[26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36]	Assuming commenter is referring to retrospective CGM, see comment #5
	9	Evidence of CGM benefits is further reflected in professional standards. The AACE Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus include the following recommendation on use of CGM in type 1 diabetes: • Arrange for continuous glucose monitoring for patients with T1DM with unstable glucose control and for	HTAS does not disagree with the use of CGM. The guideline referenced by the commenter does not specify that CGM should be retrospective.

DRAFT

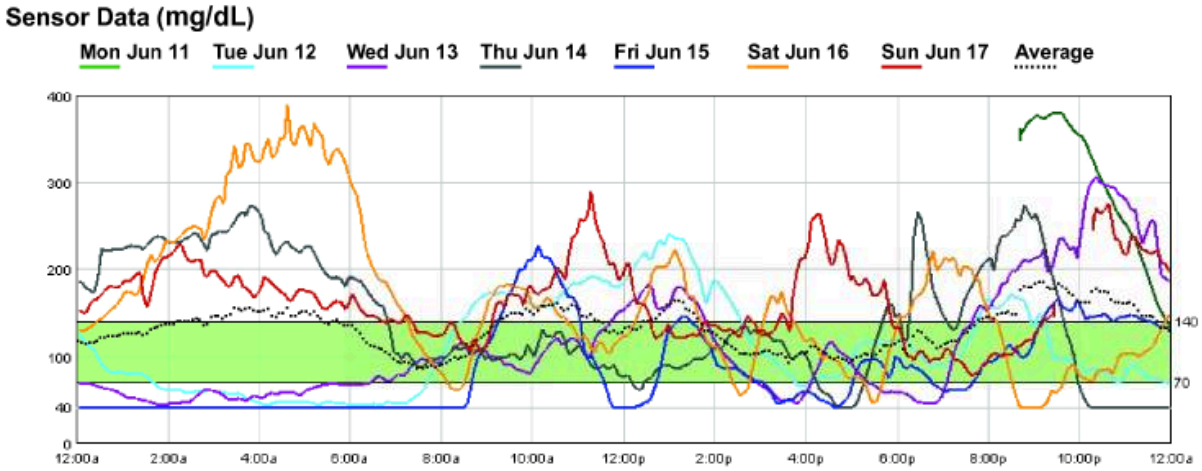
Stakeholder	#	Comment	Disposition
		patients unable to achieve an acceptable HbA1C level; continuous glucose monitoring is particularly valuable in detecting both unrecognized nocturnal hypoglycemia and postprandial hyperglycemia.[37]	
	10	The ADA's Standards of Medical Care in Diabetes - 2012 make the following CGM recommendations (Levels "A", "C", and "E", respectively)[38]: • Continuous glucose monitoring (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. (A) • 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.	See comment #9
	11	We hope that Oregon Health Authority finds this information useful in evaluating the benefits of continuous glucose monitoring technology. Should you have any questions regarding this information, please contact me.	Thank you for your comment.
Physician, Associate Professor Portland, OR	12	The purpose of this letter is to provide my opinion on the Draft Coverage Guidance on Continuous Glucose Monitoring by the Oregon Health Evidence Review Commission and Health Technology Assessment Subcommittee. Based on several clinical trials regarding the use of CGM in patients with diabetes, I am in full support of the draft guidance recommended at the June 25th meeting for Personal/Real-Time CGM. The guidance states that Personal/Real-Time CGM "should be covered for Type 1 diabetes mellitus patients with a history of recurrent hypoglycemia or HbA1c >8 for whom insulin pump management is being considered, initiated, or utilized.	Thank you for taking the time to comment.
	13	I am a specialist in diabetes and I see patients at the [*clinic name removed*] diabetes clinic. I believe that such a policy will help to minimize hypoglycemia and hyperglycemia in persons with type 1 diabetes, will minimize acute and chronic complications, and will thus improve their short-term and long-term quality of life.	Thank you for your comment.
JDRF Washington, DC	14	JDRF applauds the efforts of Health Technology Assessment Subcommittee (HTAS) in developing the draft guidance on CGM for Type 1 Diabetes. As JDRF's previous letter of June 21, 2012 to the HTAS indicates, we support broad coverage of CGM for those with type 1 diabetes (T1D), based on the extensive evidence of clinical benefit, the recommendations of all leading diabetes clinical care guidelines, and data on cost effectiveness. The Subcommittee's proposed draft guidance states that Personal/Real-Time CGM should be covered for Type 1 diabetes mellitus patients with a history of recurrent hypoglycemia or HbA1c >8 for whom insulin pump management is being considered, initiated, or utilized'. We believe this language is consistent with the clinical trial data from the 2006 JDRF funded trial and the series of published papers detailing the findings of the trial since 2008 highlighting the clinical effectiveness of CGM.	Thank you for taking the time to comment.
	15	JDRF however, has concern with the recommendation that retrospective (professional) CGM devices should not be covered and respectfully suggests that this language be reconsidered. We believe that retrospective CGM provides clinicians with critical insight to glucose excursions that otherwise would not be available. Patients'	The evidence source did not find a statistically significant difference in HgA1c levels or hypoglycemia in any

DRAFT

Stakeholder	#	Comment	Disposition
		doctors utilize the data to help guide therapy, modify treatment regimens, and teach patients how food, activity, and personal involvement impacts their ability to better manage their disease.	trial that compared a retrospective CGM to control.
	16	In addition, eliminating coverage would create disparity of care for the patients served in Oregon. All other payer entities in the state of Oregon including Medicare and all private/commercial payers including United Healthcare, Aetna, Cigna, Humana, Health Net, and WellPoint/Anthem have coverage and payment for Retrospective CGM. Thank you again for consideration of our comments.	The HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies.
Physician, Director of a diabetes health center Portland, OR	17	Thank you for your efforts in developing the guidance document on continuous glucose monitoring. I also greatly appreciated the opportunity to address the group at your meeting in June. I agree with your recommendations concerning the real-time continuous glucose monitoring systems. This is an important tool in the care of patients with type 1 diabetes that would be used sparingly and selectively to the benefit of appropriate subjects.	Thank you for taking the time to comment.
	18	During the June meeting I did not have time to comment on retrospective CGM. The guidance document refers to the lack of evidence for benefit and recommends against coverage for this tool. Although it is true that RCTs have not clearly shown benefit of retrospective CGM with regard to A1c reduction, for those of us who have used it, experience says it is a very important tool for some patients. I believe the manufacturers have not promoted extensive research in this are because the focus has been on real-time CGM. Nevertheless, most payers including Medicare have readily recognized the value of this technology. The cost is relatively low. There is plentiful evidence that CGM will identify unrecognized glucose fluctuations and hypoglycemia. The concept and intent are different than when using real-time CGM. Real-time CGM helps patients make moment-to-moment decisions on glucose values and trends as well as offering education when used to review the tracings. The emphasis with retrospective CGM is on identification of patterns that can be used by the provider to educate patients and to make safe adjustments in insulin. Most importantly, it identifies unrecognized hypoglycemia that is potentially life threatening. This is particularly important considering the fact that hypoglycemia is thought to be one of the leading causes of death in young individuals with type 1 diabetes. I have personally experienced at least a half-dozen patient deaths due to hypoglycemia and many others who have had severe injuries and other major consequences.	HTAS appreciates the concern about hypoglycemia, however, the evidence source did not find a significant difference in episodes of hypoglycemia in any trial that compared a retrospective CGM to control.
	19	Sometimes a single picture is worth a thousand words so I am including the following images from a retrospective CGM tracing done several days prior to the June meeting on a 30 year old teacher who was not aware of more than rare nocturnal hypoglycemia: [*Graph located on next page*]	While anecdotal experience has a strong influence on individual opinion, it is inherently susceptible to bias. High quality RCTs are the best way to assess true treatment effects, and the evidence examined by HTAS does not support the efficacy of retrospective CGM.

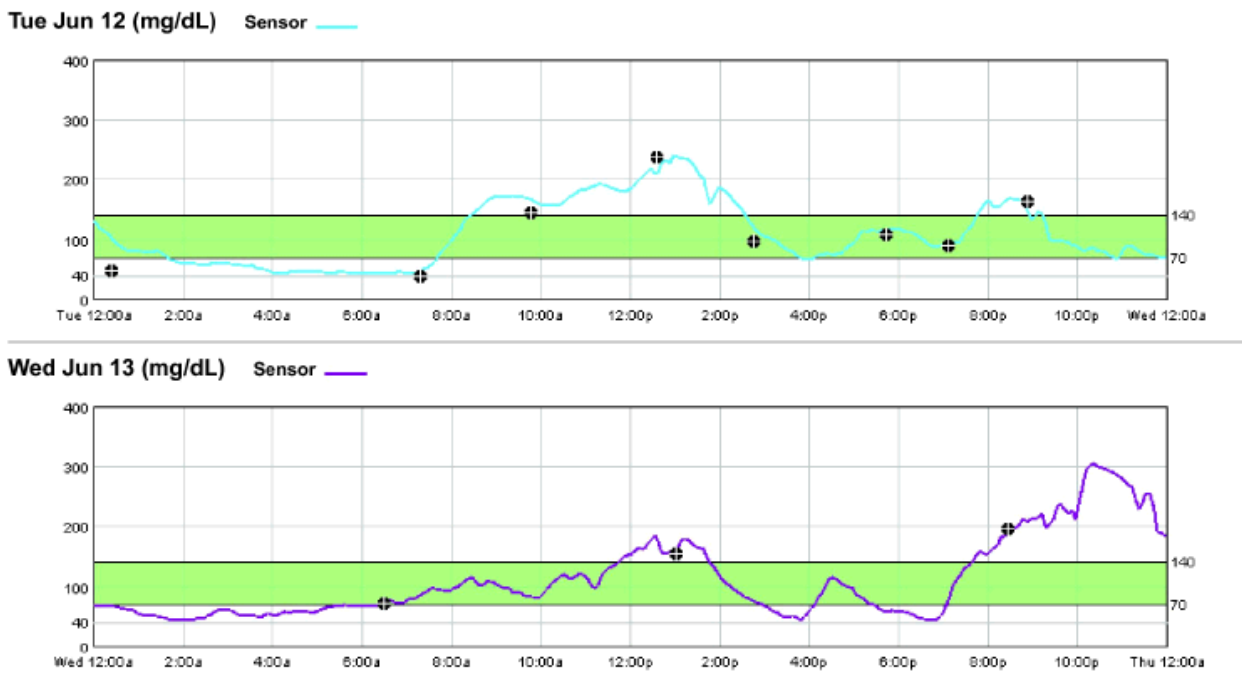
DRAFT

Stakeholder	#	Comment	Disposition



	Mon Jun 11	Tue Jun 12	Wed Jun 13	Thu Jun 14	Fri Jun 15	Sat Jun 16	Sun Jun 17	Average / Total
# Sensor Values	40	288	288	288	288	288	279	1,759
Highest	380	240	306	274	227	389	290	389
Lowest	135	43	44	40	40	40	78	40
Average	297	110	111	144	83	163	165	133
Standard Dev.	79	53	66	69	49	83	45	74
MAD %	2.1	22.5	8.4	21.5	27.6	11.2	6.5	17.3
Correlation	N/A	0.96	0.99	0.94	0.74	N/A	1.00	0.96
# Valid Calibrations	2	8	3	4	7	5	4	33
Designation	X				X			

X: Use Clinical Judgment S: No Sensor Data C: No Calibration BG's

Stakeholder	#	Comment	Disposition
	20		See comment #19
	21	This type of tracing is paired with a diary to indicate food intake, activity, insulin doses and other relevant events. As you can see, this patient had highly significant nocturnal hypoglycemia (< 50 mg/dl) on 3 of the 7 days tested by a retrospective sensor. She had no symptoms on any of these nights. It was frightening to find that she remained at dangerous levels of hypoglycemia for many hours during the night. This was definitely life-threatening and led to significant reductions in her insulin pump basal rates at night despite the fact that they were already much lower than daytime rates. I would like to think we avoided what would otherwise have been an eventual seizure or even a potential fracture falling out of bed or worst case, an arrhythmia.	See comment #19
	22	This is just one of many cases where findings on a retrospective CGM study resulted in important changes in therapy to improve safety or glucose control. In fact, I would estimate that >95% of such studies guide the provider to change insulin or behaviors to the benefit of the patient.	Thank you for providing your clinical opinion.
	23	Trying to help relate retrospective CGM to other common, covered procedures, I would have you consider ECGs, PFTs or possibly sleep studies. My guess is that ECGs in asymptomatic patients have never been shown to reduce the frequency of cardiac events by today's standards of evidence. Likewise, while PFTs can identify problems and guide therapy, they have likely never been subjected to RCT to show they directly improve outcomes.	HTAS has not reviewed the evidence on ECGs or PFTs, but would require the same rigorous evaluation if they did.

