



Health Technology Assessment Clinical Committee Meeting Program Update

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Health Technology Assessment

August 20, 2010



Presentation Overview

- **WA State Government Context**
- **Health Care Access, Quality, and Cost efforts**
- **HTA Program Introduction**
- **HTA Program Updates**
 - HTA Program Outcomes / Measures
 - Recognition
 - Program Transparency Improvement
 - 2010 Topics
- Today's Topics - Breast MRI and Spinal Cord Stimulators

Governor Gregoire's strategy : Improve quality in health care

- **Governor Gregoire's five point plan to improve health care (2005)**
 - Emphasize evidence based health care
 - Create more transparency in the health care system
 - Promote prevention, healthy lifestyles, and healthy choices
 - Better managed chronic care
 - Make better use of information technology
- **Blue Ribbon Commission (2006)**
 - Goals set for 2012
 - Four strategies
 - 16 recommendations
 - Health reform legislation, 2007 ([5930](#))

How a Large Purchaser Can Impact the Market

- **Must change the delivery system to impact cost and quality**
 - Driving change through purchasing
- **Must target manageable changes for the long haul (lesson learned from 1993)**
- **Governor targeted key initiatives early and stuck with them**
 - Five point plan, BRC
- **Focus has endured despite a bad economy and political pressure**
- **This focus has helped other employers, health plans and provider groups to think differently**
- **Working together with private sector**
 - Puget Sound Health Alliance
 - Multi-payer medical homes payment reform pilot
 - Health Technology Assessment, Prescription Drug Program, PDA/SDM and AIM
 - Health Information Technology and Health Information Exchange
 - Health Insurance Partnership

The State Budget, Health Care, and National Health Reform

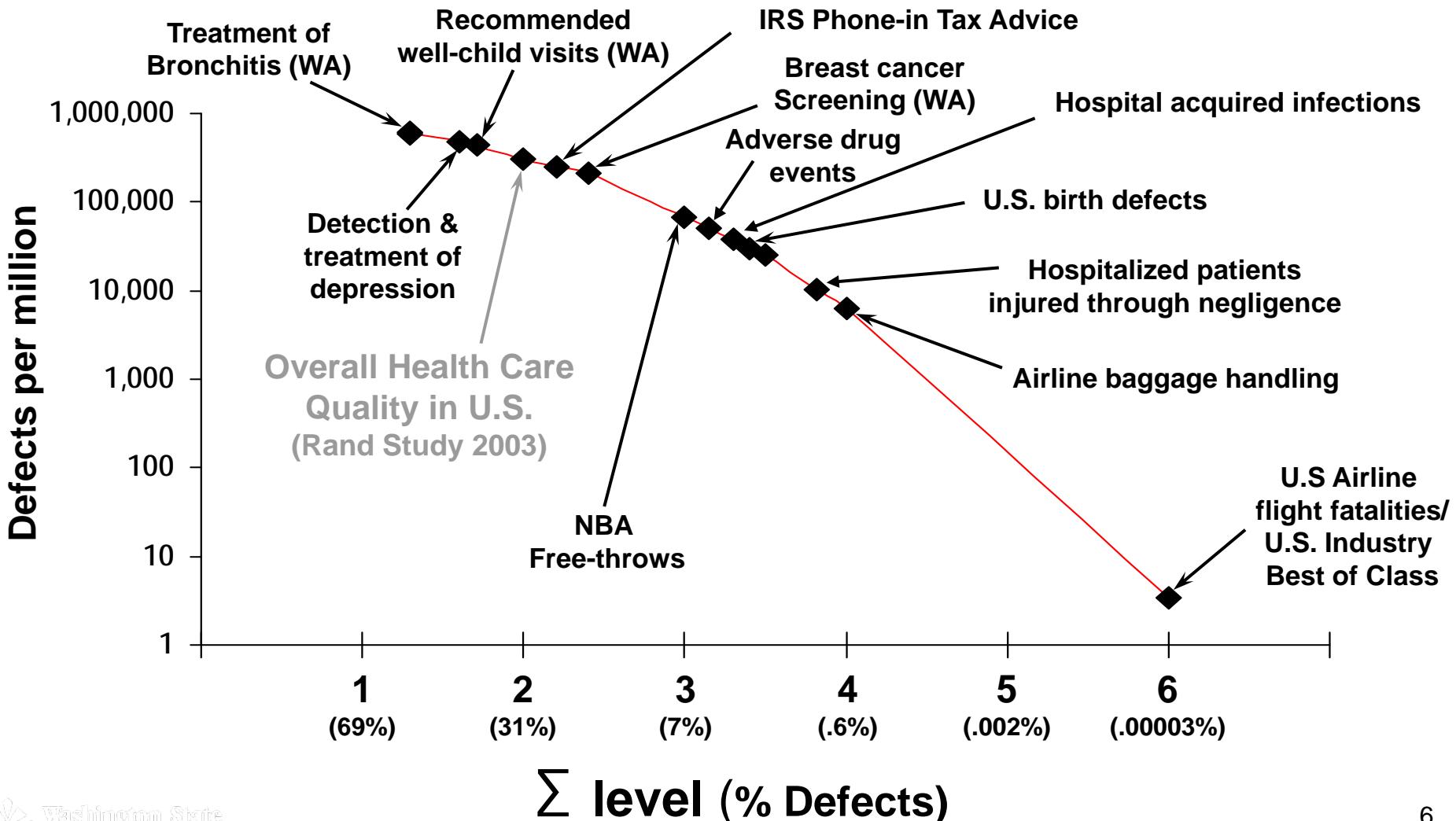
- **Budget Shortfall 2009-2011 – \$2 Billion (of \$33 Billion)**
 - Past 3 years, total of \$5.1 Billion in cuts to state budget
 - Federal funds of about \$500M anticipated; \$300M Medicaid
 - Preparing for a 4-7% across the board cut by October 2010
- **Projected shortfall for 2011-2013 is \$3 billion**
- **Total health care spending now about 1/3 of state budget, was about 1/5 in 2005**
 - Waiver request to sustain BHP, Medical Care Services programs
 - Executive order to consolidate Medicaid, public employees health purchasing, eventually all state health purchasing, under HCA
 - Executive implementation of NHR, Joint Legislative Select Committee on Health Reform Implementation
 - Low income expansion
 - Health insurance exchange
 - Health care workforce

HCA and State Health Reform Efforts

- **HCA - 330,000 public employees and retirees -\$1.1B**
 - State, higher ed, some K-12, some local governments – Self insured and MCO
 - In 2009, bid trend at 7.9%; Legislature approved 3%; Increase cost share; reduced benefits
- **HCA ~70,000 low income in Basic Health Program -\$330M**
 - Until budget reduction in 2009, program enrollment around 100,000
 - Now over 100,000 on wait list
 - Entirely state funded, waiver request for early expansion
- **Medicaid – 900,000 WA Children and Adults -\$3.5B (6.2B total)**
 - Federal and State partnership; enrollment up 9% to 1.1M in 2009
 - In 2009, ARRA one-time payment \$765,000 and some provider rate and pharmacy controls
 - Federal Health Reform 2010/2011 – require same eligibility, expect adult population to double by 2014; WA does not have waiver for co-pay; benefit reductions and LTC management under consideration
- **L&I - ~130,000 Claims (2.5M workers) - \$1.9B (Medical/Time Loss)**
 - Pharmacy controls; Claim audits; prior authorization; COHE; IIMAC
 - From higher investment returns in 2007- \$300M returned, but for 2010, rate increase of 7%

Health Care Quality Defects Occur at Alarming Rates

Sources: modified from C. Buck, GE; Dr. Sam Nussbaum, WellPoint; Premera 2004 Quality Score Card; March of Dimes



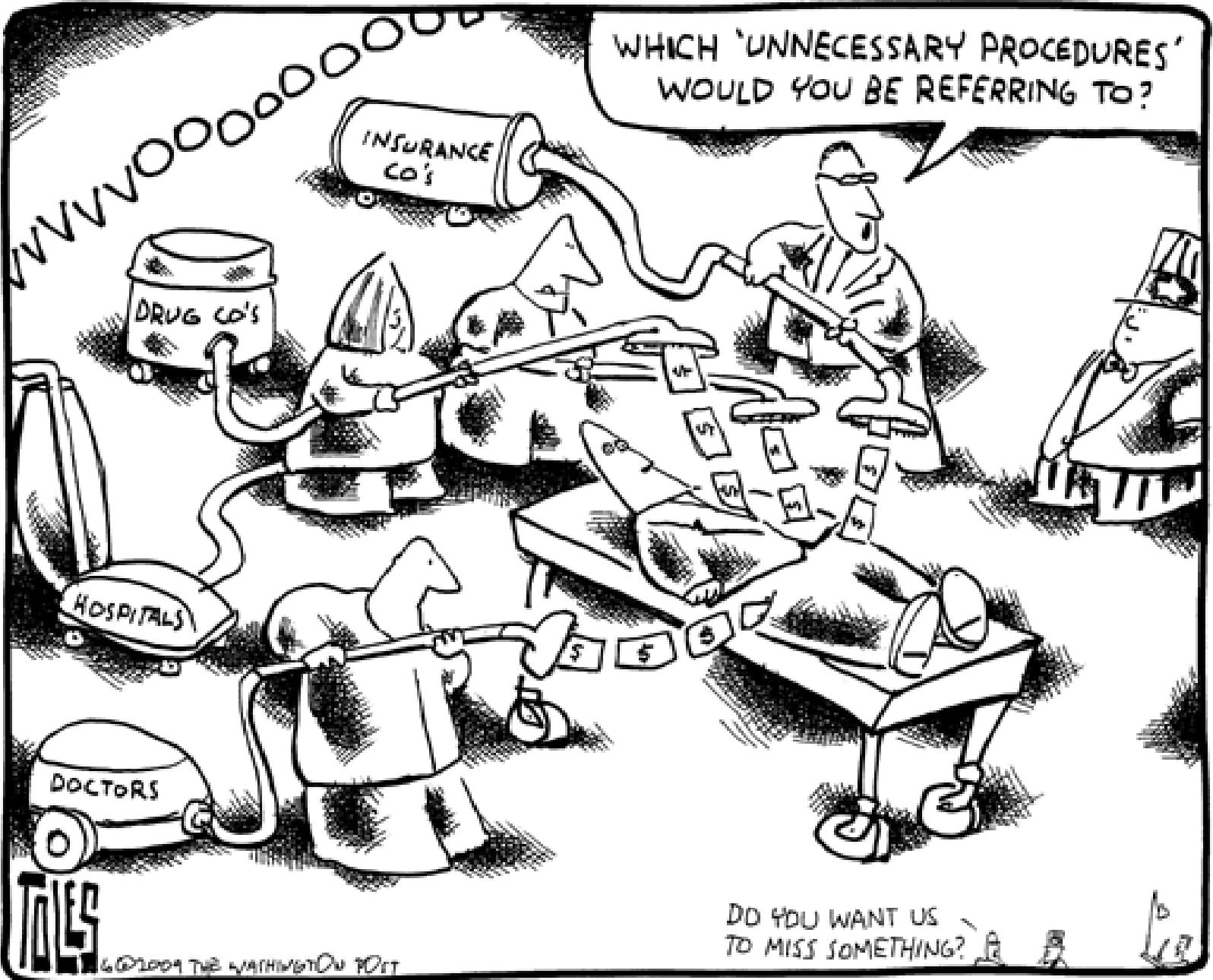
Why Health Technology Assessment?

