Health Evidence Review Commission's

Health Technology Assessment Subcommittee

November 26, 2012

Meridian Park Hospital
Community Health Education Center, Room 117
19300 SW 65th Avenue, Tualatin, OR 97062

AGENDA

HEALTH TECHNOLOGY ASSESSMENT SUBCOMMITTEE (HTAS)

Meridian Park Hospital Health
Education Center, Room 117
Tualatin, Oregon
November 26, 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 September minutes	Alissa Craft	X
3	1:10 PM	Review Final Draft Coverage Guidance 1) Vertebroplasty, Sacroplasty, and Kyphoplasty	Alison Little	X
4	1:45 PM	Review Public Comment 1) Continuous Blood Glucose Monitoring in Diabetes Mellitus 2) Diagnosis of Sleep Apnea in Adults 3) Treatment of Sleep Apnea in Adults 4) MRI for Breast Cancer Diagnosis	Darren Coffman Alison Little Wally Shaffer	X
5	2:45 PM	Review Draft Coverage Guidances 1) PET scans for breast cancer	Wally Shaffer	X
6	3:00 PM	Changes to Coverage Guidance Process	Darren Coffman	
7	3:45 PM	Confirm next meeting: Feb. 25th	Alissa Craft	
8	3:50 PM	General Public Comment		
9	4:00 PM	Adjournment	Alissa Craft	

Minutes

MINUTES

Health Technology Assessment Subcommittee
Meridian Park Community Health Education Center
19300 SW 65th Avenue, Tualatin, OR
September 24, 2012
1:00-4:00pm

Members Present: Alissa Craft, DO, MBA; Gerald Ahmann, MD; George Waldmann, MD; James MacKay, MD; Tim Keenen, MD.

Members Absent: Ed Toggert, MD.

Staff Present: Darren Coffman; Wally Shaffer, MD, MPH; Jason Gingerich.

Also Attending: Alison Little, MD (CEBP); Shannon Vandergriff (CEBP); Vinod Dasa[1] (Bioventus), Brad Bisson[1] (Depuy-Mitek), Russ Riggs[1] (Reflex Clinic), Joe Salmonese[1], Ken Hirons[1], Leonard Allen[1], Chuck Martin[1], Sherry Williams[1], Greg Carroll[1] (Reflex Clinic), George M. Douglass[1], Nancy Borden[1], Bill McKee (Roche), Carolyn Walwyn (Slocum Orthopedics), Judy Fry (American Diabetes Association), Peter Heeckt (Bioventus), Dena Scearce (Medtronics), Michael Bolen (Medtronic), Jason Lerner (Depuy Synthes), Chris Arapoff (Medtronic), Denise Taray (DMAP), Ken Lozy (Bioventus), Cari Hayes (Medtronic), Michael Pfister (Interventional & Vascular Consultants), Margaret Eastman (Sanofi), Biji Joseph[1] (Sanofi), Abby Anderson (Bioventus), Chris Browner (Bioventus), Elise Brown (ADA), Rich Hatlin (Sanofi), Jake Thielen (Orthopedica & Fracture Clinic), Joanie Cosgrove (Medtronic), Nan Hein (Oregon Association of Orthopedists), Sean Galling (Ferring Pharmaceuticals), P. Cosgrove (Medtronic), Frances Lawson (Reflex Clinics), Mary Anderson[1] (Reflex Clinics), Alec Slebel (LHNW), Andrea Bruno (American Diabetes Association), Paul Nielsen (MedImmune)

[1]Testified on Viscosupplementation

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1. CALL TO ORDER

Alissa Craft called the meeting of the Health Technology Assessment Subcommittee (HTAS) to order at 1:00 pm. She introduced Tim Keenen, MD, a new member of the subcommittee, as well as Jason Gingerich who will serve as staff for this subcommittee.

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2. MINUTES REVIEW

No changes were made to the draft June 2012 minutes.
Minutes approved 5-0.

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3. REVIEW OF PUBLIC COMMENTS

A) Vertebroplasty, Sacroplasty, and Kyphoplasty

Alison Little reviewed the written public comments and the CEbP's recommended responses as outlined in the meeting materials. No revisions were suggested by the members.

Dr. Craft then invited verbal comments.

> Jason Lehrer, from Depuy testified. He disclosed a conflict of interest by nature of his employment. He asked the subcommittee to consider the hierarchy of evidence, clinician experience and patient values. He expressed concerns about the NEJM studies, suggesting they be downgraded to the level of the other studies considered to be of lower quality.
>
> Mike Pfister, is an interventional radiologist practicing in Oregon since the late 90's. He said he has performed vertebroplasty on 350 patients. Expressed agreement with Lehrer but disagreed with the proposed coverage guideline, especially the definition of routine. He believes the Medicare local coverage determination (LCD) will guide him without a more definitive definition of what routine/nonroutine means. Departing from LCD is a big effort which may not be necessary for this committee.