Stakeholder	#	Comment	Disposition
	24	I would be happy to provide literature to highlight studies showing identification of unrecognized long exposure to hypoglycemia if requested by the committee. The fact that most attention and studies have focused on real-time CGM speaks more to the business plans of device companies than to the potential advantage for patient care. Although you may want to restrict the use to specific situations and only with a limited frequency, I believe this is a tool that will not be costly and will serve patients and experienced type 1 diabetes providers well. Please consider a change in your recommendations.	Thank you for your comment. HTAS appreciates that impact of business on driving the research agenda, but notes that the evidence is not entirely lacking for retrospective CGM, with 7 studies in the evidence source.
Citizen/Patient Portland, OR	25	I am writing in response to the proposed coverage guidance for continuous glucose monitoring (CGM) use by people with Type 1 diabetes. I applaud your proposed coverage of CGM for people who are having trouble bringing their HbA1c below 8.0 and for recurrent hypoglycemia. The use of a CGM has been repeatedly shown to help improve blood sugar control and lower HbA1c values. However, as a diabetic for over 15 years, and the father of a child with diabetes since age 5 (now 21), I can tell you that long term blood glucose control is only one (albeit very important) measure of successfully managing Type 1 diabetes. Equally important measures are the ability to reduce or eliminate dangerous high blood sugars, severe low blood sugars, the forewarning of potential ketoacidosis, effective sick day management, and finally, quality of life (the ability to sleep well without worrying about undetected hypoglycemia, for instance).	Thank you for taking the time to comment.
	26	CGM use can aid in weight management and exercise by allowing more confidence that lack of eating or heavy/prolonged exercise will result in severe lows. Importantly, where the proposed guidance is concerned, these benefits are equally important to those who have consistently maintained an HbA1C below 8.0 as to those whose HbA1c is above 8.0.	Thank you for sharing your opinion. HTAS believes the importance of lowering HbA1c is greater in patients with levels > 8.0.
	27	Although hypoglycemia is rightly cited as a reason for including coverage for CGM use, the absence of recorded hypoglycemic events should not be a reason to deny coverage for those with high or low HbA1c values. First, there is good evidence that many Type 1 diabetics do not capture the occurrence of many low blood sugar events through standard blood glucose monitoring: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group - Prolonged Nocturnal Hypoglycemia Is Common During 12 Months of Continuous Glucose Monitoring in Children and Adults With Type 1 Diabetes. *Diabetes Care May 2010 33:1004-1008*	HTAS does not debate the fact that diabetes do not capture many low blood sugar events. The Cochrane review identified four studies that measured the occurrence of severe hypoglycemia. At three months, the number of events was very low, and at six and 12 months, the risk of severe hypoglycemia was actually increased for CGM users, but the difference was not statistically significant.
	28	Those who are able to successfully use a CGM to either better control their diabetes, resulting in a lower HbA1c and avoiding recurrent hypoglycemia (the two qualifying criteria), should not be dropped from coverage of CGM	*For HTAS discussion.*

DRAFT

Stakeholder	#	Comment	Disposition
		use due to that success.	
	29	The single study referenced in the guidance focused primarily on "average blood glucose level" as expressed in the measured HbA1c. Although mentioning the importance of hypoglycemia (and an attempt to measure the occurrence) it was not deemed significant due to the low number of events which precluded their evaluation. There are other studies however, that have confirmed the benefits of CGM use in patients with well controlled glucose (HbA1c < 7.0) and in those with poorly controlled diabetes in terms of avoiding severe or prolonged hypoglycemia:	It is not clear what single study the commenter is referring to. The guidance references the Cochrane review which is a full systematic review of the evidence and includes a total of 22 studies.
	30	"An additional important observation was the remarkably low rate of severe hypoglycemic events during the extension phase of the study. The rate of severe hypoglycemia in our CGM subjects with a mean A1C of 6.8% during the 6-month extension phase was markedly lower than the rate of severe hypoglycemia in the Diabetes Control and Complications Trial (DCCT) intensive treatment group, which had mean A1C of 7.1% (7 vs. 62 events per 100 person-years) (6). The total absence of severe hypoglycemia during the second 6 months of the study in the subjects who had a baseline A1C <7.0% is particularly striking, especially because these subjects were able to maintain a mean A1C of 6.4%. It is possible that the decline in severe hypoglycemic events during the second 6 months of the study resulted from learning from prior experience, including appropriate setting of the low alarms, glucose targets, and titration of basal and bolus insulin doses. It is also intriguing to speculate that the reduction in exposure to biochemical hypoglycemia over the 12 months of the study may have protected subjects from severe hypoglycemic events by enhancing their counterregulatory hormone defense mechanisms against hypoglycemia (7)." The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group - Sustained Benefit of Continuous Glucose Monitoring on A1C, Glucose Profiles, and Hypoglycemia in Adults With Type 1 Diabetes. *Diabetes Care November 2009 32:2047-2049*	The citations listed were published before the date of the Cochrane review (last search date June 2011). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	31	We are only beginning to understand all the benefits of tight glucose control and the effects of hypoglycemia on the body, and some studies point to a possible link to development of atherosclerosis. Marga Giménez, Rosa Gilabert, Joan Monteagudo, Anna Alonso, Roser Casamitjana, Carles Paré, and Ignacio Conget - Repeated Episodes of Hypoglycemia as a Potential Aggravating Factor for Preclinical Atherosclerosis in Subjects With Type 1 Diabetes. *Diabetes Care January 2011 34:198-203*	See comment #30
	32	As a CGM user for approximately 2 years, I can tell the HERC that the use of a CGM has made my day to day life with diabetes more predictable, more successful, and more enjoyable. I believe that the use of a CGM has	Thank you for sharing your

DRAFT

Stakeholder	#	Comment	Disposition
		reduced the likelihood that I would end up in the hospital for dehydration during sick days (ketones with low blood sugar being a surprising and challenging situation to deal with) and allowed me to be a more confident and successful public servant. I believe that every person with Type 1 diabetes should be encouraged to use a CGM if they have a need, the inclination, and the motivation.	perspective.
	33	For these reasons, I believe the use of a CGM is warranted and beneficial for all with Type 1 diabetes in terms of safety, in terms of quality of life and in terms of long term health benefits and saving of health care costs. The coverage of CGM use should be possible regardless of whether one's HbA1c is above or below 8.0, or their success in avoiding (and success in documenting) recurrent hypoglycemia. Thank you for considering these comments.	Thank you for sharing your perspective.
	34	Please note there are typos on pages 2 and 4 of the proposed guidance where HbA1c is mistakenly shown as HgA1c or HgbA1c.	Thank you, typos have been corrected.
American Diabetes Association Oregon Office Portland, OR	35	The American Diabetes Association (Association) is pleased to provide additional comments to the Commission regarding the Draft Coverage Guidance on Continuous Glucose Monitoring (CGM) in Type 1 Diabetes, **and** to address particular questions posed by members of the Commission to the Association during the June 25 hearing. We appreciate your willingness to consider additional information from the Association before revising the Coverage Guidance for Self-Monitoring of Blood Glucose (SMBG) for Type 1 and Type 2 Diabetes, and we are pleased to respond to your request. [***Comments regarding SMBG will be addressed in a separate disposition***.]	Thank you for your comments.
	36	**V. Comments in response to the Draft Coverage Guidance: Continuous Glucose Monitoring in Type 1 Diabetes Mellitus issued on July 10, 2012** The Association's *Standards of Medical Care in Diabetes – 2012* includes the following recommendations: • CGM in conjunction with intensive insulin regimens can be a useful tool to lower A1C in selected adults age 25 and over 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. • In addition, CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes.	HTAS believes that the current coverage guidance supports these stated standards.
	37	The revised Draft Coverage Guidance on Continuous Glucose Monitoring in Type 1 Diabetes issued on July 10 includes the following recommendation: Real time CGM systems should be covered for Type 1 diabetes mellitus patients with a history of recurrent hypoglycemia or HbAlc > 8% for whom insulin pump management is being considered, initiated or utilized. We note that research has shown benefits for CGM in individuals with type 1 diabetes on intensive insulin therapy (*either* an insulin pump or multiple daily injections).[3] ***Thus, we recommend adding "multiple daily insulin injections or" after the words "for whom" in the Coverage Guidance document to include individuals on multiple daily injections of insulin.***	HTAS acknowledges that CGM has been shown to have a statistically significant beneficial effect on HbA1c in both insulin pump and MDI populations, however, the improvements in HbA1c are generally not considered clinically significant in the MDI patients (-

Stakeholder	#	Comment	Disposition
			0.30% to -0.36%), and there have been no studies that found improvements in quality of life, hypoglycemia, diabetic complications or mortality in this patient population.
	38	Diabetes is a complex disease to manage and can lead to short and long term complications. The goal of diabetes care is to avoid the devastating and costly complications of the disease. The costs associated with diabetes, including diagnosed and undiagnosed diabetes, prediabetes, and gestational diabetes, and their complications, accounted for $218 billion in direct and indirect costs in 2007 alone. Much of the economic burden of diabetes is related to its complications including blindness, amputation, kidney failure, heart attack, and stroke. Yet, we have made major strides in effectively managing diabetes and reducing the risk for these devastating – and costly – complications through necessary medical care, medications and other tools, patient self-management, education, and support. We appreciate the opportunity to provide comments to the Commission as it develops Coverage Guidance documents for CGM and SMBG. The Association looks forward to reviewing the revised Coverage Guidance documents.	HTAS is aware of the complexity of diabetes management, and believes that the guidance as currently written provides the needed flexibility in patient management. Thank you for taking the time to provide the HTAS with this information.

DRAFT

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: MRI FOR BREAST CANCER DIAGNOSIS

DATE: XX/XX/XXXX

HERC COVERAGE GUIDANCE

In women with recently diagnosed breast cancer, preoperative or contralateral MRI of the breast should not be a covered service.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. In addition to an evidence-based guideline developed by the Evidence-based Guideline Subcommittee and a health technology assessment developed by the Heath Technology Assessment Subcommittee, coverage guidance may utilize an existing evidence report produced in the last 5 years by the Agency for Healthcare Research and Quality, the Medicaid Evidence-based Decisions Project or the Washington Health Technology Assessment Program.

EVIDENCE SOURCE

Washington State Health Care Authority Health Technology Assessment Program. (2010). *HTA Report: Breast MRI in diagnosis and treatment of cancer in women at high risk*. Olympia, WA: Health Technology Assessment Program.Retrieved from http://www.hta.hca.wa.gov/documents/breast_mri_072310_final.pdf

The summary of evidence in this document is derived directly from this evidence source, and portions are extracted verbatim.

DRAFT

SUMMARY OF EVIDENCE

Clinical Background

In 2009, an estimated 192,370 cases and 40,170 deaths occurred in women with breast cancer. In 2002, the United States Preventive Services Task Force found adequate evidence of film mammography's sensitivity and specificity and evidence of mammography's effectiveness in decreasing breast cancer mortality in women at average risk and concluded that film mammography was the standard for detecting breast cancer in women at average risk of developing breast cancer. In women recently diagnosed with breast cancer, MRI has been used to evaluate the contralateral breast, and has also been used to assist with treatment planning prior to definitive treatment. Whether these uses of breast MRI improve patient outcomes is not clear, and is the focus of this report.

Evidence Review

Detecting Contralateral Breast Cancer in Women Recently Diagnosed
MRI detects contralateral breast lesions in a substantial proportion of women with breast cancer, but does not reliably distinguish benign from malignant findings. This evidence review identified the following results:

- Detection of suspicious findings (true positives plus false positives): 9.3% (95% CI, 5.8% to 14.7%)
- Incremental cancer detection rate (ICDR): 4.1% (95% CI, 2.7% to 6.0%)
- PPV, 47.9% (95% CI, 31.8% to 64.6%)
- True positive: false positive ratio, 0.92 (95% CI, 0.47 to 1.82).

Some women will undergo treatment changes based on false positive tests, with one study reporting that 6.9% of women with changes in treatment based on MRI were found to have benign lesions. There were no RCTs which assessed the effect of adding MRI to conventional breast cancer screening on mortality rates.

Changes in Treatment in Women with Recently Diagnosed Breast Cancer
Preoperative MRI testing in women with recently diagnosed breast cancer will change treatment plans for some women (15.7%). Conversion of wide local excision to more extensive surgery will occur in up to 11.3% of women, and conversion from wide excision to mastectomy will occur in up to 8.1% of women. In women with breast cancer with dense breast tissue, microcalcifications suspicious for carcinoma in situ or discordance between mammography and ultrasound, MRI may add clinical information which may alter treatment plans (44.3% of the time in one retrospective observational study).

Changes in Treatment – Incomplete Excision
Adding MRI will change treatment plans and result in more extensive surgery for some women, but may not change incomplete excision rates or breast cancer recurrence

DRAFT

rates. The evidence is insufficient to determine whether MRI affects the rate of incomplete cancer excision because it is conflicting. One study found no difference between groups while another found an 18% decrease in re-excision rates in women who underwent MRI preoperatively. The study reporting of no difference between groups may have been underpowered to find a difference if one existed. The evidence is insufficient to determine whether changes in treatment plans based on the results of preoperative MRI testing are beneficial.