- **Part of an overall strategy**
- **Medical technology is a primary driver of cost**
 - The development and diffusion of medical technology are primary factors in explaining the persistent difference between health spending and overall economic growth.
 - Some health experts arguing that new medical technology may account for about one-half or more of real long-term spending growth.

Kaiser Family Foundation, March 2007: How Changes in Medical Technology Affect Health Care Costs

- **Medical Technology has quality gaps**
 - Medical technology diffusing without evidence of improving quality Highly correlated with misuses, overutilization, underutilization.

Cathy Schoen, Karen Davis, Sabrina K.H. How, and Stephen C. Schoenbaum, "U.S. Health System Performance: A National Scorecard," *Health Affairs*, Web Exclusive (September 20, 2006): w459



KEY HTA Products

Pay for What Works: Better Information is Better health

- **Transparency:** Publish topics, criteria, reports, open meeting
- **Technology Assessment Report:** Formal, systematic process to review appropriate healthcare technologies.
- **Independent Coverage decision:** Committee of practicing clinicians make decisions that are scientifically based, transparent, and consistent across state health care purchasing agencies.

Key focus questions:

- Is it safe?
- Is it effective?
- Does it provide value (improve health outcomes)?

HTA Program Elements

1. HCA Administrator Selects Technology

Nominate, Review, Public Input, Prioritize

Semi-annual

2. Vendor Produce Technology Assessment Report

Key Questions and Work Plan, Draft, Comments, Finalize

2-8 Months

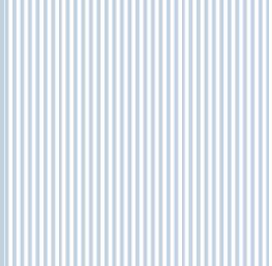
3. Clinical Committee makes Coverage Determination

Review report, Public hearing

Meet Quarterly

4. Agencies Implement Decision

Implements within current process unless statutory conflict



Evidence for use in Policy Decisions

Different Data Sources

- **Efficacy**
 - How technology functions in “best environments”
 - Randomized trials-distinguish technology from other variables
 - Meta-analysis
- **Effectiveness**
 - How technology functions in “real world”
 - Population level analyses
 - Large, multicenter, rigorous observational cohorts (consecutive pts/objective observers)
- **Safety**
 - Variant of effectiveness
 - Population level analyses
 - Case reports/series, FDA reports
- **Cost**
 - Direct and modeled analysis
 - Administrative/billing data (charge vs cost)
- **Context**
 - Mix of historic trend, utilization data, beneficiary status, expert opinion

- **Clinical Committee Decision must give greatest weight to most valid and reliable evidence**
 - Objective Factors for evidence consideration
 - Nature and Source of evidence
 - Empirical characteristics of the studies or trials upon which evidence is based
 - Consistency of outcomes with comparable studies
 - Additional evaluation factors
 - Recency (date of information)
 - Relevance (applicability of the information to the key questions presented or participating agency programs and clients)
 - Bias (presence of conflict of interest or political considerations)

HTA Measures and Outcomes

■ Transparency

- Topics, Key Questions, Draft Reports, Final Reports, Criteria Posted
- Average 83 days of public comment per technology
- All decisions made at public meeting

■ Technology Reports: Analysis completed

- Over 6,000 articles/trials reviewed
- 15 comprehensive technology assessment reports

■ Independent Coverage Decisions

- 13 decisions where reliable evidence:
 - 7 show benefit and support coverage for certain situations
 - 5 do not yet show benefit and are not covered
 - 1 shown unsafe or ineffective
- Estimated \$27 million cost avoided
- Projected Utilization impact: 3 increased; 3 same; 7 decrease

HTA Outcomes

Health Technology Assessment Program							Utilization Impact (annual figure)	
Topic	Date	Evidence		Cost-Effective	Decision			
		Safe	Effective		Health Benefit	Coverage		
Upright MRI	May-07	Equal	Insufficient	Less	N/A	No	\$2,990,000	
Ped Bariatric Surgery <18	Aug-07	Insufficient	More	Insufficient	No	No	\$0	
Ped Bariatric Surgery 18-21	Aug-07	Less	More	Insufficient	Yes	Yes/ Conditions	\$589,485	
Lumbar Fusion	Nov-07	Less	Equal/More	Less	Yes	Yes/ Conditions	\$5,240,639	
Discography	Feb-08	Insufficient	Insufficient	Insufficient	No	No	\$324,000	
Virtual Colonoscopy (CTC)	Feb-08	Equal	Equal/More	Less	No	No	\$11,100,000	
Intrathecal Pump for chronic	Feb-08	Insufficient	Insufficient	Equal	No	No	\$691,326	
Arthroscopic Knee Surgery	Aug-08	Less	Equal	Less	No	No	\$400,000	
Artificial Disc Replacement	Nov-08	Equal	Equal/More	Insufficient	Yes	Yes/ Conditions	0*	
Computed Tomographic Angiography (cardiac)	Nov-08	Equal	Equal	Equal/More	Yes	Yes/ Conditions	\$5,063,928	
Cardiac Stents	May-09	Equal	Equal/More	Less	Yes	Yes/ Conditions	\$966,760	
							\$27,366,138	

*Insufficient current data to calculate conservative estimate.

HTA Measures

WA HTA Comparison with Insurer Policies								Reference Sources	
WA HTA			Private Insurer					Medicare	BCBS TEC
Topic	Date	Coverage Decision	Aetna	Group Health	Premera-BS	Regence-BC	NCD		
Upright MRI	May-07	Not covered	Less Restrictive	No decision	Same	Same	No decision	No decision	
Ped Bariatric Surgery <18	Aug-07	Not covered	Less Restrictive	Less Restrictive	Same	Same	n/a	No decision	
Ped Bariatric Surgery 18-21		Conditional	Same	Same	Less Restrictive	Less Restrictive	Less Restrictive	Same	
Lumbar Fusion for DDD	Nov-07	Conditional	More Restrictive	No decision	Same	Same	No decision #	No decision	
Discography for DDD	Feb-08	Not covered	Less Restrictive	Same	No Decision	No decision	No decision	No decision	
Virtual Colonoscopy (CTC)-Cancer screening	Feb-08	Not covered	Same*	Same	Same	Same	Same*	Less Restrictive	

- **Summary Comparison of HTA Decisions and Private Insurers:**
 - Same as Private (some occur before, some after) - 47%
 - Private Insurer is Less Restrictive - 22%
 - Private Insurer is More Restrictive - 9%
 - Private Insurer does not have published policy - 18%

HTA Program Recognition

- **Proto (Mass General Hospital Publication)**
 - Spring 2010, Article on evidence based medicine as used by providers in setting guidelines, and payers
 - <http://protomag.com/assets/evidence-based-medicine-burden-of-proof>
- **Council of State Governments, Western Region**
 - HTA Program is Regional Finalist for the Innovations Awards
- **Invited Presentations**
 - UW Symposia on EBM Decision Making –June 2010
 - *Academy Health/State Coverage Initiatives - National Meeting* – August 2010
 - *Medicaid Medical Directors Learning Network* – Aug 2010

HTA Transparency Improvement

- **Industry and Stakeholder Meetings January – May 2010**
 - Transparency related issues:
 - Unclear Public Comment Times
 - No comprehensive information about HTA Process (begin to end)
 - No Guidance on Public Comments – when and what type of information sought
 - Suggested Medicare and NICE processes as examples
- **HTA Process Review and Description – June-July 2010**
 - *Reviewed other program processes; updated program documents; drafted full program description*
 - *Review by stakeholders in July 2010*
 - *Publication to Website for central information Aug. 2010*

- **Hyaluronic Acid**
- **Spinal Cord Stimulators**
- **Breast MRI**
- Knee Replacement Surgery
- Vertebroplasty, Kyphoplasty, Sacroplasty
- Glucose Monitoring
- Sleep Apnea Diagnosis and Treatment
- Routine Ultrasound in Pregnancy
- CT/MR for Pelvic and Abdomen
- ABA Therapy for Autism
- Spinal Injections