Discussion by the Subcommittee focused around the definition of routine and whether exceptions to the noncoverage decisions might be appropriate in certain cases.

A motion was made and seconded to accept the draft coverage guidance recommendation. **The motion carried 5-0**, and Craft requested that staff work on a definition of routine which can be forwarded to HERC for consideration during guideline development. The approved language is:

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

B) Viscosupplementation for Osteoarthritis of the Knee

Alison Little reviewed the public comments and the CEbP's recommended responses. No revisions were suggested by the members. There was extensive discussion and public comment on this topic. Thirteen individuals representing patients, providers and product manufacturers gave public comment, all in support of coverage for this procedure.

Public comments focused on several areas:

- Personal testimonies from physicians and patients reporting successful viscosupplementation treatment and urging coverage of the procedure.

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- Testimony raising concerns about the quality of the evidence used in the noncoverage determination. Concerns included inclusion of inappropropriately selected patients in the studies as well as whether the size of the effect from treatment was significant.
- Testimony that analgesics are insufficient or contraindicated for some patients. Steroids have adverse effects. The only other alternative is knee replacement, which is more expensive and more invasive.
- Testimony arguing that fluouroscopic guidance may improve effectiveness.
- Testimony observing that other similar bodies and other payers have decided to cover the procedure.

Committee members discussed these comments, but also the potential for abuse, that some patients see no benefit or experience harm from these procedures, and that the evidence considered shows a benefit which may not be clinically significant. In addition, there was discussion of the difficulty of determining which patients may be good candidates, and that pain measurement is highly subjective. Several committee members stated that this is a difficult decision.

A motion was made to approve the draft coverage guidance as written and forward to HERC. **Motion approved 4-1 (Keenen).** Coffman said that this will be taken to the next HERC meeting October 11 where there will be more limited opportunity for public comment. The approved language is:

HERC COVERAGE GUIDANCE

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

C) Continuous Glucose Monitoring in Type II Diabetes

Alison Little reviewed the public comments and the CEbP's recommended responses. No revisions were suggested by the members. There was minimal discussion.

At committee request, the coverage guidance was changed to allow for retrospective glucose monitoring for Type 1 diabetes.

It was also noted that the revised draft guidance includes a noncoverage recommendation for real-time continuous glucose monitors for type 2 diabetes based on a new AHRQ report. Since this change was not a result of public comment, the revised guidance will be reposted for an additional 21-day public comment period.

A motion was made to approve the revisions to the draft coverage guidance as written and repost it for public comment. **Motion approved 5-0.**

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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 be covered for Type 1 diabetes mellitus and should not be covered for Type 2 diabetes mellitus.

The remaining guidances on MRI for breast cancer diagnosis and the diagnosis and treatment of sleep apnea in adults were not reviewed as the time allotted for the meeting had expired.

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4. COVERAGE GUIDANCE ALGORITHM

This topic was not discussed due to insufficient time. Members were encouraged to send any comments via email to staff as the algorithm will be discussed at the October 11th HERC meeting.

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5. REVIEW OF NEW DRAFT COVERAGE GUIDANCES

A. Self-monitoring of Blood Glucose

This topic was not discussed due to insufficient time.

B. PET Scans for Breast Cancer

This topic was not discussed due to insufficient time.

C. Carotid Endarterectomy

This topic was not discussed due to insufficient time.

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6. PUBLIC COMMENT

No additional public comment was received at this time.

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7. ADJOURNMENT

The meeting was adjourned at 4:00 pm. The next meeting is scheduled for November 26, 2012 from 1:00-4:00pm in Room 117B of the Meridian Park Hospital Community Health Education Center in Tualatin.

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Review Final Draft Coverage Guidances

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.

An osteoporotic compression fracture is not "routine" if the patient is hospitalized due to pain that is primarily related to a well-documented acute fracture; if the severity of pain prevents ambulation; and if pain is not adequately controlled with oral medication, bracing, and an appropriate trial of conservative management.

Note: This coverage guidance does not address vertebral fractures related to malignancy.

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

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

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

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than conservative medical therapy, followed by equivalent levels of functioning after six months to a year.

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

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PCE rates from 0.1% to 1.7%, with insufficient information to compare rates for vertebroplasty and kyphoplasty.

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

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CODES	DESCRIPTION
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
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.

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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

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.
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.

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

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.
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.

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

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		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.

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		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.

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		• 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. Addition of the definition of when a compression fracture is not routine adds additional specificity. It is similar to the NAS coverage policy.
	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

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		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

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		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.