Changes in Treatment – Recurrence Rates

The evidence regarding the effect of preoperative MRI testing in women with early invasive breast cancer on recurrence rates is inconclusive. One retrospective observational study reported a 5.6% reduction in recurrence rates in patients receiving preoperative MRI before breast conservation surgery. Another larger observational study found that MRI was not associated with a lower recurrence rate or 8-year rate of local failure.

Safety

Gadolinium-based MRI contrast agents appear to be safe. There is no evidence of adverse events associated with MRI radiation exposure. We found no evidence that breast implants increase the risk of developing breast cancer. The evidence is insufficient to conclude that false-positive breast cancer screening or testing results lead to clinically meaningful negative psychological outcomes.

Technical and Provider Issues in MRI Testing

The evidence is insufficient to establish technical MRI specifications or provider qualifications.

[Evidence Source]

Overall Summary

MRI of the breast identifies contralateral breast lesions in women who have been recently diagnosed with breast cancer and may result in a change in treatment plans, but some women will undergo those changes based on false positive tests, and whether those changes are beneficial is unknown. Preoperative MRI testing in women with recently diagnosed breast cancer may change treatment plans, but there is no clear evidence that it changes incomplete excision rates or breast cancer recurrence rates. There is no evidence of a benefit on mortality with contralateral or preoperative MRI of the breast.

PROCEDURE

MRI of the Breast

DIAGNOSES

Breast cancer

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Codes	
V10.3	Personal history of malignant neoplasm, breast
V16.3	Family history of malignant neoplasm, breast
V76.10	Special screening for malignant neoplasms, breast, unspecified
V76.19	Special screening for malignant neoplasms, breast, other screening breast examination
V84.01	Genetic susceptibility to malignant neoplasm of breast
ICD-9 Volume 3 (procedure codes)	
None	
CPT Codes	
77058	MRI breast, with or without contrast, unilateral
77059	MRI breast, with or without contrast, bilateral
HCPCS Codes	
C8903	Magnetic resonance imaging with contrast, breast; unilateral
C8904	Magnetic resonance imaging without contrast, breast; unilateral
C8905	Magnetic resonance imaging without contrast followed by with contrast, breast; unilateral
C8906	Magnetic resonance imaging with contrast, breast; bilateral
C8907	Magnetic resonance imaging without contrast, breast; bilateral
C8908	Magnetic resonance imaging without contrast followed by with contrast, breast; bilateral

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

HERC Coverage Guidance – MRI for Breast Cancer Diagnosis
Disposition of Public Comments

General Comments

Stakeholder	#	Comment	Disposition
	1	No public comments were received for this topic.	

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: DIAGNOSIS OF SLEEP APNEA IN ADULTS

DATE: XX/XX/XXXX

HERC COVERAGE GUIDANCE

The following diagnostic tests for Obstructive Sleep Apnea (OSA) should be covered for adults:

1. Type I PSG is covered when used to aid the diagnosis of OSA in patients who have clinical signs and symptoms indicative of OSA if performed attended in a sleep lab facility.

2. Type II or Type III sleep testing devices are covered when used to aid the diagnosis of OSA in patients who have clinical signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.

3. Type IV sleep testing devices measuring three or more channels, one of which is airflow, are covered when used to aid the diagnosis of OSA in patients who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.

4. Sleep testing devices measuring three or more channels that include actigraphy, oximetry, and peripheral arterial tone, are covered when used to aid the diagnosis of OSA in patients who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

DRAFT

Coverage guidance development follows to translate the evidence review to a policy decision. In addition to an evidence-based guideline developed by the Evidence-based Guideline Subcommittee and a health technology assessment developed by the Heath Technology Assessment Subcommittee, coverage guidance may utilize an existing evidence report produced in the last 5 years by the Agency for Healthcare Research and Quality, the Medicaid Evidence-based Decisions Project or the Washington Health Technology Assessment Program.

EVIDENCE SOURCE

Gleitsmann, K., Kriz, H., Thielke, A., Bunker, K., Ryan, K., Lorish, K., & King, V. (2012). *Sleep apnea diagnosis and treatment in adults.* Portland, OR: Center for Evidence-based Policy, Oregon Health and Science University. Retrieved from http://www.hta.hca.wa.gov/documents/sleep_apnea_final_report.pdf

The summary of evidence in this document is derived directly from this evidence source, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Obstructive sleep apnea (OSA) refers to sleep-disordered breathing due to the recurrent collapse of pharyngeal tissues resulting in snoring, fitful sleep, and daytime somnolence. These episodes are characterized by either reduced airflow (hypopnea), or a complete obstruction (apnea), with a subsequent drop in oxygen saturation, interfering with gas exchange. Obstructive sleep apnea is a cause of significant morbidity and mortality and is associated with hypertension, neuropsychological impairment, motor vehicle accidents, stroke, cardiovascular disease, diabetes, and decreased quality of life. The prevalence of OSA is 2% to 7% in the general adult population. Prevalence increases steadily with age, to approximately 20% among people older than age 60.

Risk factors for OSA include male gender, age, obesity, airway characteristics, familial/genetic predisposition, smoking, and alcohol consumption. The majority of patients with OSA are asymptomatic, unaware of their sleep disordered breathing and associated health risks.

The diagnosis as well as the treatment of OSA is complicated by the difficulty in defining the syndrome. There is controversy surrounding the parameters to be used in a clinical definition as well as which diagnostic method is most appropriate to detect OSA. The current standard for diagnosing OSA is polysomnography (PSG) administered in a sleep study facility. The frequency of obstructed breathing events (i.e., the apnea-hypopnea index (AHI)), combined with multiple other clinical features of obstruction (e.g., oxygen desaturation, air flow, choking episodes) are recorded during sleep. A diagnosis of OSA is generally made when AHI is greater than or equal to 15 or greater than 5 with noticeable daytime symptoms. Considerable costs and patient inconvenience are involved in a PSG study. Portable PSG monitors, various

questionnaires, and predictive models using anatomic and demographic variables have been developed to aid in screening candidates for referral for further diagnostic testing (e.g., sleep lab PSG).

Evidence Review

Diagnosing OSA: The "Gold Standard"
Most experts consider laboratory-based PSG to be the reference standard for measuring Apnea-Hypopnea Index (AHI) in order to diagnose OSA. However, there are significant challenges that can be raised in considering PSG to be the "gold standard". This would imply that this test is essentially error-free and therefore has the ability to prognosticate patients diagnosed with OSA from those without OSA. No current established threshold level for AHI exists that indicates the need for treatment. Furthermore, several facets raise uncertainty regarding PSG's place as the diagnostic "gold standard":

- There are variations across laboratories in the definitions of OSA (using different thresholds of AHI, from 5 to 15 events/hr) and in the way that the PSG results are read and interpreted.
- Apnea-Hypopnea Index, which is used as the single metric to define OSA, can vary from night to night and does not take into account symptoms, comorbidities, or response to treatment.
- Apnea-Hypopnea Index has variable value as a predictor of clinical outcomes:
    - The strength of evidence is high (based on four trials) that high baseline (AHI>30 events/hr or range) AHI is a strong and independent predictor of all-cause mortality over several years of follow-up (2-14 years).
    - The association between baseline AHI and the other long-term clinical outcomes is less robust, having been analyzed by only one or two studies:
        - Cardiovascular (CV) disease (studies reported mixed results regarding CV death, but AHI >30 was an independent predictor of nonfatal CV disease.
        - Stroke (one study suggested that the association between AHI and stroke may be confounded by obesity).
        - Hypertension (studies had uncertain conclusions regarding the possible association between AHI and incident hypertension)
        - Non-insulin-dependent diabetes and other metabolic abnormalities (studies reported mixed results that suggested an association between AHI and incident type 2 diabetes which, in one study, was confounded by obesity)
        - Decreased quality of life (a single study found no significant association between AHI and future quality of life [SF-36 after 5 years]).
- No current established threshold level for AHI exists that indicates the need for treatment.

DRAFT

In addition to the uncertainty surrounding the clinical utility of the AHI, the measurement of this index is also subject to several sources of variability. Airflow measurements are assessed by different instruments between laboratories and are subject to variation depending on the extent of mouth breathing in the subject. Oxygen saturation sampling is also measured by different types of oximeters using different methods of sampling, and other probes which measure respiratory movements and EEGs may differ between labs.

Interpretation of the PSG results is another area of potential uncertainty. Manual versus automated PSG scoring in the same lab may yield different results. Intra- and inter-rater variability may be problematic, and the definition of hypopnea varies, which results in different AHI measurements.

Repeatability and reproducibility of PSG measurements are also a concern. Serial studies with the same patient in the same lab may result in differential classifications, especially in patients whose AHI scores are close to the OSA diagnostic cut-off point.

Polysomnograms on the same patient in different labs would be expected to have even more variation due to differing measurement apparatus.

Based on the limitations of the test as described, it is clear that while lab-based PSG indices provide the current reference standard, they alone are not a “gold standard” for diagnosing OSA. Even so, clinicians agree that from a pragmatic point of view, the PSG information is important in the management of patients with disturbed sleep. Interestingly, no “strength of evidence” was assessed for this test, although it is the reference standard used throughout this report.

Methods of Measurement
Diagnosing OSA by detailing obstructive episodes is done using a variety of types of monitors in either the laboratory or home setting, and are categorized as follows:

- Type I: PSG in sleep facility
- Type II: Portable recording; same information as Type I (3 sleep arousal channels and minimum of 2 respiratory information channels)
- Type III: Portable recording; minimum of 2 respiratory channels (with no channels which differentiate waking and sleeping)
- Type IV: Portable monitors that fail Type III criteria

Compared to the current diagnostic standard (PSG), the strength of evidence is low that that Type II monitors can accurately diagnosis OSA, although there is wide variation in estimating the actual AHI, with discrepancies between the monitors and PSG as wide as negative 36 to positive 36 events/hr. In one study, the difference between the two measurements was dependent on their average value, with the portable monitor over estimating laboratory-based measurements for AHI<20 events/hr, but under estimating it in more severe cases. For Type III and IV monitors, the strength of the evidence is moderate that they can accurately predict an elevated AHI (as determined by full PSG). Type III monitors perform better than type IV monitors at AHI cut offs of 5, 10 and 15 events/hour.

Several questionnaire designs and clinical prediction models have been used to assess sleep disordered breathing. The conclusion of study authors is that there is a low strength of evidence supporting the use of the Berlin questionnaire to screen for OSA, while other questionnaires could not be evaluated due to insufficient strength of evidence (only one study evaluating each). There is a low strength of evidence supporting the usefulness of some clinical prediction modeling in OSA diagnosis.

There was insufficient evidence for the utility of phased testing (i.e., using a screening test result to determine the next test to be performed in a series), as compared to PSG.

Predictive Utility of OSA Diagnostic Tests
There was insufficient evidence to assess the utility of preoperative screening for OSA.

With regard to the relationship between AHI and long term outcomes, using AHI greater than 30 events per hour was found to be an independent predictor of all cause mortality with a high strength of evidence. A higher AHI was also associated with incident diabetes based on a low strength of evidence. The association of diabetes and OSA may be confounded by obesity which may contribute to both conditions. There was insufficient evidence to determine an association of AHI with other clinical outcomes (e.g., cardiovascular mortality and hypertension).

Overall Summary

Although PSG (type I monitor) is considered the gold standard for diagnosing sleep apnea, the strength of evidence that AHI is a strong and independent predictor of all-cause mortality is limited to AHI > 30. The association between baseline AHI and the other long-term clinical outcomes is less robust, no current established threshold level for AHI exists that indicates the need for treatment. Type II, III and IV monitors can all accurately diagnosis OSA, although there is wide variation in estimating the actual AHI for type II monitors, and type III monitors perform better than type IV monitors. Some clinical prediction models and the Berlin questionnaire have evidence of efficacy as screening tools for OSA.