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Discography for DDD	Feb-08	Not covered	Less Restrictive	Same	No Decision	No decision	No decision	No decision
Virtual Colonoscopy (CTC)-Cancer screening	Feb-08	Not covered	Same*	Same	Same	Same	Same*	Less Restrictive
Intrathecal Pump for chronic noncancer pain	Feb-08	Not covered	Less Restrictive	Less Restrictive	No Decision	No decision	Less Restrictive	No decision
Arthroscopic Knee Surgery for Osteoarthritis	Aug-08	Not covered	Less Restrictive	Less Restrictive	No Decision	No decision	Same	No decision
Artificial Disc Repl-Lumbar	Nov-08	Conditional	Less Restrictive	No decision`	More Restrictive	More Restrictive	Same	More Restrictive
ADR- Cervical		Conditional	Same	No decision`	More Restrictive	More Restrictive	No decision	More
Computed Tomographic Angiography (cardiac)	Nov-08	Conditional	Less Restrictive	Less Restrictive	More Restrictive	More Restrictive	No decision #	More Restrictive
Cardiac Stents	May-09	Conditional	Less Restrictive	Less Restrictive	No Decision	No decision	No decision	No decision
Vagal Nerve Stim-Epilepsy	Aug-10	Conditional	Same	Same	Same	Same	Same	No decision
Vagal Nerve Stim-Depress.		Not covered	Same	Same	Same	Same	Same	Same
Bone Growth Stim-Elec.	Aug-09	Conditional	Same	Same	Same	Same	Same	No decision
Bone Growth Stim-Ultsnd		Conditional	Same	Same	No Decision	No decision	More Restrictive	No decision
Transcutaneous Electrical Neural Stimulation (TENS)	Oct-09	Not covered	Less Restrictive	No decision				
Calcium Scoring for Cardiac Disease	Nov-09	Not covered	Same	Same	Same	Same	No decision	No decision
Hip Resurfacing	Nov-09	Conditional	Same	Same	No Decision	No decision	No decision	Same
(Note: of 19 decisions)		% same	47%	47%	47%	47%	37%	16%
		% less restrictive	47%	32%	5%	5%	16%	5%
		% more restrictive	5%	0%	16%	16%	5%	16%
		% no published dec.	0%	21%	26%	26%	42%	53%

47%
22%
9%
18%

Web site reference	Access Date	Notation Key:
http://www.aetna.com/healthcare-professionals/policies-	4/20/2010	* Policy Cites HTA # CMS reviewed but no decision
http://blue.regence.com/trgmedpol/	4/20/2010	
http://www.bcbs.com/blueresources/tec/tec-assessments.html	4/21/2010	Tech specific notes on major differences
http://www.ghc.org/hosting/clinical/criteria/index.jhtml	4/28/2010	1 allows positions other than supine 2 Younger age; age not restricted; more invasive 3 Lack Structured, intensive, multi-disciplinary 7 Debridement (not lavage) permitted 'Under review at one entity'
https://www.premera.com/stellent/groups/public/docu	5/4/2010	

Policy comparison is to the HTCC Decision

Noted as same if match or similar coverage - unable generally to determine which policy first
 HTA goals: enhance consistency among agencies; ensure transparency and public process;
 base decision on evidence; use safety, efficacy, and cost-effectiveness

Questions: Compared to HTA -

1. Are plans coverage decisions as transparent and engage public?
2. Are plans making decisions?
3. Is formal analysis done?
4. When formal analysis completed, how consistent are results?
5. How consistent are policies overall?
6. Appropriateness of consistency - using same criteria?
7. Are there outlier "more restrictive" decisions that HTA should address and what criteria
8. Where no decision, are plans paying?

CURRICULUM VITAE

EDGAR E. CLARK, MD

PERSONAL

Birthdate: 10 October 1942

Birthplace: Los Angeles, California

Residence: 248 SW Kingston Ave.

Portland, Oregon 97201

Family Status: Married; two grown children

EDUCATION

College: BS in Chemistry, Stanford University; 1964

Medical School: MD, Univ. of California, San Francisco (UCSF), Calif.; 1968

Internship: Straight Medical Internship, Univ. of Washington Affiliated Hospitals,
Seattle, Wa.; 1968-9

Residency: Diagnostic Radiology, Univ. of California, San Francisco; 1971-4

Nuclear medicine, Univ. of California, San Francisco; 1974-5

Health Administration: Masters of Science in Health Administration, University of Colorado
School of Business, Denver, Colorado; 1994

ACADEMIC AWARDS AND HONORS

BS with Distinction, Stanford University, 1968

Merck Manual and Mosby Scholarship Book Award for Academic Excellence at MD
Graduation, UCSF, 1968

Alpha Omega Alpha Honor Fraternity, UCSF, 1968

Chief Resident, Diagnostic Radiology, UCSF, 1973-4

MILITARY SERVICE

General Medical Officer, Captain, US Army, 1969-71;
US Kenner Army Hospital, Ft Lee, Va.

EMPLOYMENT

Staff Radiologist, Portland Adventist Hospital, Portland, Oregon, 1975-86

Medical Director, Outpatient Radiology Center, Portland, Oregon, 1986-- 1999

Owner/Medical Director, Body Imaging Radiology, Portland, Oregon, 1998-- 1999

Staff Radiologist, Body Imaging Radiology, Portland, Oregon, 2000—2003

Medical Director for Pacific Northwest, HealthHelp, Inc. (Radiology Utilization Management). 2001-- May, 2004.
Locum Tenens Radiologist, 2004—2006.
Consultant, Center for Evidence-based Policy, Oregon Health and Science University, Portland, OR, 2006—present
Consultant, AllMed Healthcare Management, Portland, OR., 2006- present

COMMITTEES AND COMMUNITY SERVICE

*Member of Audit, Cancer, Institutional Review, Safety, Radiation Committees (Chair of *Cancer and Institutional Review Committees), Portland Adventist Hospital, 1975-88.
*Member of Radiology Chairman Search Committee, Oregon Health Science Univ.,1988
*Member of MSAC Committee, Blue Cross Blue Shield of Oregon) 1986-present
*Board, Portland Adventist Hospital IPA, 1985-8
*Board of Trustees, Oregon Episcopal School, 1988-91; Chair, Development Committee
*Clinical Instructor, Department of Public Health and Preventive Medicine, Oregon Health Science University, 1994—1997
*Volunteer, The Nature Conservancy, 2000-- present; work with Cynthia Beckwith in Development and Dan Salzer on Assessment and Monitoring project
*Board of Trustees, The Nature Conservancy of Oregon, 2007-- present

MEMBERSHIPS IN PROFESSIONAL SOCIETIES

Diplomate, American Board of Radiology, 1974
Diplomate, American Board of Nuclear Medicine, 1975
Member, American College of Radiology and Oregon Radiological Society, 1976- 2005
Member, Multnomah Medical Society, 1975- present
Member, Oregon Medical Association, 1975- present
American Roentgen Ray Society, 2003- 6

PUBLICATIONS

Clark, EE and Hattner, RS. Brain Scintigraphy in Recurrent Medulloblastoma, Radiology 119: 633-6, June 1976.
Clark, EE and Hattner, RS Recurrent Medulloblastoma, Yearbook of Nuclear Medicine 1977, 156-7
Stevens, JS and Clark, EE. Liver Metastases of Colon Adenocarcinoma Demonstrated on 99m Tc Pyrophosphate Bone Scan. Clinical Nuclear Medicine 2: 270, 1977.
Burke, LF and Clark, EE. Ileocolic Intussusception: A Case Report. J. Clinical Ultrasound 5: 346, 1977.

**Washington State Health Care Authority, HTA Program
FINAL Key Questions and Background
Breast MRI in Diagnosis and Treatment of Cancer**

Introduction

HTA has selected using magnetic resonance imaging (MRI) of the breast used in diagnosis and treatment of cancer to undergo a health technology assessment where an independent vendor will systematically review the evidence available on the safety, efficacy, and cost-effectiveness. HTA posted the topic and gathered public input on all available evidence. Key questions guide the development of the draft evidence report.

Breast cancer is the second most common malignancy affecting women, and is an important public health concern. Accurate diagnosis and appropriate treatment are critical. Patients identified as having a possible abnormality on screening mammography or physical examination or who are at high risk may undergo additional tests, including imaging, and physical examination. An ideal diagnostic test to evaluate risk/breast abnormalities would provide accurate information appropriate to guide patient-management decisions. Such test would accurately distinguish patients who need to have a biopsy from those who can safely avoid one as well as accurately identify extent or location of malignancy (e.g. detection of contra lateral disease) for optimizing treatment. In order to appropriately guide decisions, a person who has a negative test result should be very confident that the result is correct. There are concerns about the safety, cost, and efficacy of MRI to diagnose and stage women at high risk or with breast cancer.