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		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

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		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.	With the addition of a definition of when a compression fracture is not routine, the guidance is no longer a "unilateral non-coverage determination". Coverage is allowed for non-routine fractures, which is similar to appropriateness criteria.
	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	HTAS did not include guidance on treatment of pathologic fractures due to limitations of the evidence base.

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		vertebral augmentation.	
Oregon Association of Orthopaedists, Inc. Portland, OR	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. 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.	Thank you for this information and for taking the time to comment.
	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,	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)

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		peripheral arterial disease, deep vein thrombosis, uterine fibroids, cancer and stroke patients.	
	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 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.	HTAS agrees that because of similarity of VP and KP procedures, considering the procedures together is reasonable. Since as the commenter states, "patient outcomes 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	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.

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		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*	
	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 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.*	The assumption that if the original enrollment target had been met, the study 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.

Stakeholder	#	Comment	Disposition
	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 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).	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 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	Since evidence of effectiveness has not

Stakeholder	#	Comment	Disposition
		"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.	been established, it is inappropriate to calculate an ICER.
	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	Defining a period for conservative treatment is not needed for procedures that are not effective.

Stakeholder	#	Comment	Disposition
		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 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	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.

Stakeholder	#	Comment	Disposition
		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.	
	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 affected by VCF produces better clinical outcomes and that this is also cost effective.	HTAS disagrees that early intervention with VP produces better clinical outcomes, since 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.
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	Thank you for your comment. Definition of non-routine fracture matches your

Stakeholder	#	Comment	Disposition
		fracture and whose pain cannot be rapidly brought under control to the point of discharge to home should be allowed to have immediate kyphoplasty.	recommendation.
	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 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.	See comment #66.

Review Public Comment

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 be covered for Type 1 diabetes mellitus and should not be covered for 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 October, 29, 2012 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 October, 29, 2012 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.

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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

DIAGNOSES

Type 1 Diabetes Mellitus
Type 2 Diabetes Mellitus

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
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

DRAFT

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.

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HERC Coverage Guidance – Continuous Glucose Monitoring in Diabetes Mellitus
Disposition of Public Comments – Second Posting

General Comments

Stakeholder	#	Comment	Disposition
American Diabetes Association Oregon Office Portland, OR	1	On behalf of the people with diabetes in Oregon, the American Diabetes Association (Association) is pleased to provide additional comments to the Commission regarding the revised *Draft Coverage Guidance on Continuous Glucose Monitoring (CGM) in Diabetes Mellitus*. 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.	Thank you for taking the time to comment. HTAS is aware of ADA recommendations.
	2	The revised *Draft Coverage Guidance on Continuous Glucose Monitoring in Diabetes Mellitus* issued on September 24 includes the following recommendation: Real time CGM systems should be covered for Type 1 diabetes mellitus patients with HbAlc > 8% or a history of recurrent hypoglycemia or for whom insulin pump management is being considered, initiated or utilized, and should not be covered for individuals with type 2 diabetes mellitus. Research has shown benefits for CGM in individuals with type 1 diabetes on intensive insulin therapy, through *either* an insulin pump or multiple daily injections.[1] ***As such, we recommend anyone on multiple doses of insulin or continuous subcutaneous insulin infusion with recurrent hypoglycemic episodes or persistently high HbA1c levels be given the option of real-time CGM***. [1] 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.	The citations listed were published before the date of both evidence reviews (last search dates June and July 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. Both evidence sources found significantly greater improvement in HgA1c in patients using insulin pumps than in those using multiple daily injections,

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Stakeholder	#	Comment	Disposition
			and no difference in risk of severe hypoglycemia.
	3	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 the Coverage Guidance document for CGM.	HTAS is aware of the implications and costs of diabetes. Thank you for your comment.

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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

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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.* Produced for the Washington HTA Program. Olympia, WA: Center for Evidence-based Policy, Oregon Health and Science University for the Washington Health Technology Assessment Program. Retrieved September 13, 2012, 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]).

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- No current established threshold level for AHI exists that indicates the need for treatment.

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

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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

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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.

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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

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.

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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.* Produced for the Washington HTA Program. Olympia, WA: Center for Evidence-based Policy, Oregon Health and Science University for the Washington Health Technology Assessment Program. Retrieved September 13, 2012, 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

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patients with OSA are asymptomatic, unaware of their sleep disordered breathing and associated health risks.

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

[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.

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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, 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]

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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	

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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.

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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.

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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.

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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 May 7, 2012, 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.

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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

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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
174.0-9	Malignant neoplasm of female breast
233.0	Carcinoma in situ 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.	

Review Draft Coverage Guidances

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

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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

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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

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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

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