[Evidence Source]

PROCEDURE

Diagnostic testing for OSA

DIAGNOSES

Obstructive sleep apnea

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
327.20	Organic sleep apnea, unspecified
327.21	Primary central sleep apnea

327.23	Obstructive sleep apnea (adult) (pediatric)
327.27	Central sleep apnea in conditions classified elsewhere
327.29	Other organic sleep apnea
478.29	Nasopharyngeal obstruction
780.5	Sleep disturbance, unspecified
780.51	Insomnia with sleep apnea, unspecified
780.53	Hypersomnia with sleep apnea, unspecified
780.54	Hypersomnia, unspecified
780.57	Unspecified sleep apnea
ICD-9 Volume 3 (Procedure Codes)	
89.17	Polysomnogram
89.1	Other sleep disorder function tests
93.90	Non-invasive mechanical ventilation (CPAP)
CPT Codes	
95800	Sleep study, unattended, simultaneous recording: heart rate, O2 sat, respiratory analysis, sleep time
95801	Sleep study, unattended, simultaneous recording: heart rate, O2 sat, respiratory analysis
95803	Actigraphy
95805	Multiple sleep latency test
95806	Sleep study, unattended, simultaneous recording: heart rate, O2 sat, respiratory airflow and effort
95807	Sleep study,simultaneous recording: ventilation, respiratory effort, ECG or heart rate, O2 sat, attended by technologist
95808	Polysomnography: sleep staging with 1-3 additional parameters, attended by technologist
95810	Polysomnography: sleep staging with 4 or moe additional parameters, attended by technologist
95811	Polysomnography: sleep staging with 4 or more additional parameters, with initiation of CPAP, attended by technologist
HCPCS Codes	
G0398	Home sleep study test (HST) with type II portable monitor, unattended; minimum of 7 channels: EEG, EOG, EMG, ECG/heart rate, airflow, respiratory effort and oxygen saturation
G0399	Home sleep test (HST) with type III portable monitor, unattended; minimum of 4 channels: 2 respiratory movement/airflow, 1 ECG/heart rate and 1 oxygen saturation
G0400	Home sleep test (HST) with type IV portable monitor, unattended; minimum of 3 channels

Note: Inclusion on this list does not guarantee coverage

DRAFT

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT

HERC Coverage Guidance – Diagnosis of Sleep Apnea in Adults
Disposition of Public Comments

General Comments

Stakeholder	#	Comment	Disposition
	1	No public comments were received for this topic.	

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: TREATMENT OF SLEEP APNEA IN ADULTS

DATE: XX/XX/XXXX

DRAFT

HERC COVERAGE GUIDANCE

Coverage of treatment for Obstructive Sleep Apnea (OSA) in adults should be limited, as follows:

CPAP should be covered initially when all of the following conditions are met:

- 12 week 'trial' period to determine benefit. This period is covered if apnea-hypopnea index (AHI) or respiratory disturbance index (RDI) is greater than or equal to 15 events per hour, or if between 5 and 14 events with additional symptoms including excessive daytime sleepiness (Epworth Sleepiness Scale score > 10) or impaired cognition, or documented hypertension, ischemic heart disease, or history of stroke;
- Providers must provide education to patients and caregivers prior to use of CPAP machine to ensure proper use; and
- Positive diagnosis through polysomnogram (PSG) or Home Sleep Test (HST).

CPAP coverage subsequent to the initial 12 weeks should be based on documented patient tolerance, compliance, and clinical benefit. Compliance (adherence to therapy) is defined as use of CPAP for at least four hours per night on 70% of the nights during a consecutive 30 day period.

Coverage of mandibular advancement devices (oral appliances) should be provided.

Intensive weight loss programs (if provided in the benefit package) should be covered for patients with obesity and obstructive sleep apnea.

Surgical options may be covered for treatment of OSA when a diagnosis has been made, CPAP or other non-invasive treatments are not effective or not tolerated, and patients have been informed of the benefits and risks of surgery.

Oregon Health Authority

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

EVIDENCE SOURCE

Gleitsmann, K., Kriz, H., Thielke, A., Bunker, K., Ryan, K., Lorish, K., & King, V. (2012). *Sleep apnea diagnosis and treatment in adults.* Portland, OR: Center for Evidence-based Policy, Oregon Health and Science University. Retrieved from http://www.hta.hca.wa.gov/documents/sleep_apnea_final_report.pdf

The summary of evidence in this document is derived directly from this evidence source, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Obstructive sleep apnea (OSA) refers to sleep-disordered breathing due to the recurrent collapse of pharyngeal tissues resulting in snoring, fitful sleep, and daytime somnolence. These episodes are characterized by either reduced airflow (hypopnea), or a complete obstruction (apnea), with a subsequent drop in oxygen saturation, interfering with gas exchange. Obstructive sleep apnea is a cause of significant morbidity and mortality and is associated with hypertension, neuropsychological impairment, motor vehicle accidents, stroke, cardiovascular disease, diabetes, and decreased quality of life. The prevalence of OSA is 2 to 7% in the general adult population. Prevalence increases steadily with age, to approximately 20% among people older than age 60. Risk factors for OSA include male gender, age, obesity, airway characteristics, familial/genetic predisposition, smoking, and alcohol consumption. The majority of patients with OSA are asymptomatic, unaware of their sleep disordered breathing and associated health risks.

DRAFT

There have been various modalities developed to treat OSA, most attempting to reduce the airway obstructive component. Continuous positive airway pressure (CPAP) is the first-line therapy for OSA and opens the airway with compressed air. However, the CPAP machinery required is poorly tolerated and compliance is a major concern. Various oral appliances, which attempt to splint open the airway, have been used as an alternative to CPAP. Surgical procedures, including various surgeries on the oropharyngeal anatomy to alter airway mechanics, are performed to treat OSA. Bariatric surgery may be performed to reduce the volume of obstructive tissues. Other interventions that have been used to treat OSA include: weight loss regimens; smoking cessation; caffeine and alcohol avoidance; positional therapy; oropharyngeal physical therapy to strengthen the musculature and reduce obstruction; arrhythmia treatment for nocturnal bradycardia; complementary and alternative medicine (e.g., acupuncture), and a variety of pharmacologic agents.

Evidence Review

Continuous Positive Airway Pressure

A moderate strength of evidence was found for the effectiveness of treatment of OSA with CPAP. However, there was insufficient evidence to determine which patients CPAP might benefit the most. The reviewed studies report sufficient evidence supporting large improvements in sleep measures with CPAP compared with control (e.g., reducing apnea hypopnea index (AHI), improving symptoms as measured by the Epworth Sleepiness Scale[1], reducing arousal index, and raising the minimum oxygen saturation). Weak evidence demonstrated no consistent benefit in improving quality of life, neurocognitive measures or other intermediate outcomes. Despite no or weak evidence for an effect of CPAP on clinical outcomes, given the large magnitude of effect on the intermediate outcomes of AHI and Epworth Sleepiness Scale, the strength of evidence that CPAP is an effective treatment to alleviate sleep apnea signs and symptoms was rated moderate. However, the link between AHI reduction and long term clinical outcomes is not directly proven. There was insufficient evidence regarding most comparisons of various different CPAP devices, including nasal vs. oral, bilevel vs. fixed, flexible bilevel vs. fixed and humidified vs. non-humidified. However, there was a low strength of evidence that C-Flex (a proprietary CPAP technology that reduces the pressure slightly at the beginning of exhalation) is not significantly different than fixed CPAP in compliance or other outcomes, and a moderate strength of evidence that autoCPAP and fixed CPAP result in similar compliance and treatment effects.

Other Treatments for Obstructive Sleep Apnea

Mandibular advancement devices (oral appliances) had moderate strength of evidence supporting their use as an effective treatment for OSA. However, as with CPAP, there was insufficient evidence to indicate which patients might benefit from their use. There was moderate evidence that the use of CPAP is superior to mandibular advancement devices with regard to improved sleep study measures, bu weak evidence that there is minimal difference between the two for improving compliance, treatment response,

[1] A self-administered questionnaire that measures sleep propensity, total score ranges 0-24. Reference range is defined as ≤ 10, with 1 point change considered clinically significant. Sensitivity 49% and specificity 80% for detecting OSA using an AHI cutoff of 5 events/hour, based on one high quality study.

quality of life or neurocognitive measures. There was insufficient evidence to compare the different oral devices, other than mandibular advancement devices.

Six surgical interventions for the treatment of OSA were reviewed (uvulopalatopharyngoplasty (UPPP), laser-assisted uvulopalatoplasty (LAUP), radiofrequency ablation (RFA), and combinations of pharyngoplasty, tonsillectomy, adenoidectomy, genioglossal advancement septoplasty, radiofrequency ablation of the inferior nasal turbinates, or combination nasal surgery) compared to sham, conservative therapy or no treatment. No surgical interventions were compared to each other. Overall there was insufficient evidence with which to evaluate their efficacy. When each modality was compared to CPAP, the evidence was insufficient to determine their relative merits. No evidence that met inclusion criteria was identified for any other surgical procedures.

Of the other treatments for OSA that were considered, only intensive weight loss programs were an effective treatment in obese patients with OSA with a low strength of evidence. The remainder of the other management modalities (e.g., atrial overdrive pacing, medications, palatal implants, oropharyngeal exercises, tongue-retaining devices with positional alarms either in isolation or in combination, bariatric surgery, acupuncture, and auricular plaster) had insufficient evidence to determine the effects of using them for treatment of OSA.

Compliance with Treatment

Compliance in OSA patients prescribed nonsurgical treatments had moderate strength of evidence that compliance was greater with CPAP use with more severe OSA and insufficient evidence regarding potential predictors of mandibular advancement devices compliance.

The strength of evidence is low for indentifying any specific intervention which may improve CPAP compliance. No intervention type (e.g., education, telemonitoring) was more promising than others.

Overall Summary

CPAP is effective for improving sleep measures (e.g., reducing AHI, improving symptoms as measured by the Epworth Sleepiness Scale, reducing arousal index, and raising the minimum oxygen saturation), but there is no evidence of consistent benefit in improving quality of life, neurocognitive measures or other intermediate outcomes. AutoCPAP and fixed CPAP result in similar compliance and treatment effects. Mandibular advancement devices are effective treatment for OSA, although CPAP is superior to mandibular advancement devices with regard to improved sleep study measures. The evidence is insufficient to evaluate the efficacy of all surgical procedures and other treatments except intensive weight loss for obese patients with OSA.

[Evidence Source]

DRAFT

PROCEDURE

Continuous positive airway pressure
Uvulopalatopharyngoplasty
Mandibular maxillary osteotomy
Tracheostomy

DIAGNOSES

Obstructive sleep apnea

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
327.20	Organic sleep apnea, unspecified
327.21	Primary central sleep apnea
327.23	Obstructive sleep apnea (adult) (pediatric)
327.27	Central sleep apnea in conditions classified elsewhere
327.29	Other organic sleep apnea
780.5	Sleep disturbance, unspecified
780.51	Insomnia with sleep apnea, unspecified
780.53	Hypersomnia with sleep apnea, unspecified
780.54	Hypersomnia, unspecified
780.57	Unspecified sleep apnea
ICD-9 Volume 3 (Procedure Codes)	
21.31	Nasal surgery (remove polyps)
21.88	Other septoplasty
27.64	Insertion of palatal implant
27.69	Uvulopalatopharyngoplasty
28.2	Tonsillectomy
28.3	Tonsillectomy/adenoidectomy
28.6	Adenoidectomy
31.29	Tracheostomy
93.9	CPAP
CPT Codes	
21198	Osteotomy, mandible
21199	Osteotomy, mandible, with genioglossus advancement
21206	Osteotomy, maxilla
21685	Hyoid myotomy and suspension
24145	Uvulopalatopharyngoplasty
31600	Tracheostomy
41512	Tongue base suspension, permanent suture technique
41530	Radiofrequency reduction of the tongue base
42299	Unlisted procedure, palate, uvula (use for laser assisted uvulopalatoplasty (LAUP), somnoplasty, palatal implants)
HCPCS Codes	

DRAFT

CODES	DESCRIPTION
A4604	Tubing with integrated heating element for use with positive airway pressure device
A7033	Pillow for use on nasal cannula type interface, replacement only, pair
A7034	Nasal interface (mask or cannula type) used with positive airway pressure device, with or without head strap
A7035	Headgear used with positive airway pressure device
A7036	Chinstrap used with positive airway pressure device
A7037	Tubing used with positive airway pressure device
A7038	Filter, disposable, used with positive airway pressure device
A7039	Filter, nondisposable, used with positive airway pressure device
A7524	Tracheostoma stent/stud/button, each
E0470	Respiratory assist device, bi-level pressure capability, without backup rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)
E0471	Respiratory assist device, bi-level pressure capability, with back-up rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)
E0472	Respiratory assist device, bi-level pressure capability, with backup rate feature, used with invasive interface, e.g., tracheostomy tube (intermittent assist device with continuous positive airway pressure device)
E0485	Oral device/appliance used to reduce upper airway collapsibility, adjustable or nonadjustable, prefabricated, includes fitting and adjustment
E0486	Oral device/appliance used to reduce upper airway collapsibility, adjustable or nonadjustable, custom fabricated, includes fitting and adjustment
E0601	Continuous airway pressure (CPAP) device

Note: Inclusion on this list does not guarantee coverage

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT

HERC Coverage Guidance – Treatment of Sleep Apnea in Adults
Disposition of Public Comments