Key Questions

For women at risk of breast cancer based on presentation of with an abnormal mammogram; palpable breast abnormality; or relevant demographic and clinical risk factors:

1. What is the evidence that Breast MRI has the ability to diagnose or exclude breast cancer compared to current tests including mammography?
 - a. Describe sensitivity, specificity, and other key test characteristics
2. What is the evidence that breast MRI improves health outcomes for patients with suspected or diagnosed breast cancer? Including consideration of:
 - a. reduced need for other tests
 - b. more accurate diagnosis
 - c. change in treatment plan
 - d. reduced mortality and morbidity
3. What is the evidence of the safety of breast MRI?
4. What is the evidence that breast MRI has differential efficacy or safety issues in sub populations? Including consideration of:
 - a. Age, breast tissue characteristics; breast implants
 - b. Other patient characteristics or evidence of appropriate patient selection criteria
 - c. Type of scanning machine and software, reader training, and other operational factors
 - d. Provider type, setting or other provider characteristics
 - e. Health care system type, including worker's compensation, Medicaid, state employees

5. What is the evidence about the cost implications and cost effectiveness of breast MRI?

Technology Background

Technology: Breast MRI is being investigated as an adjunct to mammography for screening of high-risk women since its accuracy is not affected by breast density, it does not use radiation, and it has high sensitivity. The goal of providing early, accurate diagnosis and reducing the mortality rate associated with breast cancer is an important public health goal. Important questions include the how accurate breast MRI is in detecting breast cancer compared with conventional techniques; does imaging with a breast MRI as a supplement to mammography reduce biopsy, use of other tests, produce appropriate changes in treatment, and reduce morbidity or mortality? Further, have definitive patient selection criteria for the use of breast MRI in screening and staging been established?

Introduction and Background:

These commentaries are based on more than 18 years of clinical and research experience with contrast enhanced magnetic resonance (MR) imaging of the breast at First Hill Diagnostic Imaging (FHD) in Seattle. FHD is internationally recognized as a leading clinical and development site for MR in breast cancer. We currently perform more than 2700 breast cancer MR exams per year and evaluate and stage an average of 750 new breast cancer patients per year. We are the primary development site worldwide for Siemens for breast MR imaging and host seminars and fellowships each year attended by physicians from Australia to Europe, Asia, Canada and South America. Patients come here from other countries as well to be scanned and cared for by our team.

With the expansion of breast MR to community practice it is important and appropriate to review its strengths and limitations, as well as its best and less appropriate indications. Also you need to be aware of some limitations of the current literature on this subject, which is often outdated and not representative of current practice in the Pacific Northwest, which has led the world in the clinical development of this exam due to the efforts of FHD and the Seattle Cancer Care Alliance (University of Washington- Connie Lehman, MD, PhD). With this communication I will address some of the clinical indications and issues that the commission should be aware of to appropriately assess the current and future role of MR in breast cancer. Since the commission has indicated they have extensively reviewed the literature on this subject, only selected references will be used.

Comments:

- **High risk surveillance:** The superiority of MR for early detection of the often high grade rapidly growing tumors in the BrCa patient population and others at significant risk for breast cancer has been definitively established (1). MR detects small (5-10 mm) cancers in these pre-menopausal women with dense negative mammograms and when MR detected, they are twice as likely to be small and node negative! Decades of experience have shown that small, node negative cancers have a much more favorable prognosis. Additionally, the negative predictive value of MR even in this group with high prevalence has been established by Lehman, et.al. (2) At 99%, which makes this one of the most reliable tests in medicine in one of the most difficult and challenging situations. Determination of high risk status is still somewhat in evolution, but this is a key indication for MR.
- **Mammographically Occult Breast Cancer:** Classically these are patients who present with malignant axillary nodes but negative mammograms, clinical exams, and ultrasound. We and others have established that MR detects and can localize the usually small tumors in approximately 80% of these women, allowing them the option of breast conservation vs. mastectomy that was previously necessary. This concept has expanded to include detection of clinically and mammographically occult contralateral tumors in patients with newly diagnosed breast cancer.

MR detects contralateral occult cancers in between 3 and 10% of newly diagnosed cases. Our last assessment at FHDI was a contralateral detection rate of approximately 5%. This allows treatment of both cancers at the time of initial diagnosis, rather than a second expensive and morbid treatment episode several years later for the opposite breast when the contralateral tumor becomes apparent with conventional clinical and mammographic evaluation.

- **Pre-operative determination of tumor extent and multi-focality:** Surgical removal of multi-focal tumors is essential to both decreasing in breast recurrence and in mortality. Although this has become a primary indication for breast MR at the Swedish Medical Center facilities and SCCA, the literature was recently clouded by a poorly done prospective study from the UK (COMICE Trial (3)). This unfortunate attempt at science has caused significant concern and uncertainty and is regarded by many as misleading and poorly designed. They concluded that MR did not improve re-excision rates; we and others have found the opposite result (Beatty and Porter (4)).

A quick summary of the deficiencies of the COMICE study follows: There were 45 centers involved, many which had very limited experience with MR- it took these 45 centers almost 6 years to generate 800 cancers, which approximates the number FHDI *alone* evaluates in one year. Very few centers had MR biopsy available, CAD was not used, the re-excision rate in the control group was only 10% which is remarkably low and indicates that large surgical specimens were likely the norm. The detection rate for contralateral cancers was only 1.6 % which is half of the lowest rate reported elsewhere. 70 % of patients were post-menopausal and there was no control on the definition of *%adequate margins+*(it was left to the judgment of the individual surgeon). Finally the image slice thickness and resolution of the MR exams would not be considered current and is much inferior to the standard in the Pacific NW.

- **Affect of MR on mastectomy and re-excision rates:** Early studies concluded that mastectomy rates increase with MR utilization and this appears to be variably true for some centers, and not for others. This is again very dependent on the experience *and cooperation* of the surgeons, pathologists and radiologists. Newer data from experienced sites with coordinated evaluations between specialties have different conclusions: Recent data on this from Sweden from Drs. Tabar, Ingvarsson, and Tot are presented below and in my opinion more representative of the current status in Seattle and of future trends elsewhere:

*Comparison of surgery on breast cancer patients
Falun, Sweden 2005 vs 2008/2009 combined ***

	Before preop. MR 238 cases	MR era 428 cases
Primary mastectomy	40.3% (96/238)	38.1% (163/428)
Breast conservation	59.7% (142/238)	61.2% (262/428)
Re-op frequency after breast conserv. surgery <i>(re-excision or mastectomy)</i>	26.1% (37/142)	18.7% (49/262)

**Courtesy of Laszlo Tabar, MD June 2010

Dr. Tabar is the world's foremost expert on mammography. His experience with MR began in 2006; after review of their data, presented above, his current recommendation is for routine pre-operative use of MR in newly diagnosed breast cancer due to its beneficial effect on pre-operative determination of extent and for detection and subsequent surgical removal of previously unsuspected multifocal breast cancer. As noted above, the mastectomy rate did not increase but the re-excision rate for inadequate margins dropped significantly. I have consulted on their MR technique and trained their physicians on breast MR since 2007 and anticipate that their re-operation rate will diminish even further. Decreasing reoperation rates for positive or inadequate surgical margins saves substantial cost and morbidity.

- **Safety:** Breast MR uses no ionizing radiation and the contrast materials used are considered very safe when used in patients with normal or adequate renal function. Renal function is currently screened with estimates of glomerular filtration rates from serum creatinine levels and historical data.
- **Differential efficacy:** MR is not adversely affected by breast density or the presence of implants, and therefore is particularly effective in a population of women who are not only at greater risk for cancer because of breast density, but also have a lower likelihood of early detection due to the well established limitations of mammography in dense breasts. Our surgeons find pre-operative MR particularly

valuable for surgical decision-making in patients with large and dense breasts. This advantage is naturally greater in pre-menopausal than post-menopausal patients, however.

- **Lobular carcinoma and ductal carcinoma *in situ* (DCIS):** Lobular carcinoma is a most insidious tumor. It is more commonly diffuse or multi-focal and is twice as likely as ductal carcinoma to be bilateral at diagnosis. It is frequently occult to mammography until large, but not to MR which detects the abnormal vascularity associated with this challenging tumor even when it is small. DCIS is increasingly recognized to have benign and malignant variants. The most malignant types are readily visualized in their full extent, even without calcification and can be characterized by MR pre-operatively. This allows better surgical planning and fewer re-operations for inadequate or positive margins and therefore saves cost, time and morbidity.
- **Equipment, software, training and CAD:** Significant differences in equipment capabilities and non-standardized methods remain in breast MR. The American College of Radiology just recently released guidelines for Breast MR and a pathway for certification in this subspecialty area (____). This has been much needed and will, over time, allow the kind of standardization of equipment, training, and methodology that is now applied to mammography. Specific training in breast MR for the radiologist and technologist will be required as will the capability of providing MR guided biopsy. CAD systems are invaluable in breast MR for kinetic analysis, motion correction, 2D and 3D reconstructions, for comparison to prior studies and reproducibility. They allow interpretation of extremely large image files that may number more than 3000 images per exam. The ability of these sophisticated systems to correct for patient motion frequently saves a study that would otherwise need to be repeated.
- **Provider type and setting:** These very specialized exams are best performed at sites with a multi-disciplinary team of surgeons, pathologists, oncologists and radiologists and significant volumes of breast cancers. In addition to dedicated MR equipment such as breast imaging coils, MR-guided biopsy, breast ultrasound and biopsy and mammography must be available as well.

Bruce A. Porter, MD, FACP
Medical Director
Swedish/First Hill Diagnostic Imaging
Seattle, Washington



Agency Medical Director Comments

**Health Technology Clinical Committee
MRI of the Breast**

■ AMDG Perspective

- **Technology is not new, but the application is changing**
 - Screening of high risk (BRCA1 and 2) and high risk is changing (post cancer treatment surveillance)
 - Screening the contra-lateral breast prior to mastectomy
 - Screening breast when dense tissue or implants are present
- **Prevention is a shared agency focus: increased number of individuals screened for Breast cancer results in better health**
 - Are there better outcomes with this new technology?
- **A key question: Will this additional method increase benefits when lesser cost screening has known outcomes?**
 - Adding more expensive, additional test increases costs
 - Is the measure of a new test only SN/SP and PPV, and
 - Are there better outcomes?

Current State Agency Policy

State Agencies Policies – no current formal coverage/non coverage, no current restrictions.

- DSHS allows MRI of the Breast in
 - Hayes recommendations
 - High Risk Clients
- UMP allows MRI
 - Hayes recommendations

- **State Agencies Questions (Breast Cancer Preventive Screening)**
 - **Safety:** Benefit vs. Harms Issues?
 - Do less expensive screenings (mammography and ultra sound) have less risk for false positives moving onto chemo and radiation therapies
 - Does the identification of non-specific findings lead to unnecessary interventions?

■ State Agencies Questions

□ Effectiveness

- Is the evidence of sensitivity, specificity, and reliability enough to make a benefit decision?
- Can we define when screening mammogram vs. MRI is needed in a “high risk” population?

□ Cost

- Higher cost, proposed additional test
- Do added tests, if suspicious lesions, equivocal results or poor study add to inappropriate costs?
- What is the impact of differential activity in the community?

Codes for Breast MRI and Breast Surgery

Related Medical Codes		
Codes	Number	Description
CPT - MRI	77058	MRI, single breast (since 2006))
	77059	MRI, both breasts (since 2006)
	0159T	MRI add-on (since 2006) (use as part of cost, not a separate procedure)
	C8903-8	MRI of the Breast (still in use)
	76093-4	DEL-MRI Breast w/wo contrast, uni/bi (until 2005-6)
Breast Surgery	19301-7	Breast surgery – mastectomy partial-radical
Diagnosis codes	174.*	Primary malignant breast cancer, female
	233.0,233.3	
	239.3	Neoplasm, cancer in situ, breast
Other diagnostic procedures for breast cancer		
Mammogram	77051-77057	Mammogram, diagnostic or screening, interpretation and guidance
	G0202-7	Screening mammogram, digital, bilateral

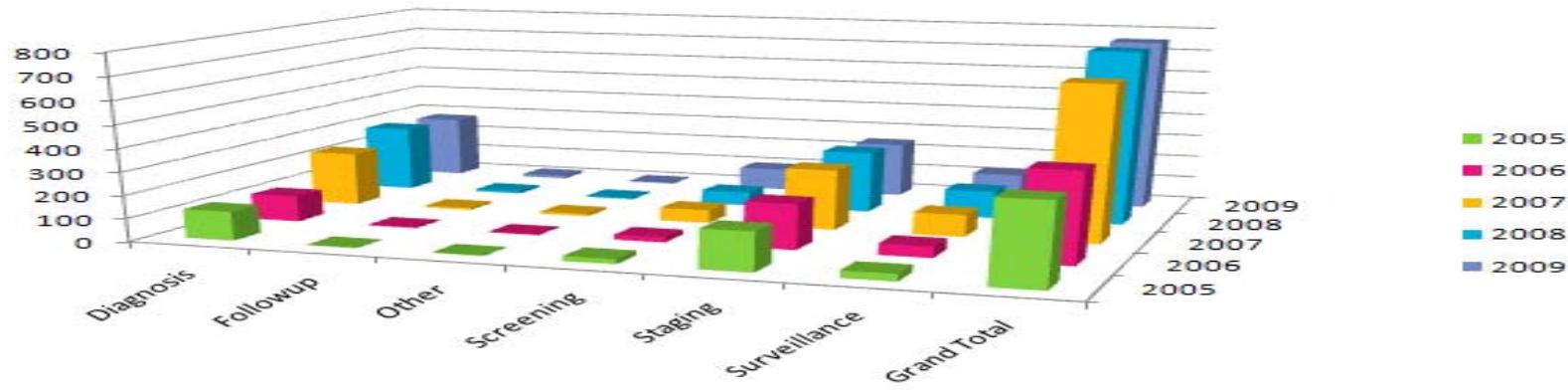
State Agency Utilization (SFYs 2005 and 2009)

Figure 1. Washington State Agency Annual Reimbursement Costs for Breast MRI, 2005-2009

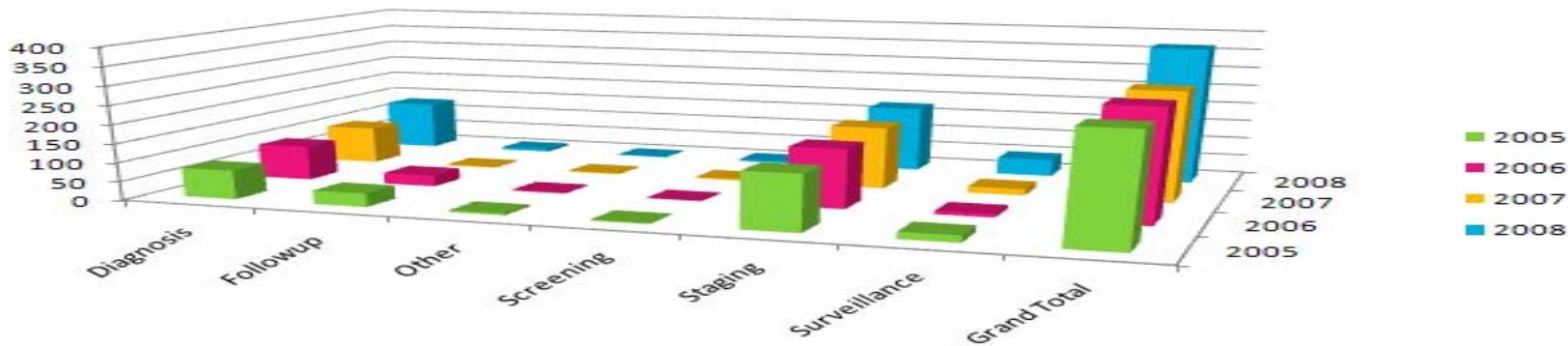
Year/Agency	2005	2006	2007	2008	2009	5 Year Total
UMP/PEP						
Annual Total Cost	\$388,836	\$434,526	\$707,429	\$787,489	\$793,663	\$3,111,943
BMRI Count¹	352	391	676	761	756	2936
Average cost¹	\$1,105	\$1,111	\$1,046	\$1,035	\$1,050	\$1,060
DSHS						
Annual Total Cost	\$95,210	\$112,996	\$46,520	\$93,869	\$117,854	\$466,449
BMRI Count²	160	180	90	156	248	834
Average cost²	\$595	\$628	\$517	\$602	\$475	\$559
Totals						
Annual Total Cost	\$484,046	\$547,522	\$753,949	\$881,358	\$911,517	\$3,578,392
BMRI Count	512	571	766	917	1004	3770
Average cost	\$945	\$959	\$984	\$961	\$908	\$949

There is Differential Use Across Populations and Reasons: Do we know why?

UMP BMRI Counts by Diagnosis Code Classification, 2005-2009

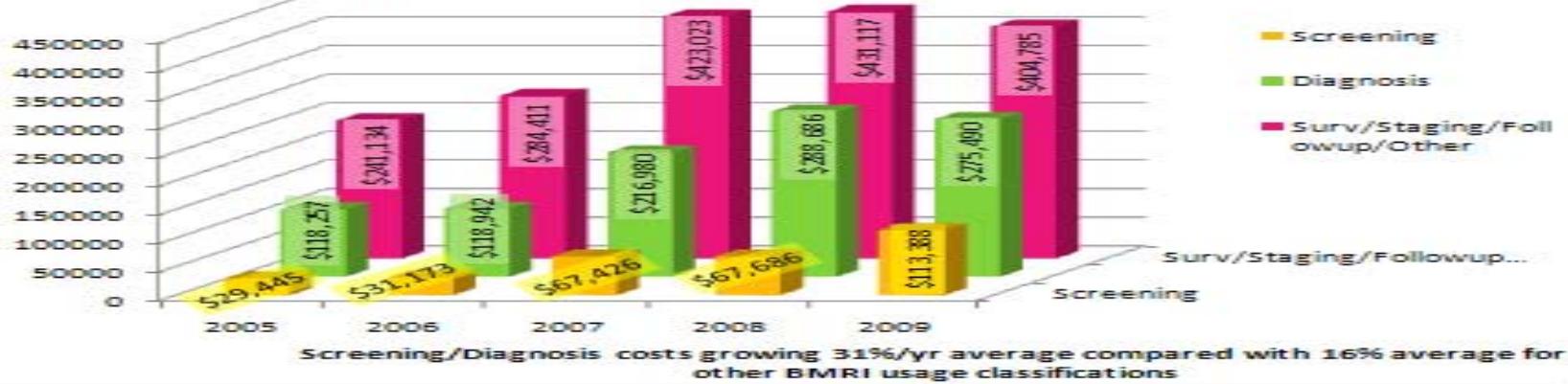


DSHS BMRI Counts by Diagnosis Classification, 2005-2008



Are Reimbursements causing Differential?

UMP BMRI \$ for Screening and Diagnosis Compared with Other Classifications

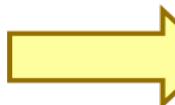


DSHS BMRI \$ for Diagnostics Compared with Other Classifications

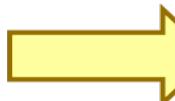


Should there be a screening Mammogram before an MRI?