General Comments

Stakeholder	#	Comment	Disposition
Medical Director, Health Plan Portland, OR	1	Regarding the Coverage Guidance, I have several suggestions for consideration. First would be to enhance the statement regarding excessive daytime sleepiness to require an objective evaluation of daytime sleepiness, presumably the Epworth Sleepiness Scale. This would avoid the subjectivity involved in any statement on the part of provider or DME supplier claiming member has "excessive sleepiness", without requirement of at least a standardized assessment. Likewise, "impaired cognition" is problematic in its subjectivity, although probably not wise to try and establish a standardized requirement for that condition, as it would likely lead to neuropsych testing requests, which would be of limited value in many cases (particularly if no baseline exists, as would be the case in almost every situation).	Thank you for your comment. Guidance changed to incorporate ESS into coverage guidance box. Eight trials evaluated the effect of CPAP on neurocognitive or psychological tests, all found significant benefit from CPAP. *Consider deleting reference to impaired cognition.*
	2	It might be of value to consider whether provider needs to test for alcohol use, as recommendations for abstinence from alcohol is a standard recommendation whether or not a patient is using CPAP.	Evidence source does not address this, except to list avoidance of alcohol as the conservative management arm compared to surgery.
	3	It might also be of value to specify that the provider education should cover avoidance of alcohol, avoidance of CNS-affecting medications, and the contribution of obesity to OSA, when applicable. It could even be required to document (by requesting provider) that a review of medications has been performed, focusing on current use of contraindicated medications, and avoidance of them in the future.	Evidence source does not address this, except to list weight loss, positional therapy, and avoidance of alcohol and sedatives as the conservative management arm compared to surgery. Regarding obesity, three trials of weight loss interventions (primarily diets) found a significant improvement in AHI, ESS and O2 saturation. Regarding provider education, 9 studies evaluated extra support or education to improve compliance with CPAP, however results were inconsistent. *Counseling regarding weight loss added to guidance box.*
	4	I also believe the literature suggests that compliance with CPAP can be predicted in most cases by usage in the first few weeks, if not sooner. Is there need to have the trial period be 12 weeks-that would seem to be excessive, and given the likely high rate of non-compliance, is a 3 month trial necessary? It seems not, and a significant cost to the system. A shorter trial period might also promote the DME supplier to ensure member awareness of compliance requirements. I would propose a two-stage trial period-the first of 4-6 weeks to establish compliance, and if that first criteria is met, a second criteria at 12-16 weeks to evaluate for effectiveness.	The evidence source identified 5 studies that evaluated predictors of compliance, which included higher AHI, higher ESS score, younger age, snoring, lower CPAP pressure, higher BMI, higher mean O2 sat. One of those trials evaluated compliance at 4 weeks and found the only significant predictor to be high baseline AHI. There was a small (3%) decrease in the number of patients compliant with CPAP use between 4 weeks and 12 weeks. No other trials evaluated compliance or predictors of compliance at 4-6 weeks.

DRAFT

Stakeholder	#	Comment	Disposition
	5	It also might be helpful to objectify "effectiveness" or clinical benefit if possible. Thank you for your consideration.	Effectiveness is explained in the text, as follows: "sufficient evidence supporting large improvements in sleep measures with CPAP compared with control (e.g., reducing apnea hypopnea index (AHI), improving symptoms as measured by the Epworth Sleepiness Scale, reducing arousal index, and raising the minimum oxygen saturation). Weak evidence demonstrated no consistent benefit in improving quality of life, neurocognitive measures or other intermediate outcomes."
Industry Location Unknown	6	In response to the draft coverage guidance: Treatment of sleep apnea in adults, I guess my first response would be; is this the full policy? It appears that it may be a summary of medical necessity but does not have guidelines which currently exist in this policy such as when to bill for the sale of the item. For example the current policy has has "a three month trial (rental) period for CPAP is required prior to purchase", the draft does not mention a change in therapy, existing policy states "If a CPAP device was used more than three months and the client is switched to a RAD, then the clinical re-evaluation would occur between the 61st and 91st day following initiation of the RAD".	This document provides general guidance only. Specific implementation of the policy is left to individual payers.
	7	I guess my overall confusion is what is the reasoning for the "draft" is it just in terms of medical appropriateness and nothing further or is the "draft" intended to replace the current rule? If it is intended to replace the current rule it appears to be missing many factors that are vital to providers. Thank you.	Yes, the intent is to address general medical appropriateness, not to replace the current DMAP rule.

DRAFT

Draft Coverage Guidance Review

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: SELF-MONITORING OF BLOOD GLUCOSE FOR TYPE 1 & TYPE 2 DIABETES

DATE: XX/XX/XXXX

HERC COVERAGE GUIDANCE

For patients with Type 2 diabetes mellitus not requiring insulin, home blood glucose monitors and related diabetic supplies should only be covered for those who have HbA1c levels greater than 8% and in sufficient quantity to allow once a week testing. Such coverage should include a structured education and feedback program for self-monitoring of blood glucose. For most adults with type 2 diabetes using oral hypoglycemics (without insulin) or diet only, the routine use of SMBG is not recommended. For patients with insulin-requiring diabetes mellitus, home blood glucose monitors and related diabetic supplies should be covered and should include a structured education and feedback program for self-monitoring of blood glucose.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

DRAFT

EVIDENCE SOURCE

Gerrity, M., Kriz, H., & Little, A. (2010). Self-monitoring of blood glucose for type 1 and type 2 diabetes. Portland, OR: Center for Evidence-based Policy, Oregon Health and Science University.

Sources Cited In MED Report

Clar, C., Barnard, K., Cummins, E., Royle, P., & Waugh, N. (2010). Self-monitoring of blood glucose in type 2 diabetes: systematic review. Health Technology Assessment, 14(12), 1-140. doi: 10.3310/hta14120

The Diabetes Control and Complications Trial Research Group. (1993). The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. New England Journal of Medicine, 329(14), 977-986. doi: 10.1056/NEJM199309303291401

The summary of evidence in this document is derived directly from these evidence sources, and portions may be extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Diabetes mellitus (DM) is a serious chronic disease with significant morbidity, mortality, and cost. According to the Centers for Disease Control and Prevention, over 23 million (7.6% of the population) Americans have diagnosed (17.9 million) or undiagnosed (5.7 million) DM. Of the 17.9 million people with diagnosed diabetes, 2.2 million (14.5%) use insulin only, 10.3 million (57.6%) use oral medications only, 2.6 million (14.5%) use both, and 2.8 million (15.6%) do not take diabetes medications. An estimated $174 billion in health care costs are either directly or indirectly related to DM, and 16% of total Medicaid expenses are for individuals with DM. Supplies for self-monitoring of blood glucose (SMBG) are an important portion of this expense. Self-monitoring of blood glucose is used to guide the day-to-day management of blood glucose through appropriate changes in diet, exercise, and/or medications to improve overall glycemic control and clinical outcomes. However, there is controversy about the benefits and frequency of SMBG particularly for diabetics who do not use insulin.

DRAFT

Evidence Review

Type 1 Diabetes

No studies address the frequency of SMBG for type 1 diabetes except as a component of an intensive program to improve glycemic control. Recommendations for frequent (two to four times per day) and individualized SMBG in patients with type 1 diabetes are based on the Diabetes Control and Complications Trial (DCCT), clinical expertise, and the practical issues associated with adjusting insulin dosing.

Type 2 Diabetes

A good quality systematic review (Char 2010) published in 2010 included 26 RCTs that varied in quality (15 poor, 7 fair, and 4 good quality). Most of the RCTs had more than 100 participants, but varied between 30 to over 800. The duration of the studies ranged from 12 weeks to 30 months, and participants were generally 50 to 65 years old. Fewer than half of the studies found that SMBG interventions improved HbA1c compared to the control, and all of these studies included an education and/or feedback component. The authors performed four separate meta-analyses, and report the following results:

- No study addressed the impact of SMBG on clinical outcomes (e.g., myocardial infarction, retinopathy).The main outcome evaluated was HbA1c, a surrogate outcome.
- SMBG decreases HbA1c by a mean of -0.21% (95% confidence interval [CI], -0.31% to -0.10%). A clinically important change in HbA1c has been defined as 0.5% or greater. Thus, a decrease in HbA1c of -0.21% may not be clinically important. Many of the interventions did not describe the educational component done in conjunction with SMBG.
- Structured education and feedback aimed at improving glycemic control may be necessary to achieve reductions in HbA1c through SMBG. Although not statistically significant, SMBG in conjunction with structured education and feedback (enhanced SMBG) decreased HbA1c by a mean of -0.20% (95% CI, -0.44% to 0.03%) compared to SMBG alone. Enhanced SMBG compared to no SMBG decreased HbA1c by a mean of -0.52% (95% CI, -0.98% to -0.06%). This decrease is clinically as well as statistically significant.
- One meta-analysis performed by Clar compared frequency of testing. The results of this analysis found that frequent testing (3-7 times/week) compared to less frequent testing (1X/week or as usual) resulted in a mean difference in HbA1c of 0.20% (-0.01% to 0.41%) favoring the *less* frequent testing group, although the result was not statistically significant.
- The 26 RCTs did not provide enough subgroup data to assess the impact of SMBG on patient subgroups, except for baseline HbA1c.

DRAFT

- Patients using diet alone or oral agents and having a higher baseline HbA1c (≥ 8%) may achieve greater reductions in HbA1c with SMBG compared to those with a lower baseline HbA1c (< 8%). For patients with a baseline HbA1c > 10%, SMBG may decrease HbA1c by a mean of -1.23% (95% CI, -2.31% to -0.14%) compared to no SMBG; for those with a baseline HbA1c 8% to 10%, SMBG may decrease HbA1c by a mean of -0.27% (95% CI, -0.40% to -0.14%); and those with baseline HbA1c < 8% may decrease HbA1c by a mean of -0.15% (95% CI, -0.33% to 0.03%). The reduction in HbA1c for patients with a baseline HbA1c < 8% is not statistically significant or clinically important.

- Few studies reported data on harms of SMBG. Seven RCTs suggested the frequency of mild to moderate hypoglycemia may be increased with frequent SMBG, but results were inconsistent. One good quality cost-utility study found quality of life decreased slightly with intensive SMBG compared to standard care. Thirteen RCTs reported on weight and/or BMI and found no effect from SMBG. Two studies found an increase in depression with SMBG while two studies did not.

    - Two good quality cost-effectiveness studies found that SMBG was not cost effective compared to standard care. In one study, SMBG (about nine times per week) compared to no SMBG had an incremental cost per life-year gained was approximately US$92,301 and cost per quality adjusted life-year gained was US$107,331 (or approximately $1 million dollars over ten years).

Overall Summary

Although no studies address the frequency of SMBG for Type 1 diabetes, frequent and individualized SMBG is recommended based on the practical issues associated with adjusting insulin dosing. For Type 2 diabetes, no study addressed the impact of SMBG on clinical outcomes. Overall, SMBG decreases HbA1c by a mean of -0.21%, although this is likely not clinically important. With regard to frequency of testing, there was no significant difference in HbA1c when comparing a frequency of three to seven times per week to one time per week. Patients using diet alone or oral agents and having a higher baseline HbA1c (≥ 8%) may achieve greater reductions in HbA1c with SMBG compared to those with a lower baseline HbA1c (< 8%). Although few studies reported data on harms of SMBG, the frequency of mild to moderate hypoglycemia may be increased with frequent SMBG, and quality of life may be slightly decreased with intensive SMBG compared to standard care.

PROCEDURE

Self-monitoring of blood glucose

DIAGNOSES

Diabetes mellitus

DRAFT

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
249	Secondary Diabetes Mellitus
250	Diabetes Mellitus
ICD-9 Volume 3 (Procedure Codes)	
None	
CPT Codes	
83036	Hemoglobin; glycosylated (A1C)
83037	Hemoglobin; glycosylated (A1C) by device cleared by FDA for home use
97802- 97804	Medical nutrition therapy
98960-98962	Education and training for patient self-management by a qualified, nonphysician health care professional using a standardized curriculum, face-to-face, with the patient (could include caregiver/ family) each 30 minutes
99078	Physician educational services rendered to patients in a group setting (eg, prenatal, obesity, or diabetic instructions)
HCPCS Codes	
A4233-6	Batteries for home blood glucose monitors
A4253	Blood Glucose test strips, box of 50
A4255	Platforms for home blood glucose monitor, 50/box
A4256	Calibrator solutions/chips
A4258	Spring-powered device for lancet, each
A4259	Lancets, per box of 100
E0607	Blood glucose monitor
E2100	Blood glucose monitor with voice synthesizer
E2101	Blood glucose monitor with integrated lancer
G0108-G0109	Diabetes outpatient self-management training services
G0270-G0271	Medical nutrition therapy; reassessment and subsequent intervention(s) following second referral in same year for change in diagnosis, medical condition or treatment regimen (including additional hours needed for renal disease)
S9140	Diabetic management program, follow-up visit to non-MD provider
S9141	Diabetic management program, follow-up visit to MD provider

Note: Inclusion on this list does not guarantee coverage

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT

American Diabetes Association

August 1, 2012

Health Evidence Review Commission
State of Oregon
General Services Building
1225 Ferry Street, Suite C
Salem, Oregon 97301

Re: Response to information request on Self-Monitoring of Blood Glucose for Type 1 & Type 2 Diabetes; and Comments on the Draft Coverage Guidance: Continuous Glucose Monitoring in Type 1 Diabetes Mellitus

The American Diabetes Association (Association) is pleased to provide additional comments to the Commission regarding the Draft Coverage Guidance on Continuous Glucose Monitoring (CGM) in Type 1 Diabetes, **and** to address particular questions posed by members of the Commission to the Association during the June 25 hearing. We appreciate your willingness to consider additional information from the Association before revising the Coverage Guidance for Self-Monitoring of Blood Glucose (SMBG) for Type 1 and Type 2 Diabetes, and we are pleased to respond to your request. In particular these comments address:

I. The Association's treatment guidelines for SMBG
II. Clinical information on hypoglycemia in relation to SMBG
III. Clinical information on HbA1c levels and SMBG
IV. Additional Recommendations
V. Comments on the Draft Coverage Guidance: Continuous Glucose Monitoring in Type 1 Diabetes Mellitus issued on July 10, 2012

I. The Association's treatment guidelines for SMBG

The Association's *Standards of Medical Care in Diabetes – 2012*[1] addresses the importance of assessing the effectiveness of an individual's diabetes management plan on glycemic control through patient self-monitoring of blood glucose or interstitial glucose, and A1C (attached, pages S-16 to S-18). In particular, the *Standards of Medical Care in Diabetes – 2012* include the following recommendations:

- SMBG should be carried out three or more times daily for patients using multiple insulin injections or insulin pump therapy.
- For patients using less-frequent insulin injections, noninsulin therapies or medical nutrition therapy alone, SMBG may be useful as a guide to management.
- To achieve postprandial glucose targets, postprandial SMBG may be appropriate.
- When prescribing SMBG, ensure that patients receive initial instruction in, and routine follow-up evaluation of, SMBG technique and their ability to use data to adjust therapy.