UMP/PEP Patients w/wo Mammogram Prior to BMRI	2005	2006	2007	2008	2009	Grand Total
Count of BMRI Patients						
With a prior Mammogram	100	165	572	694	714	2245
Without a prior Mammogram	252	226	104	67	42	691
Total	352	391	676	761	756	2936
Percent of BMRI Patients						
With a prior Mammogram	28%	42%	85%	91%	94%	76%
Without a prior Mammogram	72%	58%	15%	9%	6%	23%
Mammogram patients using BMRI						
Count of Mammogram Pts	5436	9633	34428	40039	42583	132118
Percent Mammogram pts w/BMRI	1.6%	1.7%	1.9%	1.9%	1.8%	1.8%



DSHS Patients w/wo Mammogram Prior to BMRI	2005	2006	2007	2008	Grand Total
Count of BMRI Patients					
With a prior Mammogram	42	88	266	457	853
Without a prior Mammogram	243	236	142	137	759
Total	285	324	408	594	1612
Percent of BMRI Patients					
With a prior Mammogram	15%	27%	65%	77%	53%
Without a prior Mammogram	85%	73%	35%	23%	47%
Mammogram patients using BMRI					
Count of Mammogram Pts	1592	3900	12182	12564	30238
Percent Mammogram pts w/BMRI	2.6%	2.3%	2.2%	3.6%	2.8%



Breast MRI: Other Centers, Agencies and HTAs

□ *Hayes Inc.* (06)

- Screening MRI for Women at Average Risk for Breast Cancer
 - **D** for use of contrast-enhanced breast MRI in screening women at average risk for breast cancer.
- Magnetic Resonance Imaging for Breast Cancer Screening in Women at High Risk
 - **B** for supplementing current breast cancer screening procedures in women who are at high risk for breast cancer, especially those for whom mammography is less sensitive; and **D** for screening women at average risk for breast cancer.

□ *Centers for Medicare & Medicaid Services (CMS):*

- Annual breast cancer screening with clinical examination and mammography is covered by Medicare, breast cancer screening with MRI is not covered as a routine preventive measure. However, breast MRI may be covered as a diagnostic procedure (CMS, 2007).

□ *National Cancer Institute (NCI):*

- MRI “has been used to evaluate palpable breast masses and to discriminate between cancer and scar, but any role MRI might have in breast cancer screening has not been established” (NCI, 2006b).

Breast MRI: Other Centers, Agencies and HTAs

- ***American Cancer Society (ACS): (Saslow et al., 2007):***
 - Carry *BRCA 1* or *BRCA 2* mutation.
 - Have a first-degree relative with *BRCA 1* or *BRCA 2* mutation and are untested.
 - Lifetime risk of breast cancer $\geq 20\%$ to 25% using standard risk assessment models.
 - Received radiation treatment to the chest between ages 10 and 30, such as for Hodgkin's disease.
 - Carry or have a first-degree relative who carries a genetic mutation in the *TP53* or *PTEN* genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes).
- ***National Comprehensive Cancer Network (NCCN 2007):***
 - Does the increase in cancer detection confer a mortality benefit given the large increase in false-positive rates, and
 - The possibility of over diagnosis.
 - All of the published studies are observational studies
 - No patient outcomes (including morbidity, survival, or mortality) to show improvement when women are screened with breast MRI.

The USPSTF

- **Potential Preventable Burden.** Studies of the use of contrast-enhanced MRI very high-risk populations:
 - ❖ Detected more cases of cancer than did mammography
 - ❖ Unknown if this detection results in lower mortality.
- **Potential Harms.**
 - ❖ Reactions from the injection of contrast material.
 - ❖ More false-positive results than does mammography.
 - ❖ Potential for over diagnosis
- **Costs.** Magnetic resonance imaging is much more expensive than either film or digital mammography.
- **Current Practice.** Magnetic resonance imaging is not currently used for screening women at average risk for breast cancer.

Breast MRI: Other Centers, Agencies and HTAs

- The USPSTF concludes that the current evidence is insufficient to assess the additional benefits and harms of either digital mammography or magnetic resonance imaging (MRI) instead of film mammography as screening modalities for breast cancer.

Grade I Statement

- the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.)

■ State Agencies Summary View

- MRI in Breast Cancer Screening
 - Improved Sen/Spe but no outcome data
 - Data is best in BRC1 and 2
 - No evidence that increase screenings improves health outcomes
- Safety Issues not resolved
 - Increased incident of biopsies stemming from false positive is not known
- Costs Issues
 - Added test adds cost
 - Costs Effectiveness studies are limited
 - Tests performance has wide variability in the community

■ State Agencies Summary View

- Consistent with Medicare and 3 evidence based guidelines, Breast MRI is of unknown benefit or no benefit in screening
 - ❖ Average risk women (not within scope here)
 - ❖ Dense breasts and breasts with implants
 - ❖ High Risk
- If coverage for high risk, limited to only the highest risk women due to high false-positives, unknown health outcome benefit, and very high test cost
 - BRCA 1 and 2 and other high risk mutations for breast cancer , with mammogram screening first
- Pre-operative staging - current evidence that changes treatment but no evidence on outcome, at least limit to
 - ❖ Contra-lateral mastectomy decision making

?Questions?

Breast Magnetic Resonance Imaging (MRI) In Diagnosis and Treatment of Cancer in Women at High Risk

Provided by Delfini Group, LLC

Project Manager: Michael Stuart, MD

1

Definitions

- High risk: High risk for developing breast cancer is variously defined in clinical trials but frequently refers to women
 - With a calculated lifetime risk of 20% or greater
 - With a calculated risk of greater than 1% per year
 - With genetic BRCA 1 or BRCA 2 mutation
 - With a history of breast cancer
 - With a family history consistent with a hereditary breast cancer syndrome
- Other risk factors such as age, ethnicity, age at menarche, previous breast biopsy, parity, age at first birth are included in some risk calculation models

2

Definitions

- **Sensitivity (SN):** Correct identification of a disease or condition by a screening test- of all subjects with a disease, the percent testing positive (true positives)
- **Specificity (SP):** Correct identification by a screening test as not having a disease – of all subjects without the disease, the percent testing negative (true negatives)
- **Positive Predictive Value (PPV):** Of all subjects testing positive, the percent who have the disease, based on the population's prevalence of disease

3

Definitions

- **Re-excision:** Refers to additional surgery performed after initial breast cancer excision. Re-excision is determined by histopathological examination of the surgically excised specimen to see if the borders are cancer-free
- **MRI and Treatment Plans:** Information provided by MRI testing is used to plan the extent of surgical excisions. This is **one part** one of cancer staging (which includes evaluation of histopathology, cancer size, local, nodal and distant cancer spread)
- **Recurrence of breast cancer:** Refers to reappearance of cancer in similar location and with similar histology to the index cancer (in contrast to the development of a second breast cancer)

4

Background

- 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** based on randomized controlled trials (RCTs) and concluded that **film mammography was the standard for detecting breast cancer in women at average risk** of developing breast cancer (USPSTF 2002)

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Background

- USPSTF concludes (Grade I) that the current evidence is insufficient to assess the additional benefits and harms of magnetic resonance imaging (MRI) instead of film mammography.
 - Noted evidence related to higher detection rate in women at high risk, but did not separately recommend
- **American Cancer Society (ACS) 2007** recommends women at high risk of breast cancer be also screened with MRI -no evidence cited in recommendation
 - High risk defined as MRI screening for women starting at age 30 if their lifetime risk is approximately 20% to 25% - no evidence cited
- **National Cancer Institute** recommends mammography and clinical breast exams and self breast exams citing fair evidence of benefit; no recommendation for MRI

6

Aim of Evidence Review

- To systematically review, critically appraise and analyze research evidence regarding the accuracy, efficacy, effectiveness and safety of MRI in the detection of breast cancer in women at high risk for developing breast cancer

7

Evidence Review: Key Questions

For women at risk of breast cancer based on presentation of with an abnormal mammogram; palpable breast abnormality; or relevant demographic and clinical risk factors:

1. What is the evidence that Breast MRI has the ability to diagnose or exclude breast cancer compared to current tests including mammography?
2. What is the evidence that breast MRI improves health outcomes for patients with suspected or diagnosed breast cancer
3. What is the evidence of the safety of breast MRI?
4. What is the evidence that breast MRI has differential efficacy or safety issues in sub populations?
5. What is the evidence about the cost implications and cost effectiveness of breast MRI?

8

Levels of Evidence (LOE)

- LOE is “high” if we find more than one grade B (valid and possibly useful) study reporting consistent results
- LOE is “moderate” if we find at least one grade B study
- LOE is “borderline” if we find at least two grade B-U (possible to uncertain validity and usefulness) studies with consistent findings
- LOE is “inconclusive” if we find single grade B-U studies or grade B-U studies with conflicting results or only grade U studies (uncertain usefulness or validity)

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KEY POINTS

Adding MRI to Annual Screening With Mammography (MX) in Women at High Risk...

- Will increase sensitivity over MX alone in screening for breast cancer in women at high risk and will detect approximately **2 to 5 additional breast cancers per 100 breast screenings**
- Will increase detection of breast cancer in women with increased breast density
- Will increase incidence of false positives (benign biopsies) – **up to 11 false positives (benign biopsies) per 100 MRI exams**
- Will change treatment plans including wider excisions and conversion to mastectomy for some women undergoing surgical planning for recently diagnosed breast cancer
- May or may not change re-excision rates, cancer recurrence rates or mortality rates

10

KEY POINTS Safety

Adding MRI to Annual Screening With MX in Women at High Risk

- No reliable evidence for harm from increased radiation exposure
- No reliable evidence to suggest that gadolinium-based contrast agents are associated with adverse outcomes in the fetus, infants or children
- No reliable evidence for meaningful adverse psychological outcomes from false-positive MRI test results in women at high risk for breast cancer
- No reliable evidence for increased cancer in women with breast implants

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KEY POINTS Cost and Cost-effectiveness

Adding MRI to Annual Screening With MX in Women at High Risk

- Adding MRI to mammographic breast cancer screening in women at high risk of breast cancer will increase diagnostic and therapeutic costs
- Accurately predicting mortality reduction and other health outcomes in high-risk women may not be possible unless results from valid RCTs become available
- Cost per QALYs gained range from approximately \$25,000 to \$311,000 depending upon assumptions about various costs, yearly risk, mortality reduction with the addition of MRI, frequency of screening, etc.

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KEY QUESTION 1: DIAGNOSTIC ACCURACY—FINDINGS

What is the evidence that breast MRI has the ability to diagnose or exclude breast cancer compared to current tests including mammography (MX)?

- a. Describe sensitivity, specificity and other key test characteristics
 - Adding yearly screening with MRI to mammographic screening **will increase detection of breast cancer**
 - Adding yearly screening with MRI to mammographic screening **will result in a higher rate of false positive tests, benign breast biopsies and more extensive surgeries**

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KEY QUESTION 1: DIAGNOSTIC ACCURACY—Lifetime Risk 20% or Greater—Sensitivity (SN)

- Lord 07: Systematic Review (Best evidence for accuracy)
 - 5/91 relevant studies included in review based on acceptable quality criteria
 - Sensitivity with addition of MRI to mammography (3 studies) women high risk
 - **94% (95% CI, 86% to 98%)**
 - **Incremental sensitivity (over MX) was 58% (95% CI, 47% to 70%)**
 - Level of Evidence (LOE): Borderline

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KEY QUESTION 1: DIAGNOSTIC ACCURACY— Lifetime Risk 20% or Greater—Sensitivity (SN)

- Detection of breast cancer in contralateral breast in women with breast cancer by adding MRI to mammography
- Brennan 09: meta-analysis 22 studies
- **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**

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KEY QUESTION 1: DIAGNOSTIC ACCURACY— Lifetime Risk 20% or Greater—Specificity (SP)

- Lord 07 Systematic Review
- **Specificity:** Study results were inconsistent, but suggested a 3-5-fold higher risk of patient recall for investigation of false positive results with the addition of MRI
- **False positive recall rates (two studies) ranged from 6 to 106 per 1000 MRI exams**
- LOE: inconclusive

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KEY QUESTION 1: DIAGNOSTIC ACCURACY— Recent Diagnosis of Breast Cancer—SN/SP

- Lehman 07: prospective observational study, N=969, recent diagnosis of breast cancer, negative mammogram and clinical exam of contralateral breast within 90 days before enrollment
- MRI detected clinically and mammographically occult breast cancer in the contralateral breast in 30 of 969 women (3.1%)
- **Sensitivity of MRI in the contralateral breast was 91%**
- **Specificity of MRI in contralateral breast was 88%**

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Adding MRI to MX For Yearly Screening in High Risk Women

SUMMARY

- Will result in—
 - An increased detection of approximately **2 to 5 breast cancers** per 100 breast screenings
 - An increased incidence of false positives (benign biopsies)—**up to 11 false positives** (benign biopsies) per 100 MRI exams

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KEY QUESTION 2: IMPROVED OUTCOMES

What is the evidence that breast MRI improves health outcomes for patients with suspected or diagnosed breast cancer?

- a. reduced need for other tests**
- b. more accurate diagnosis**
- c. change in treatment plan**
- d. reduced mortality and morbidity**

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Reduced Need for Other Tests

- Breast cancers may be missed if MRI or mammography is omitted from screening high risk women (Lord 07, Berg 08, Weinstein 09, Kuhl 10)
- Reducing the need for other tests becomes a **judgment call based on evidence and other factors such as patient preference, breast density, contraindications to MRI contrast and cost**
- LOE: Inconclusive

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Reduced Need for Other Tests

Lord 07

Diagnostic Test	Sensitivity	Specificity
MX Alone	25% to 59%	NR
MX+MRI	94% (95% CI, 86% to 98%)	True value not calculated in meta-analysis but studies reported from 77% to 96% for MRI+conventional testing
MX+US	49% to 67%	NR
MRI+Mammography + US	86% to 100%;	NR

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Change in Treatment Plans

- Preoperative MRI testing in women with recently diagnosed breast cancer will change treatment plans for some women (LOE: Borderline)
- The evidence is insufficient to determine whether changes in treatment plans based on the results of preoperative MRI testing are beneficial (LOE: Insufficient)

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Change in Treatment Plans

Houssami 08: meta-analysis of 19 retrospective observational studies of 2610 women with breast Ca

- 16% increase in detected ipsilateral breast cancer with MRI compared to conventional testing
- **11.3% underwent more extensive resections**
- Conversion from wide local excision (WLE) to **mastectomy was 8.1%** (95% CI, 5.9 to 11.3)

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Change in Treatment Plans

Lim 10: Retrospective cohort study of patients with newly diagnosed breast cancer (N=535) with planned breast conservation surgery

- 18.3% had additional suspicious lesions on breast MRI, but not detected with conventional methods
- 8.8% had additional malignancies
- 6.9% had benign lesions
- **15.7% had a change in surgical treatment plans based on the MRI results**
- Mastectomy rate did not change significantly (OR 0.98; 95% CI, 0.95 to 1.00; P = 0.059)

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Change in Treatment Plans

Pengel 09: Retrospective cohort study of women with invasive breast cancer; N=349

- **Treatment changes in MRI group: mastectomy (8.7%) or wider excision (2.3%)**

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Change in Re-excision Rates

- LOE for effect of preoperative MRI testing on re-excision rates following surgical treatment: Inconclusive

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Change in Re-excision Rates

Mann 10: Retrospective study using pathological and oncological databases; invasive lobular carcinoma; N=267

- Significant difference in re-excision rate
 - **27% re-excision rate** in patients not receiving preoperative MRI compared to
 - **9% re-excision rate** in the MRI group, OR 3.64 (95% CI, 1.30 to 10.20, P = 0.010).

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Change in Re-excision Rates

Pengel 09: Retrospective cohort study; N=349

- No significant difference in incomplete excision rates between the MRI group, 13.8%, and the non-MRI groups, 19.4% (P = 0.17)

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Change in Re-excision Rates

Turnbull 10: The first randomized controlled trial (RCT) to assess whether preoperative breast MRI in early-stage breast cancer can decrease reoperation rates (6 mos) for incompletely excised breast cancer included 1623 women with early breast cancer

- **No significant difference in re-excision rates;** with MRI 10.4% vs 11.2% (no MRI)

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Change in Re-excision Rates

Turnbull 10 (CONT)

- However, results of this RCT are inconclusive because 15 (26%) of the 58 women undergoing mastectomy did not have preoperative verification of breast cancer

30

Recurrence Rates

- There is insufficient evidence to determine if preoperative MRI testing in women with early invasive breast cancer reduces recurrence rates or mortality rates
- Adequately powered prospective trials are lacking
- LOE: Inconclusive

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Recurrence Rates

Fischer 04: Retrospective study of 346 patients

- Local recurrence rate after breast conservation treatment was 6.8% (9/133) in patients without a breast MRI and 1.2% (1/86) in patients with a breast MRI ($P < .001$).

32

Recurrence and Mortality

Solin 08: Retrospective cohort study of 756 women with early stage invasive breast carcinoma or ductal carcinoma in situ who underwent breast conserving surgery (BCS)+irradiation

- There were **no statistically significant differences** between the two groups for—
 - **8-year local failure rate (3% vs 4%, P=.32)**
 - **8-year rates of overall survival (86% v 87%, P=.51)**
 - **Freedom from distant metastases (89% v 92%, P=.16)**
 - **Contralateral breast cancer (6% v 6%, P=.39)**

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Key Question 2: Health Outcomes SUMMARY

- Adding preoperative MRI testing for surgical planning in women with diagnosed breast cancer—
 - **Will change treatment plans for some women** and result in wider local excisions and conversion from wide local excision to mastectomy
 - May or may not change
 - **Rates of re-excision**
 - **Rates of breast cancer recurrence**
 - **Mortality rates**

34

Key Question 3: Safety

What is the evidence of the safety of breast MRI?

Radiation Exposure: There is no reliable evidence to suggest that MRI radiation exposure from screening or testing results in adverse outcomes for women at high risk of breast cancer (LOE: Inconclusive)

- MRI uses non-ionizing radiation

Pregnancy: There is no reliable evidence to suggest that gadolinium-based contrast agents are associated with adverse outcomes in the fetus, infants, children (Chen 08)

- Classified as category C drug: Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal or other) and there are no controlled studies in women, or studies in women and animals are not available

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Key Question 3: Safety

What is the evidence of the safety of breast MRI?

Chronic Kidney Disease

Shellock 06: 79 observational studies of gadolinium chelates in conjunction with MRI imaging

- Data and totaled more than 1.5 million applications of gadolinium agents
- Adverse event rates were similar in the contrast agent group (13%) and placebo group (17%)

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Key Question 3: Safety

What is the evidence of the safety of breast MRI?

Adverse Psychological Outcomes

- The evidence is insufficient to conclude that false-positive MRI test results in women at high risk for breast cancer lead to meaningful adverse psychological outcomes (LOE: Borderline)
 - Indirect evidence from MX studies in average risk women
- Brewer 07: narrative review of 313,967 women at average risk for breast cancer reported no long-term symptoms of depression in women with false positive mammograms

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KEY QUESTION 4: SUBPOPULATIONS

What is the evidence that breast MRI has differential efficacy or safety issues in subpopulations? Including consideration of—

- a. Age, breast tissue characteristics; breast implants
- b. Other patient characteristics or evidence of appropriate patient selection criteria
- c. Type of scanning machine and software, reader training, and other operational factors
- d. Provider type, setting or other provider characteristics
- e. Health care system type, including worker's compensation, Medicaid, state employees

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Question 4: Breast Implants

- No clinical trials designed to evaluate differential risk of breast cancer in women with breast implants

Howshaw 01: Meta-analysis of 10 cohort and case-control studies totaling more than 152,000 women with implants followed from 10 to 20 years found **no increased risk** in breast cancer in women with implants

- LOE: Inconclusive

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Question 4: Increased Breast Density

- The evidence is suggestive that adding MRI to mammography increases sensitivity for detecting breast cancer in women with **increased breast density** or fibroglandular breast tissue

Sardanelli 04: Patients with planned mastectomy; N=90

- Breasts with fibroglandular dense pattern sensitivity for MX was **60% vs 81% for MRI, P<0.001**

40

Question 4: Technical and Provider Issues

- The evidence is insufficient for establishing optimal technical specifications for MRI testing

Warren 09: post-hoc assessment of the effect of technical aspects of MRI on diagnostic performance based on the Houssami 08 meta-analysis

- None of the technical parameters (year of study, slice thickness or repetitions after contrast-medium injection) were associated with True Positive:False Positive (TP:FP) ratio or significant performance differences
- LOE: Inconclusive

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QUESTION 5: COST IMPLICATIONS

What is the evidence about the cost implications and cost effectiveness of breast MRI?