[1] American Diabetes Association. Standards of Medical Care In Diabetes – 2012. Diabetes Care. January 2012; 35 (Supplement 1): S11-S63. Available at: http://care.diabetesjournals.org/content/35/Supplement_1/S11.full.pdf+html

For care of patients with diabetes, treatment must be comprehensive and individualized. Diabetes affects individuals very differently and it is critically important people with diabetes have access to the type and amount of diabetes testing supplies that meet their particular needs. SMBG is a component of effective therapy, which allows patients to evaluate their individual response to therapy and assess whether glycemic targets are being achieved. SMBG is especially important for patients treated with insulin to monitor for and prevent asymptomatic hypoglycemia and hyperglycemia. For most patients with type 1 diabetes and pregnant women taking insulin, SMBG is recommended three or more time daily. For these populations, significantly more frequent testing may be required to reach A1C targets safely without hypoglycemia and for hypoglycemia detection prior to critical tasks such as driving. We note that, for patients using insulin to manage their diabetes, the recommendation for SMBG three times per day is a minimum, and there are numerous reasons why a person may need to test more often.

Further, the American Diabetes Association statement on the *Care of Children and Adolescents with Type 1 Diabetes*[2] along with the Association's *Standards of Medical Care in Diabetes – 2012*, provide expert guidance on current standards of care for children and adolescents with diabetes and call for checking blood glucose levels before eating and when there are symptoms of high and low blood glucose levels as well as periodically after meals, before and after exercise, and at night. To be clear, all experts in pediatric diabetes agree that checking blood glucose multiple times per day is absolutely essential to the health and safety of children with type 1 diabetes. In addition, recently published and ongoing clinical trials in pediatric diabetes include SMBG as intrinsic components of family focused, school based, and community clinical interventions. Children with diabetes face special challenges including the inability of younger children to self-identify the warning signs of dangerous blood glucose levels, the hormone changes in older children, and growing bodies for all.

SMBG may also be useful as a guide to management for patients using noninsulin therapies. SMBG serves to alert patients to acute decompensation of their glucose in times of illness, and may also be important to prevent hypoglycemia in patients treated with sulfonylureas and under good glycemic control. The frequency and timing of SMBG should be dictated by the particular needs and goals of the patient and the recommendations of the treating clinician for that particular patient.

We applaud the Commission for including a structured education and feedback program in the Draft Coverage Guidance on Self-Monitoring of Blood Glucose. Results of SMBG add value to care only when they are integrated into the treatment plan. Diabetes self-management education (DSME) is an essential element of diabetes care and national standards are based on evidence for its benefits. DSME helps patients optimize metabolic control based upon the results of SMBG, prevent and manage complications, and maximize quality of life in a cost-effective manner.

[2] A statement of the American Diabetes Association. *Care of Children and Adolescents With Type 1 Diabetes*. 2005. Available at: http://care.diabetesjournals.org/content/28/1/186.full

Because DSME can result in cost-savings and improved outcomes, DSME should be adequately reimbursed by third-party payers.

II. Clinical information on hypoglycemia in relation to SMBG

Results of SMBG can be useful in preventing hypoglycemia and adjusting medications (particularly prandial insulin doses), MNT, and physical activity. Efforts to achieve good glycemic control are imperative to reduce the risks of diabetic microvascular complications. Many therapies, specifically insulin and sulfonylureas, have the capacity to cause dangerously low glucose levels. Therapy with sulfonylureas, particularly for individuals with hemoglobin A1c levels in the less than 7% range, may necessitate routine SMBG monitoring to identify hypoglycemia risk and inform reductions in medication dose or the need to ingest rapid-acting carbohydrate to prevent severe hypoglycemia. It is important to note that for insulin users, the risk for hypoglycemia is present at *any* A1c value.

III. Clinical information on HbA1c levels and SMBG

The Draft Coverage Guidance on SMBG states that home glucose monitors and testing supplies should only be covered for individuals with type 2 diabetes not requiring insulin who have HbA1c levels greater than 8% and in sufficient quantity to allow once a week testing. SMBG provides vital information concerning extremes of glucose. We urge you to consider that individuals on sulfonylurea therapy are at risk for hypoglycemia, particularly when their hemoglobin A1c is well controlled. Thus, the HbA1c cutoff of 8% would exclude those on sulfonylureas with greatest need for SMBG to protect them from hypoglycemia. Additionally, SMBG during times of acute illness is critical to identify dangerous decompensation of glucose, either diabetic ketoacidosis or hyperosmolar nonketotic states, even in those individuals otherwise in good glycemic control.

IV. Additional Recommendations pertaining to SMBG: Need for flexibility and exceptions

For care of patients with diabetes, treatment must be comprehensive and individualized. Diabetes affects individuals very differently and it is critically important people with diabetes have access to the type and amount of diabetes testing supplies that meet their particular needs. ***The Association strongly recommends, if coverage limits are set for diabetes testing supplies, an exceptions process be provided based on individual circumstances. Such a process should not be overly burdensome on the patient or clinician.***

V. Comments in response to the Draft Coverage Guidance: Continuous Glucose Monitoring in Type 1 Diabetes Mellitus issued on July 10, 2012

The Association's *Standards of Medical Care in Diabetes – 2012* includes the following recommendations:

- CGM in conjunction with intensive insulin regimens can be a useful tool to lower A1C in selected adults age 25 and over 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.
- In addition, CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes.

The revised Draft Coverage Guidance on Continuous Glucose Monitoring in Type 1 Diabetes issued on July 10 includes the following recommendation: Real time CGM systems should be covered for Type 1 diabetes mellitus patients with a history of recurrent hypoglycemia or HbAlc > 8% for whom insulin pump management is being considered, initiated or utilized. We note that research has shown benefits for CGM in individuals with type 1 diabetes on intensive insulin therapy (*either* an insulin pump or multiple daily injections).[3] ***Thus, we recommend adding "multiple daily insulin injections or" after the words "for whom" in the Coverage Guidance document to include individuals on multiple daily injections of insulin.***

Diabetes is a complex disease to manage and can lead to short and long term complications. The goal of diabetes care is to avoid the devastating and costly complications of the disease. The costs associated with diabetes, including diagnosed and undiagnosed diabetes, prediabetes, and gestational diabetes, and their complications, accounted for $218 billion in direct and indirect costs in 2007 alone. Much of the economic burden of diabetes is related to its complications including blindness, amputation, kidney failure, heart attack, and stroke. Yet, we have made major strides in effectively managing diabetes and reducing the risk for these devastating – and costly – complications through necessary medical care, medications and other tools, patient self-management, education, and support. We appreciate the opportunity to provide comments to the Commission as it develops Coverage Guidance documents for CGM and SMBG. The Association looks forward to reviewing the revised Coverage Guidance documents. Should you have any questions, please contact Laura Keller at 206-295-5532 or at lkeller@diabetes.org.

Sincerely,

Laura Keller
Director State Government Affairs Oregon

[3] Tamborlane WV, Beck RW, Bode BW, et al.; Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med 2008;359:1464-1476.

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: PET SCANNING FOR BREAST CANCER

DATE: XX/XX/XXXX

HERC COVERAGE GUIDANCE

PET scanning should not be covered in initial staging of breast cancer at low risk for metastasis (asymptomatic individuals with newly identified ductal carcinoma in situ, or clinical stage I or II disease).

PET scanning should not be covered as a modality to [routinely] monitor response to treatment of breast cancer.

PET scanning should not be covered as routine surveillance testing for asymptomatic individuals who have been treated for breast cancer with curative intent.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

EVIDENCE SOURCES

Choosing Wisely®, the ABIM Foundation. (2012). Lists. Retrieved July 6, 2012, from http://choosingwisely.org/?page_id=13

DRAFT

HAYES, Inc. (2010). *Positron emission tomography (PET) and combined positron emission tomography-computed tomography (PET-CT) for breast cancer staging*. Lansdale, PA: HAYES, Inc.

National Collaborating Centre for Cancer (NCCC). (2009). *Advanced breast cancer: diagnosis and treatment – Evidence review*. Cardiff, Wales: National Collaborating Centre for Cancer. Retrieved May 23, 2012, from http://guidance.nice.org.uk/index.jsp?action=download&o=44046

Pennant, M., Takwoingi, Y., Pennant, L., Davenport, C., Fry-Smith, A., Eisinga, A., et al. (2010). A systematic review of positron emission tomography (PET) and positron emission tomography/computed tomography (PET/CT) for the diagnosis of breast cancer recurrence. *Health Technology Assessment, 14*(50).

Schnipper, L.E., Smith, T.J., Raghavan, D., Blayney, D.W., Ganz, P.A., Mulvey, T.M., et al. (2012). American Society of Clinical Oncology identified five key opportunities to improve care and reduce costs: The top five list for oncology. *Journal of Clinical Oncology*, *30*(14), 1715-1724.

The summary of evidence in this document is derived directly from these evidence sources, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Breast cancer affects 1 in 13 women in their lifetime. Treatment options have developed significantly over the past decade and have had an impact on survival. Initial staging and the diagnosis of BC recurrence is important to allow appropriate treatment. Positron emission tomography (PET) and positron emission tomography/computed tomography (PET/CT) are technologies that have application in the detection and management of cancer. The adoption of PET or PET/CT depends not only on their diagnostic accuracy but also on their comparative advantage over existing diagnostic approaches.

Choosing Wisely® Campaign 2012

In 2010, Howard Brody, MD, PhD, Director of the Institute for Medical Humanities and a family medicine professor at the University of Texas, challenged medical specialty societies to identify five tests and treatments that are commonly performed in their respective fields despite a lack of evidence that they provide meaningful benefit to major categories of patients. Dr. Brody's commentary, "Medicine's Ethical Responsibility for Health Care Reform—The Top Five List," was published in the *New England Journal of Medicine,* and spawned the American Board of Internal Medicine (ABIM) Foundation's *Choosing Wisely®* campaign. *Choosing Wisely®* is part of a multi-year effort of the ABIM

Foundation to help physicians be better stewards of finite health care resources. Originally conceived and piloted by the National Physicians Alliance through a Putting the Charter into Practice grant, nine medical specialty organizations, along with Consumer Reports, have identified five tests or procedures commonly used in their field, whose necessity should be questioned and discussed. Each participating organization was free to determine how to create its own list, provided that it used a clear methodology and adhered to the following set of shared guidelines:

- Each item should be within the specialty's purview and control.
- The tests and/or interventions should be used frequently and/or carry a significant cost.
- Each recommendation should be supported by generally accepted evidence.
- The selection process should be thoroughly documented and publicly available on request.

One of the organizations that chose to participate in the *Choosing Wisely*® campaign is the American Society of Clinical Oncologists (ASCO). The Cost of Care Task Force of ASCO worked for several months to identify a list for ASCO to consider as its Top Five, first by suggesting a number of practices they believed were overused, then by performing a literature search to ensure that the items identified were supported by available evidence.

Two of the recommendations on ASCO's top five list pertain to PET scanning, and are presented below, along with clinical rationale. Citations supporting these recommendations are provided in the text with superscripted numerals. Full references can be found at the end of this document.

Don't perform PET, CT, and radionuclide bone scans in the staging of early breast cancer at low risk for metastasis.