Cost Outcomes

- The evidence is suggestive that adding MRI to mammographic breast cancer screening in women at high risk of breast cancer will increase diagnostic and therapeutic costs

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Cost-Effectiveness

- Accurately estimating cost-effectiveness may not be possible because RCTs evaluating the mortality reduction with screening or testing women at high-risk for breast cancer have not been conducted
- LOE for Cost-Effectiveness: Inconclusive

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Cost-Effectiveness

- QALYs gained by adding MRI to mammographic breast cancer screening in women at high risk for breast cancer vary greatly depending upon assumptions, e.g.,
 - Sensitivity of MRI
 - Number and frequency of diagnostic tests
 - Type and costs of therapeutic interventions
 - Risk of recurrence
 - Mortality assumptions

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Cost-Effectiveness

Population At High Risk For Breast Cancer	Breast Cancer Prevalence Rate*	Cost Per QALYs Gained With Addition of Annual MRI Screening to MX Screening
Women With BRCA 1/2	4%	\$25,277
High Risk Without BRCA 1/2: Scenario 1	3%	\$45,000
High Risk Without BRCA 1/2: Scenario 2	2%	\$72,360
High Risk Without BRCA 1/2: Scenario 3	1%	\$151,642
High Risk Without BRCA 1/2: Scenario 4	0.5%	\$310,616

Data from Taneja 09

- *5 Year Risk of Developing Breast Cancer Based on Gail model available From NCI Breast Cancer Assessment Tool (available at <http://www.cancer.gov/bcrisktool/Default.aspx>)
- Plevritis 06 : Cost-effectiveness study assumed 14% breast cancer mortality reduction for yearly mammography alone (based on RCT data average risk women) and **38% mortality reduction** for mammography plus MRI ages 25 to 69 with BRCA 1 (**based on modeling**)
- LOE Cost-effectiveness: Inconclusive

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HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on these questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective¹ as expressed by the following standards.²

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms.³

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

¹ Based on Legislative mandate: See RCW 70.14.100(2).

² The principles and standards are based on USPSTF Principles at: <http://www.ahrq.gov/clinic/ajpm suppl/harris3.htm>

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Using Evidence as the basis for a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. Availability of Evidence:

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. Sufficiency of the Evidence:

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence⁴ using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- the amount of evidence (sparse to many number of evidence or events or individuals studied);
- consistency of evidence (results vary or largely similar);
- recency (timeliness of information);
- directness of evidence (link between technology and outcome);
- relevance of evidence (applicability to agency program and clients);
- bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. Factors for Consideration - Importance

At the end of discussion at vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- risk of event occurring;
- the degree of harm associated with risk;
- the number of risks; the burden of the condition;
- burden untreated or treated with alternatives;
- the importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- the degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- value variation based on patient preference.

⁴ Based on GRADE recommendation: <http://www.gradeworkinggroup.org/FAQ/index.htm>

Medicare Coverage and Guidelines

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
CMS		Annual breast cancer screening with clinical examination and mammography is covered by Medicare. Breast cancer screening with MRI is not covered as a routine preventive measure. (preventive services must be specifically covered). However, breast MRI may be covered as a diagnostic procedure (CMS, 2007).	No	n/a
Guidelines – WA HTA Page: 65 American College of Radiologists (ACR)	2010	Annual mammogram and annual MRI starting by age 30, but not before age 25, or 10 years before the age of the youngest affected relative, whichever is later. Annual mammogram and annual MRI starting 8 years after treatment. Annual mammography from time of diagnosis (breast cancer, ovarian cancer, etc). The addition of ultrasound to screening mammography may be useful for incremental cancer detection.	Yes	Poor
Guidelines – WA HTA Page: 65 & 66 European Society of Breast Cancer Specialists (EUSOMA) working group	2010	Use of MR units with magnets with intensity filed P1.0 T and gradients P20 mT/m, equipped with bilateral dedicated coils, preferably multichannel; regular checks using standardized quality control of MR units according to national regulations; in order to reduce the risk of false positives, premenopausal women undergo the examination ideally on day 6-13 of the menstrual cycle, even when oral contraceptive is used; and in case of hormone replacement therapy, MRI be performed at least 4 weeks after discontinuation of treatment.	Consensus	Poor
Guidelines – WA HTA Page: 67 USPSTF: Breast Cancer Screening	2009	If a women has an abnormal mammographic finding on screening or a concerning finding on physical examination, additional imaging and biopsy may be recommended. Additional imaging may help classify the lesion as a benign or suspicious finding to determine the need for biopsy. Breast MRI improved local staging in almost 20% of patients and that preoperative breast MRI studies may be particularly useful in surgical planning for, and managing of, patients with lobular carcinoma.	The focus of the guideline is on women at average risk of breast cancer. Relevant evidence mentioned by the USPSTF is retrospective observational data and from expert opinion and is rated as at medium risk or high risk of bias.	High

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
Guidelines – WA HTA Page: 67 <i>National Comprehensive Cancer Network (NCCN)</i>	2009	Women with a strong family history of breast cancer, genetic predisposition or hereditary ovarian cancer should undergo mammography, MRI and clinical breast exam starting at age 25 every 6-12 months or annually. Consider MRI as an adjunct to mammography and clinical breast exam every 6-12 months if a woman has a lobular carcinoma in situ (LCIS) or atypical hyperplasia.	Based on a combination of "lower quality" evidence and consensus. Risk of bias is at least medium.	Poor
Guidelines – WA HTA Page: 68 <i>American Cancer Society</i>	2007	Screening MRI is recommended for women with – approximately 20-25% or greater lifetime risk of breast cancer, including women with a strong family history of breast cancer or ovarian cancer and women who were treated for Hodgkin disease.	No	Poor
Guidelines – WA HTA Page: 68 <i>National Institute for Health and Clinical Excellence (NICE)</i>	2006	Adding MRI to mammography increases sensitivity over mammography alone in screening for breast cancer in women at high risk; mammography may be useful adjunct to MRI in the high risk group; MRI is more sensitive than mammography in BRCA1 carriers; MRI combined with mammography is a cost-effective intervention in women with BRCA1 mutation aged 30-49; annual MRI combined with mammography is a cost-effective intervention in non-BRCA1 women aged 30-39 with an 8% or greater 10-year risk; and MRI combined with mammography is a cost-effective intervention in non-BRCA1 women aged 40-49 with a 20% or greater 10-year risk.	Accuracy estimates were based on two studies at medium risk of bias.	Fair
Guidelines – WA HTA Page: 68 <i>National Cancer Institute</i>	2010 (last update)	Based on fair evidence, screening mammography in women aged 40 to 70 years decreases breast cancer mortality. The benefit is higher for older women, in part because their breast cancer risk is higher. The role of MRI in screening high-risk women or very high-risk women (such as BRCA1/2 carriers) remains uncertain.	Evidence evaluation and method of grading cited.	High

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

	Breast MRI
Safety Outcomes	Safety Evidence
Mortality or morbidity	
Radiation Exposure	
Gadolinium-based Contrast Agents	
Psychological Issues	
Over diagnosis	
Other Adverse Events	
Efficacy – Effectiveness Outcomes	Efficacy / Effectiveness Evidence
Diagnostic Accuracy <ul style="list-style-type: none"> - Sensitivity - Specificity 	
Reduces Need for Other Tests	
Diagnosis Accuracy	
Change in Treatment Plan(s)	
Re-excision Rates	
Breast Cancer Recurrence	
Reduce Morbidity or Mortality	
Other	
Special Population / Considerations Outcomes	Special Population Evidence
Age	
Breast Tissue Density Characteristic	
Breast Implants	
Patient Selection Criteria	
Type of screening Machine and Software	

Reader training	
Provider Type of Setting	
Healthcare System Type - Worker's Compensation - Medicaid - State Employees	
Other	
Cost	Cost Evidence
Cost Implications	
Cost Effectiveness	

Clinical Committee Evidence Votes

First voting question

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	Equivalent (yes)	Less (yes)	More (yes)
Effective				
Safe				
Cost-effective				

Discussion

Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second vote

Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

Not Covered. Covered Unconditionally. Covered Under Certain Conditions.

Discussion Item

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Clinical Committee Findings and Decisions

Next Step: Cover or No Cover

If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions

If covered with conditions, the Committee will continue discussion.

- 1) Does the committee have enough information to identify conditions or criteria?
 - Refer to evidence identification document and discussion.
 - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
 - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.
- 2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
 - What are the known conditions/criteria and evidence state
 - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Efficacy Considerations:

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
 - Direct outcome or surrogate measure
 - Short term or long term effect
 - Magnitude of effect
 - Impact on pain, functional restoration, quality of life
 - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value

- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy
 - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
 - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
 - Adverse effect on health that can result in lasting harm or can be life-threatening.
- Other morbidity concerns
- Short term or direct complication versus long term complications
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?