Early-stage breast cancer (including ductal carcinoma in situ, and clinical stages I and II) is a potentially curable disease and a common problem faced by surgical, medical, and radiation oncologists.[1] Curative treatment of localized breast cancer can be accomplished by excision of the primary tumor followed with radiation therapy, or by mastectomy. Depending on a variety of factors, including the biomarkers associated with the primary cancer, systemic treatment—including hormonal therapy, chemotherapy, and biologic therapy—may be appropriate. Because the staging determination is critical to appropriate application of surgical, radiation, and systemic treatment with their associated short-term and long-term toxicities, there is great pressure to accurately assess disease stage in each patient.

Clinical staging (based on history and a physical examination by an oncology-trained physician), combined with serum tests of liver function and alkaline phosphatase, is the standard method to separate early breast cancer from metastatic or locally advanced breast cancer. Patients with locally advanced breast cancer (e.g., stage III) have a higher risk of occult metastatic disease, which may be discovered by FDG PET or PET/CT scanning, and use of these tests in this setting is appropriate.

The available evidence-based guideline does not recommend FDG PET or CT scanning for patients with stages I, IIa, and IIb breast cancer who are asymptomatic and have no findings on routine clinical and pathologic staging to suggest a more advanced stage.[2] The guideline is based on information available from retrospective studies of imaging in early-stage breast cancer. These studies show that the low incidence of occult liver and bone metastases (< 6%) is mostly in patients with stage III cancer, not in those with stages I and II,[3,4] and many of the findings are falsely positive (i.e., not due to metastatic cancer).[5] FDG PET is inferior to physical examination and sentinel lymph node biopsy for detecting axillary lymph node metastases.[6,7] In patients with large, stage III tumors or inflammatory breast cancer, FDG PET detects occult metastases in 10% to 21% of patients.[8-12]

In addition to excess cost, unwarranted testing leads to needless exposure of the patient to dangers of invasive procedures stimulated by false-positive results, the inherent anxiety and uncertainty associated with a false positive result, and unjustified exposure to ionizing radiation in women at low risk of dying as a result of breast cancer.[13]

Don't perform surveillance testing (biomarkers) or imaging (PET, CT, and radionuclide bone scans) for asymptomatic individuals who have been treated for breast cancer with curative intent.

Surveillance testing with serum tumor markers or imaging with PET, CT, and radionuclide bone scans has been shown to have clinical value for certain cancers (e.g., colorectal). However for breast cancer that has been treated with curative intent, several studies have shown there is no benefit from routine imaging or serial measurement of serum tumor markers in asymptomatic patients. False-positive tests can lead to harm through unnecessary invasive procedures, overtreatment, and misdiagnosis.

The majority of patients with breast cancer diagnosed today present with early-stage, node-negative disease that is found on screening mammography.[1] As a result of earlier diagnosis and the efficacy of adjuvant therapies (chemotherapy, radiation, endocrine therapy), most of these women have a normal life expectancy and a low risk for recurrence. Surveillance for breast cancer recurrence in this setting is particularly low yield given the low prevalence of recurrence. For a surveillance or screening test to be

considered useful, it must have high sensitivity and specificity, as well as a significant positive predictive value, the latter being highly dependent on the prevalence of the condition. Furthermore, screening tests need to add value through detecting early-stage disease for which treatment will improve survival outcomes. To date, there is no evidence from randomized trials that earlier detection of asymptomatic breast cancer recurrence (outside of the breast, as a local recurrence, or new primary) improves survival outcomes.[14,15,16-18] In addition, these studies suggest that most breast cancer recurrence is detected through clinical symptoms and not through screening. Thus, making patients aware of the potential symptoms of a breast cancer recurrence (e.g., pain, new lumps, dyspnea) is an important strategy in breast cancer surveillance.

Other imaging strategies such as standard chest radiograph, bone scans, and abdominal ultrasound did not change survival outcomes in the two randomized trials conducted in the 1990s,[17,18] and thus are not recommended for routine surveillance. Chest and abdominal CT scans or whole-body PET scans have not been evaluated as surveillance strategies for follow-up of early-stage breast cancer, even though they may be of value for the diagnostic evaluation of clinically evident recurrent breast cancer.[14] Given the low prevalence of distant recurrence in early-stage breast cancer, and the high likelihood of false-positive findings and/or incidental findings that will lead to further testing, there is no evidence to support the use of these imaging strategies.[14,16]

Evidence Review

The evidence sources presented below pertain to the diagnostic characteristics of PET scanning compared to other diagnostic modalities for various stages of breast cancer. None of the literature identified pertains to whether any imaging is indicated in each clinical situation.

<u>Staging</u>

Hayes 2010

Detection of Axillary Lymph Node Metastasis: Twelve of the studies compared the accuracy of the interventions to that of axillary lymph node dissection alone or in combination with sentinel lymph node biopsy. The sensitivity of PET in detecting axillary lymph node metastasis was reported as poor (27% to 61%) in five studies, moderate (68% and 80%) in two studies, and high (90.1% and 94.4%) in two studies. The corresponding specificity of PET was reported as moderate (67% to 89%) in four studies and high (95 to 100%) in five studies. The sensitivity of PET/CT was moderate (70% and 80%) in two studies and poor (48.5%) in one study. The specificity was moderate (84%) in one study and high (100%) in a second study. One study did not report on specificity, and none of the studies directly compared the performance of PET with PET/CT; therefore, there is no evidence that assesses the incremental impact that

PET/CT has on detecting metastasis. Direct comparison was made between PET and only one other imaging technique. Technetium 99 methoxyisobutylisonitrile (^{99m}Tc-MIBI) SPECT with or without planar scintigraphy demonstrated a slightly lower sensitivity of 38% (compared with 50%) in detecting axillary lymph node metastasis. Specificity was equivalent to that of PET/CT.

Detection of Distant Metastasis: Four studies assessed the performance of ^{18}F-FDG PET relative to conventional imaging or biopsy in identifying distant metastasis. In the three studies that reported the results per patient, sensitivity was in the range from 80% to 100% and specificity was 83% to 96.7%. The study population sizes ranged from 40 to 119. Two of the studies were retrospective. In the fourth study, in which the results were reported per lesion, PET sensitivity was 95.2% and specificity was 90.9% in 40 patients. The analysis in this study was also retrospective. Two of the studies compared the performance of ^{18}F-FDG PET with technetium-99m-labeled hydromethylene diphosphonate (^{99m}Tc-HMDP). In one study, ^{99m}Tc-HMDP was less sensitive but more specific than PET, while in the second study, ^{99m}Tc-HMDP was less accurate than PET. In a third study, ^{99m}Tc-MDP was as sensitive as ^{18}F-FDG PET but significantly less specific in a population of 40 patients. The fourth study reported that ^{18}F-FDG PET in 119 patients was more sensitive and less specific than conventional imaging in 116 patients.

Surveillance/Detection of Recurrence

NCCC 2009

Two systematic reviews and 15 small comparative studies or case series formed the evidence base for the topic on imaging to determine disease extent. Other than the reviews, papers were generally of poor to medium quality, and many were retrospective studies. Magnetic resonance imaging (MRI) and FDG-PET were equal to or better than scintigraphy in visualizing bone metastases, other than osteoblastic lesions, but whole body MRI was better than FDG-PET at detecting distant metastases, particularly in abdominal organs, brain, and bone. Magnetic resonance imaging also detected previously unidentified metastases, including those that were non-skeletal, and in one study, the treatment plan was changed accordingly in ~43% of patients. Computed tomography had a high diagnostic value in detecting local breast cancer recurrence and, when the field was extended to include the pelvis, also had a higher diagnostic accuracy in detecting bone metastases than scintigraphy.

Pennant 2010

In studies where direct comparisons of PET were made to conventional imaging tests (X-rays, CT, ultrasound and bone scintigraphy) and test performance was assessed based on individual patients (rather than lesions), PET had significantly higher sensitivity (89% vs. 79%) and significantly higher specificity (93% vs. 83%). Test

DRAFT

performance did not appear to vary according to the type of conventional imaging test that was compared with PET. Indirect comparisons gave similar findings. For studies that assessed test accuracy based on lesions, no significant differences in sensitivity or specificity between PET and conventional imaging tests were observed.

In studies where direct comparisons of PET/CT were made to CT (no studies of PET/CT and other imaging tests were identified), PET/CT had significantly higher sensitivity (95% vs. 80%), but the increase in specificity was not significant. Indirect comparisons gave the same findings.

For studies where test performance was assessed based on individual patients, three studies compared PET with different types of MRI technology. In each of these studies, there were no significant differences in the sensitivity or specificity of PET compared with MRI. One study compared PET/CT and MRI on a lesion basis, and there were no significant differences in sensitivity or specificity for PET/CT compared with MRI.

In the analysis of studies directly comparing PET/CT and PET, PET/CT had significantly higher sensitivity (96% vs. 85%), but the increase in specificity was not significant compared with PET (89% vs. 82%). The same pattern of results was observed for the indirect comparison of all PET/CT and PET studies. For studies that assessed test accuracy based on lesions, indirect comparison of PET/CT and PET showed no significant differences in sensitivity or specificity between PET/CT and PET.

Changes in patient management in study participants ranged from 11% to 74% (median 27%). These changes included initiation and avoidance of medical treatment such as hormone therapy and chemotherapy. In the three studies where only changes in management directly due to PET or PET/CT were considered (patients were not correctly diagnosed by conventional imaging techniques), estimates ranged from 11% to 25%.

In subgroup analysis, the accuracy of PET did not appear to be related to the location of disease or to whether PET was conducted with or without knowledge of previous clinical history and imaging studies. Characteristics of patient populations varied in many respects, and it was not possible to draw definite conclusions about patient characteristics that may have an impact on test accuracy.

Monitoring response to treatment

NCCC 2009

The evidence available to address this question is limited to six small (n=18 to 274) case series. Reviewed imaging modalities include MRI (comparing fat-suppressed-long-echo-time-inversion images to T1-weighted-sequence images), plain radiography, FDG-

PET and fluoroestradiol-PET. The paucity and poor quality of studies prevents meaningful analysis of efficacy.

Overall Summary

The *Choosing Wisely*® campaign recommends that PET scanning NOT be performed in early stage (DCIS, stage I, IIa and IIb) breast cancer because there is no evidence demonstrating a clinical benefit, and unnecessary imaging can lead to harm through unnecessary invasive procedures, over-treatment, and unnecessary radiation exposure. It also recommends that PET scanning NOT be performed for surveillance of asymptomatic patients who have been treated for breast cancer with curative intent.

For initial staging, compared to axillary lymph node dissection alone or in combination with sentinel lymph node biopsy, the sensitivity of PET in detecting axillary lymph node metastasis was reported as widely variable, ranging from 27% to 94%. The corresponding specificity of PET ranged from 67% to 100%. Assessment of the accuracy of PET/CT was limited to three trials, which reported sensitivity ranging from 48% to 80%, while the specificity ranged from 84% to 100%. For detection of distant metastases at the time of initial staging, accuracy results for PET relative to conventional imaging or biopsy were mixed, with sensitivity ranging from 80% to 100% and specificity from 83% to 96.7%.

For detection of recurrence, PET had significantly higher sensitivity and specificity compared to conventional imaging tests. Positron emission tomography/CT had a higher sensitivity than CT, no significant difference in specificity. Magnetic resonance imaging and PET have similar accuracy, and were equal to or better than scintigraphy in visualizing bone metastases, other than osteoblastic lesions.

For monitoring response to treatment, the evidence is insufficient to draw conclusions.

PROCEDURE

PET scanning

DIAGNOSES

Cancer of the breast

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
174	Malignant neoplasm of female breast
233.0	Carcinoma in situ of breast

DRAFT

CODES	DESCRIPTION
ICD-9 Volume 3 (Procedure Codes)	
92.18	Radioisotope scan; total body
92.19	Radioisotope scan; other sites
CPT Codes	
78811-3	PET imaging
78814-6	PET/CT imaging
79005-99	Systemic radiopharmaceutical therapy
HCPCS Codes	
None	

Note: Inclusion on this list does not guarantee coverage

ASCO References

1. American Cancer Society: Breast cancer facts and figures. http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-030975.pdf
2. Carlson RW, Allred DC, Anderson BO, et al: Invasive breast cancer. J Natl Compr Canc Netw 9:136-222, 2011
3. Barry MC, Thornton F, Murphy M, et al: The value of metastatic screening in early primary breast cancer. Ir J Med Sci 168:248-250, 1999
4. Puglisi F, Follador A, Minisini AM, et al: Baseline staging tests after a new diagnosis of breast cancer: Further evidence of their limited indications. Ann Oncol 16:263-266, 2005
5. Norum J, Andreassen T: Screening for metastatic disease in newly diagnosed breast cancer patients. What is cost-effective? Anticancer Res 20:2193-2196, 2000
6. Wahl RL, Siegel BA, Coleman RE, et al: Prospective multicenter study of axillary nodal staging by positron emission tomography in breast cancer: A report of the staging breast cancer with PET Study Group. J Clin Oncol 22:277-285, 2004
7. Kumar R, Zhuang H, Schnall M, et al: FDG PET positive lymph nodes are highly predictive of metastasis in breast cancer. Nucl Med Commun 27:231-236, 2006
8. van der Hoeven JJ, Krak NC, Hoekstra OS, et al: 18F-2-fluoro-2-deoxy-d-glucose positron emission tomography in staging of locally advanced breast cancer. J Clin Oncol 22:1253-1259, 2004
9. Mahner S, Schirrmacher S, Brenner W, et al: Comparison between positron emission tomography using 2-[fluorine-18]fluoro-2-deoxy-D-glucose, conventional imaging and computed tomography for staging of breast cancer. Ann Oncol 19:1249-1254, 2008
10. Fuster D, Duch J, Paredes P, et al: Preoperative staging of large primary breast cancer with [18F]fluorodeoxyglucose positron emission tomography/computed tomography compared with conventional imaging procedures. J Clin Oncol 26:4746-4751, 2008
11. Groheux D, Moretti JL, Baillet G, et al: Effect of (18)F-FDG PET/CT imaging in patients with clinical Stage II and III breast cancer. Int J Radiat Oncol Biol Phys 71:695-704, 2008
12. Carkaci S, Macapinlac HA, Cristofanilli M, et al: Retrospective study of 18F-FDG PET/CT in the diagnosis of inflammatory breast cancer: Preliminary data. J Nucl Med 50:231-238, 2009

DRAFT

13. Huang B, Law MW, Khong PL: Whole-body PET/CT scanning: Estimation of radiation dose and cancer risk. Radiology 251:166-174, 2009
14. Khatcheressian JL, Wolff AC, Smith TJ, et al: American Society of Clinical Oncology 2006 update of the breast cancer follow-up and management guideline in the adjuvant setting. J Clin Oncol 24:5091-5097, 2006
15. Harris L, Fritsche H, Mennel R, et al: American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. J Clin Oncol 25:5287-5312, 2007
16. Rojas MP, Telaro E, Russo A, et al: Follow-up strategies for women treated for early breast cancer. Cochrane Database Syst Rev 1:CD001768, 2005
17. Rosselli Del Turco M, Palli D, Cariddi A, et al: Intensive diagnostic follow-up after treatment of primary breast cancer: A randomized trial—National Research Council Project on Breast Cancer followup. JAMA 271:1593-1597, 1994
18. Liberati A: The GIVIO trial on the impact of follow-up care on survival and quality of life in breast cancer patients: Interdisciplinary Group for Cancer Care Evaluation. Ann Oncol 6:41-46, 1995 (suppl 2)

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

DRAFT COVERAGE GUIDANCE: CAROTID ENDARTERECTOMY VS. MEDICAL MANAGEMENT

DATE: XX/XX/XXXX

HERC COVERAGE GUIDANCE

Carotid endarterectomy should be a covered service in patients with 70-99% carotid stenosis without near-occlusion.

Carotid endarterectomy should not be covered for patients with less than 50% carotid stenosis.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

EVIDENCE SOURCE

Rerkasem K, Rothwell PM. Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane Database of Systematic Reviews* 2011, Issue 4. Art. No.: CD001081. DOI: 10.1002/14651858.CD001081.pub2.

DRAFT

U.S. Preventive Services Task Force. (2007). Screening for carotid artery stenosis: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*, *147*(12), 854-859.

Chambers BR, Donnan G. Carotid endarterectomy for asymptomatic carotid stenosis. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD001923. DOI: 10.1002/14651858.CD001923.pub2.
Publication status and date: Edited (no change to conclusions), published in Issue 4, 2008.

The summary of evidence in this document is derived directly from this evidence source, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Stroke is the third leading cause of death and probably the most important cause of long-term disability. The case fatality rate is between 15% and 35% with the first attack and rises to 65% for subsequent strokes. The majority of recurrences occur within one year and in the same anatomic region as the first stroke. Eighty-five percent of strokes are ischemic. Carotid endarterectomy was introduced in the 1950s and increasing numbers of patients have undergone this procedure over the last three decades.

There have been five randomized controlled trials of endarterectomy in patients with a recent symptomatic carotid stenosis. The first two studies were small, performed over 30 years ago, included a high proportion of patients with non-carotid symptoms and did not stratify results by severity of stenosis. In 1991, the Veterans Affairs trial (VACSP) reported a non-significant trend in favor of surgery but this trial was stopped early when the two largest trials, the European Carotid Surgery Trial (ECST) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET) reported their initial results. The final reports for ECST and NASCET were published in 1998. The European Carotid Surgery Trial reported benefit from surgery only in patients with 80% to 99% stenosis, and further limited this to 90% to 99% stenosis in women. In contrast, NASCET reported significant benefit from surgery in patients with 50% to 99% stenosis. In the previous version of this review, an attempt was made to reconcile and pool these apparently conflicting results. However, the differences between the trial results were partly due to differences in the methods of measurement of the degree of carotid stenosis on the pre-randomization catheter angiograms; the method used in ECST producing higher values than the method used in the NASCET and VACSP trials. There were also other differences, such as in the definitions of outcome events. Only by detailed re-analysis of the individual patient data and reassessment of the original angiograms can the results be properly compared or combined. In this version of the review, we have also included a pooled analysis of individual patient data from the three largest trials, in which the original angiograms were reassessed and analyses done using the same method of measurement of stenosis and the same definitions of outcomes. Neither the ECST nor the NASCET were powered to determine the effect of

surgery in subgroups. Subgroup analyses of pooled individual patient data from these two trials have greater power to determine subgroup-treatment interaction reliably and therefore several such clinically important analyses have been added in this review.

Evidence Review

The three trials noted above (NASCET, VACSP and ECST) were included in this review. As the trials differed in the methods of measurement of carotid stenosis and in the definition of stroke, a pooled analysis of individual patient data on 6092 patients (35,000 patient years of follow-up) from all three trials was completed after reassessment of the carotid angiograms and redefinition of outcomes when needed.

Inclusion criteria were similar for all three trials, with minor differences. All patients were symptomatic (i.e., had recent (within the last four to six months) TIA or minor ischemic stroke in the territory of the artery that was stenotic). The control group was best medical therapy, which included aspirin (79-83%), lipid-lowering medications (8-16%), antihypertensives (60%) and other antithrombotics. The exact surgical intervention was left to the discretion of the surgeon, but all surgeries were classified as endarterectomy. There were no imbalances in baseline characteristics between surgical and medical groups in the original trials.

Crossovers (patients who were randomized to one group but elected the alternate therapy) were similar for patients randomized to surgical therapy who chose medical therapy instead (0 to 3.4%) but significantly different for medical to surgical crossovers, with 22.8% of patients in the NASCET crossing over to surgery, compared to 9.2% to 9.8% in the other two trials. However, the average time to cross over to the surgical treatment was over 500 days in the two largest trials.

On re-analysis, there were no statistically significant differences between the trials in the risks of any of the main outcomes (operative risk of stroke, stroke morbidity and death) in any of the stenosis groups for either treatment group. There were likewise no statistically significant differences between trials in the effects of surgery on the relative risks of the main outcomes at five year follow up. Therefore, further analyses were performed on pooled data.

For the purposes of analysis, patients were stratified based on the degree of carotid stenosis (< 30%, 30% to 49%, 50% to 69%, 70% to 99%, near occlusion). Sub-group analysis was undertaken based on gender, age (<65, 65-74, ≥ 75) and time from most recent event to randomization (<2 weeks, 2-4 weeks, 4 to 12 weeks or > 12 weeks), type of primary event (ocular, cerebral TIA, stroke), presence of diabetes, irregular or ulcerated carotid plaque and contralateral occlusion. All of these factors had a significant effect on the risk of ipsilateral stroke in the medical group with the exception of contralateral occlusion. Male gender, older age, decreased time from ischemic event, presence of diabetes or an ulcerated plaque and those presenting with cerebral (non ocular) events all had a higher risk.

Surgery increased the five-year risk of ipsilateral ischemic stroke in patients with less than 30% stenosis (N = 1746, absolute risk reduction (ARR) -2.2%, P = 0.05), had no

significant effect in patients with 30% to 49% stenosis (N = 1429, ARR 3.2%, P = 0.6), was of marginal benefit in patients with 50% to 69% stenosis (N = 1549, ARR 4.6%, P = 0.04), and was highly beneficial in patients with 70% to 99% stenosis without near-occlusion (N = 1095, ARR 16.0%, P < 0.001). However, there was no evidence of benefit (N = 262, ARR -1.7%, P = 0.9) in patients with near-occlusions (defined as > 95% stenosis). The authors note that it is possible that intention to treat analysis may have underestimated the benefit of surgery in this group because of the relatively high rate of endarterectomy in follow up in the medical treatment group. However, the rate of endarterectomy was similarly high in the 70% to 99% stenosis group, and significant benefit with surgery was seen, making this explanation less likely.

Three of the prespecified subgroup analyses showed statistically significant differences. Benefit from surgery was greatest in men (no statistically significant benefit in women) and patients aged 75 years or over, although all age categories showed some benefit from surgery. Patients who were randomized within two weeks after their last ischemic event showed the greatest benefit from surgery, and there was decreasing benefit with increasing delay, with no benefit evident if the last ischemic event was more than 12 weeks previous. Overall, there was a 7% operative risk of death or any stroke within 30 days.

[Evidence Source]

Asymptomatic Patients – Surgery

A Cochrane review last updated in 2008 evaluated carotid endarterectomy in asymptomatic patients. Three trials with a total of 5223 patients were included. In these trials, the overall net excess of operation-related perioperative stroke or death was 2.9%. For the primary outcome of perioperative stroke or death or any subsequent stroke, patients undergoing CEA fared better than those treated medically (relative risk (RR) = 0.69, 95% confidence interval (CI) 0.57 – 0.83). Similarly, for the outcome of perioperative stroke or death or subsequent ipsilateral stroke, there was benefit for the surgical group (RR = 0.71, 95% CI 0.55 – 0.90). For the outcome of any stroke or death, there was a non-significant trend towards fewer events in the surgical group (RR = 0.92, 95% CI 0.83 – 1.02). Subgroup analyses were performed for the outcome of perioperative stroke or death or subsequent carotid stroke. CEA appeared more beneficial in men than in women and more beneficial in younger patients than in older patients although the data for age effect were inconclusive. There was no statistically significant difference between the treatment effect estimates in patients with different grades of stenosis but the data were insufficient. Patients were randomized to surgery only if they had stenosis of 60% to 99% in two trials, or 50% to 99% in the other trial.

Asymptomatic Patients - Screening

The US Preventive Services Task Force issued recommendations pertaining to screening asymptomatic patients for carotid artery stenosis (CAS) in 2007. They concluded the following:

The USPSTF recommends against screening for asymptomatic CAS in the general adult population. This is a grade D recommendation.

Benefits of Detection and Early Intervention
Good evidence indicates that in selected, high-risk trial participants with asymptomatic severe CAS, carotid endarterectomy by selected surgeons reduces the 5-year absolute incidence of all strokes or perioperative death by approximately 5%. These benefits would be less among asymptomatic people in the general population. For the general primary care population, the benefits are judged to be no greater than small**.**

Harms of Detection and Early Intervention
Good evidence indicates that both the testing strategy and the treatment with carotid endarterectomy can cause harms. A testing strategy that includes angiography will itself cause some strokes. A testing strategy that does not include angiography will cause some strokes by leading to carotid endarterectomy in people who do not have severe CAS. In excellent centers, carotid endarterectomy is associated with a 30-day stroke or mortality rate of about 3%; some areas have higher rates. These harms are judged to be no less than small.

USPSTF Assessment
The USPSTF concludes that, for individuals with asymptomatic CAS, there is moderate certainty that the benefits of screening do not outweigh the harms.

[Evidence Source]

Overall Summary

Endarterectomy is of some benefit for 50% to 69% symptomatic stenosis and highly beneficial for 70% to 99% stenosis without near occlusion. Benefit in patients with carotid near-occlusion is uncertain. These results are generalizable only to surgically-fit patients operated on by surgeons with low complication rates (less than 7% risk of stroke and death). Benefit from endarterectomy depends not only on the degree of carotid stenosis, but also on several other factors, including the delay to surgery after the presenting event. The benefit in asymptomatic patients is small. The benefits of screening asymptomatic individuals do not outweigh the harms.

PROCEDURE

Carotid endarterectomy

DIAGNOSES

Carotid artery occlusion

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
433.1	Occlusion and stenosis of precerebral arteries; carotid

DRAFT

ICD-9 Volume 3 (Procedure Codes)	
38.02	Incision of vessel (embolectomy/ thrombectomy); other vessels of head and neck
38.12	Endarterectomy; other vessels of head and neck
CPT Codes	
35301	Thromboendarterectomy; carotid, vertebral, subclavian, by neck incision
HCPCS Codes	
None	

Note: Inclusion on this list does not guarantee coverage

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT