Washington State Health Care Authority

Health Technology Assessment

Appropriate Imaging for Breast Cancer Screening in Special Populations

Draft Evidence Report: Comment & Response

December 10, 2014

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Public Comment and Response

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Response to Public Comments

The Institute for Clinical and Economic Review (ICER) is an independent vendor contracted to produce evidence assessment reports for the Washington HTA program. For transparency, all comments received during the public comment period are included in this response document. Comments related to program decisions, process, or other matters not pertaining specifically to the draft key questions, project scope, or evidence assessment are acknowledged through inclusion only.

This document responds to comments from the following parties:

Draft Report

- Kara Carlson, MD, Medical Director, EvergreenHealth Breast Care
- Jennifer Shook, MD, PhD, Swedish Medical Center
- Khai Tran, MD, Medical Director, Carol Milgard Breast Center
- Matt Larson, MBA, Health Economics & Payer Relations, Hologic, Inc.
- Pooja Voria, MD, MBA, Vice President, Washington State Radiological Society & Swedish Breast Centers, Radia, Inc., PS

	Comment	Response
Kara Carlson, MD, Medical Director, EvergreenHealth Breast Care		
1	EvergreenHealth was one of the first breast centers in the Pacific Northwest to offer DBT as a supplementary screening tool. We have utilized DBT since 2011 and have truly realized the impact of 3D technology. We have had an increase in cancer detection rate and decrease in recall rates. In our first two years of DBT screening, 48 cancers were diagnosed and seen only by 3D technology in women with dense breast tissue. DBT has also altered the work flow in our center by its efficiency and drop in recall rates. We have been fortunate to share these experiences as co-authors of the 2014 JAMA study, "Breast Cancer Screening Using Tomosynthesis in Combination With Digital Mammography," by Friedewald, et al.	*Thank you for your comments. No changes to the evidence review. The Friedewald study mentioned is included in the review.*
2	Because of our positive experiences with DBT, we decided to inform women of their breast tissue density in the layman letter as of July 1, 2014 at EvergreenHealth. Our goal was to empower women with the knowledge of their breast tissue density. But to do this successfully without creating anxiety around this topic of density, we realized the importance of educating the referring providers at EvergreenHealth on the next steps. We created an easily understandable flowchart for them (see attached) to reference. Our breast center website (link included in layman letter) also has breast density information available for our patients: www.evergreenhealth.com/breastcenter	*Thank you for your comments. No changes to the evidence review.*
Jennifer Shook, MD, PhD, Swedish Medical Center		
1	Because of its high specificity DBT not only reduces the call back rate from DM screening exams, it also often decreases the number of additional diagnostic tests to make the diagnosis. By reducing masking effect DBT offers much greater detailed margin analysis of masses such that often patients who are called back for a mass can go straight to ultrasound without the need for diagnostic spot views for evaluate margins and morphology. And frequently women who are called back for asymmetries can avoid ultrasound by DBT which can exclude a mass or distortion because of the absence of masking effect. And in the event of findings seen only by DBT, biopsy can be performed by DBT guided stereotactic percutaneous core needle biopsy or by DBT guided wire localization for open biopsy/treatment. Despite little evidence, ABUS is being heavily	*Thank you for your comments. No changes to the evidence review. The potential advantages of DBT are highlighted at several points throughout the review.*

	Comment	Response
2	promoted as the test of choice for supplemental screening of women with dense breasts. However, neither HHUS or ABUS can match DBT in sensitivity, specificity (decreased number of call backs), number of cancers detected and number of additional diagnostic tests and biopsies avoided. The false positive rate of ABUS is significantly higher than DBT and each call back from ABUS initiates a cascade of other tests required to confirm the findings and to biopsy the abnormalities found. For instance, if an abnormality is seen by ABUS the patient is recalled for 2nd look with HHUS and HHUS guided biopsy if indicated and possible. But if the ABUS finding cannot be reproduced with HHUS - there is no way to biopsy the abnormality with the ABUS system. Additional diagnostic mammographic exams and even MRI would be required to confirm with reasonable confidence that the ABUS finding is safe to follow with short interval 6 month ABUS exams for two years per BIRADS 3 protocol.	*No changes to the evidence review. All available published evidence for ABUS and HHUS has been summarized in the review, and the potential budgetary impact has been assessed in the model.*
3	MRI is by far the most sensitive breast imaging modality available, however the poor specificity frequently results in additional standard diagnostic tests and unnecessary biopsies. MRI guided biopsy is available for findings seen only by MRI. Screening MR is the most expensive and invasive of all screening tests requiring an iv and contrast injection. The average breast MRI exam takes 15 – 20 minutes, time is dependent on ease of placing an iv and the mobility of the patient and their ability to lie prone with their breasts suspended in the coils. MRI is also limited by weight and girth, renal disease, contrast allergies, pace makers and other metallic implants and claustrophobia.	*No changes to the evidence review. The potential advantages/disadvantages of MRI, as well as its potential budgetary impact, have been summarized in the review.*
4	In addition the recently published article by Christoph Lee et al is the first study to compare effectiveness of DM and DBT on a national level and should be included in the final HTA report.	*The economic evaluation by Lee and colleagues has been summarized in the final report, and differences between the approach taken in that study (biennial frequency, in women with dense breasts only) and our own model have been noted.*
Khai Tran, MD, Medical Director, Carol Milgard Breast Center		
1	There are two issues I want to comment on. First, I have concerns about the cohort model that was constructed, which does not account for downstream costs and does not accurately portray significant cancer detection rate increases like we are seeing at Carol Milgard Breast Center, corroborated in a number of published clinical trials. Secondly, it is my	*Thank you for your comments. No changes to the evidence review. The cohort model accounted for screening and diagnostic follow-up costs over one year, consistent with a budgetary impact approach for a payer interested in the additional expenditure required. In addition a sensitivity analysis was performed that included an improved cancer*

	Comment	Response
	humble suggestion that you should organize your efforts to identify and capture all the costs of breast cancer, through detection and treatment, prior to publishing DBT premium payment tiers in the Final Draft.	*detection rate with DBT (i.e., an additional one case per 1,000 screened). We also acknowledge the limitation of not including treatment costs in our modeling approach.*
2	Both the national ACR and Washington State Radiological Society have released statements on DBT that support its use in the general screening population. Those statements are attached.	*Both society statements have been included in the final report.*
3	The FDA has approved the Affirm biopsy device to be used with the Hologic DBT system to biopsy lesions that are only seen on DBT. Many sites in the state currently use the Affrim biopsy with the Hologic DBT system on a regular basis with success. The FDA document is attached.	*Mention of the biopsy device and its use with DBT has now been included in the final report.*
4	It should be noted that 3D mammography is not indicated for screening use without concurrent use of traditional 2D mammography. Therefore, it can be reasonably expected that mammography with breast tomosynthesis will be at least as beneficial as 2D mammography alone.	*No changes to the evidence review. Our conclusions and evidence ratings for DBT say essentially the same thing.*
5	A 2014 paper by Houssami et al followed the Italian (Ciatto et al) trial patients for a minimum of 13 months (19.2 month median follow-up period). This paper reported a significantly higher ($p<0.05$) comparative sensitivity for breast tomosynthesis vs 2D alone. [1] These results held true for both single reader (85% for BT vs 54% for 2D alone) and double reader (91% for BT vs 60% for 2D alone) paradigms.	*This paper is now summarized in the final report.*
6	While I agree that it would be helpful to have additional follow up information for women with negative screening results, I disagree that this could possibly change the conclusions regarding the performance of breast tomosynthesis: improvement in invasive cancer detection and decreases in false positive results. Any negative screening results subsequently determined to be a false negative, i.e. a missed cancer, would not change the conclusions, because these false negative screening results were missed by both conventional 2D and by breast tomosynthesis.	*No changes to the evidence review. We do not say that conclusions of the report would change, only that missing data on interval cancers in many studies introduces uncertainty.*
7	Findings published October 31st, 2014 by the Society for Women's Health Research (SWHR) recently found that four in five women agree that access to	*No changes to the evidence review. We could find no published citation for this study.*

	Comment	Response
	mammograms that offer better detection and lower their chances of being called back for more testing is important (81% and 82%, respectively). In addition, the SWHR found that 88% believe that the 3D mammography exam, which offers these benefits, should be covered by insurance. The survey findings fact sheet is attached.	
8	The Regence Group, Premera Blue Cross and Health Net policies are based on the Blue Cross Blue Shield Association (BCBSA) review of DBT from July 2014. The BCBSA review is out of date with regard to many of its claims and in my opinion has not understood the technology or the published literature. In addition, the BCBSA does not include the latest medical society guidance or October 31st, 2014 ruling by CMS that valued DBT at $57 in addition to 2D mammography alone.	*No changes to the coverage policy section of the evidence review. However, the CMS final rule on payment for DBT is acknowledged in the final report and included in the model.*
9	In 2013, the American College of Obstetricians and Gynecologists published an updated statement which concludes "… digital mammography plus tomosynthesis produces a better image, improved accuracy, and lower recall rates compared with digital mammography alone."	*This statement has been added to the section on guideline statements in the final report.*
10	Additionally, the 2013 The American Society of Breast Disease "Statement on Digital Breast Tomosynthesis" concludes…	*This statement has been added to the section on guideline statements in the final report.*
Matt Larson, MBA, Health Economics & Payer Relations, Hologic, Inc.		
1	The Cohort lays out A, B, C and D scenarios with various cancer detection rates. The most reasonable scenario is scenario D, which assumes a 30% increase in cancer detection. However, the DBT basecase used is well below the average increase in cancer detection found in the published studies of 33%. It is suggested that The Cohort be adjusted to reflect accurate cancer detection rates as established in the spectrum of published peer-reviewed clinical trials.	*Thank you for your comments. No changes to the evidence review. As noted previously, we modeled increased cancer detection in one of our scenarios because available studies indicate that DBT improves cancer detection over digital mammography alone; however, without consistent data on interval cancer rates, absolute levels of cancer detection cannot be known with certainty. In addition, we are unsure why our 30% increase in cancer detection in model scenario D is considered "well below" the crude average mentioned in the comments (33%).* *Many of these comments make use of crude pooled averages; as explained in our review, we did not quantitatively synthesize available data because of a high degree of heterogeneity between studies and serious quality concerns with some assessments.*

	Comment	Response
2	Five studies also report the invasive cancer detection rate and all report an increase in detection with breast tomosynthesis (Table 2). Invasive cancer detection is important because it is known to progress more rapidly than non-invasive cancers (ie: DCIS) and requires more aggressive treatment.	*No changes to the evidence review. We note that the magnitude of improvement with invasive cancers is similar to that for all cancers, and differences for invasive cancers were not tested statistically or statistically-significant in 2 of the 5 studies described.*
3	Using the approach of estimating recall based on cases sent to arbitration for the Norwegian (Skaane) and Italian (Ciatto) studies, every peer reviewed paper reporting on the performance of 3D mammography has shown a decrease in recall/false positive rates. The average in the trials laid out below is 27%.	*No changes to the evidence review. As noted above, we caution against drawing any conclusions from crude pooled rates, given quality concerns with several of these studies. Also of note, reduction in recall rates in the largest, prospective and/or multicenter studies included appears to be consistent and in a remarkably tight range (15-17%).* *We further note that new studies have been published, which have now been included in the final report (Greenberg, 2014; McCarthy, 2014; Lourenco, 2014). However, two of these studies appear to be conducted at participating centers in the large multicenter Friedewald study (Friedewald, 2014); we are unsure of the degree of data overlap.*
4	Fortunately, the Truven data set allows for the tracing of downstream costs tied to each patient who undergoes screening mammography. In their study, costs associated with patients who receive additional imaging and other diagnostic procedures, including biopsies were traced for 6 months following a screening mammogram. To account for interval cancers, women with any breast imaging procedure or a breast cancer diagnosis in the 12 month pre-index period was excluded from results.	*No changes to the evidence review. This seems to imply that our model evaluated the economic impact of screening costs alone. This is not true; costs of recall, diagnostic workup and biopsy, and detection of interval cancers were all considered over 12 months of follow-up.* *The study described based on this dataset appears to have been presented only as a poster, and does not currently exist in published form, so we cannot fully investigate the methods used.*
5	Truven data show an average recall rate of 13.4% in the PNW region, or 134.0/1,000 women screened. A 27% reduction in recalls, the average in clinical trials, would bring this down to 9.8%, or 98.0/1,000 women screened.	*Please see comment above regarding the unpublished nature of this study. We consider the recall rates from the Friedewald study (91 and 107 per 1,000 for DBT and DM respectively) defensible, as the source was largest US multicenter study conducted to date and findings were adjusted for reader-specific differences.*
6	Using the Truven model and the assumptions noted above, a $57 increased payment for DBT would yield a significant cost savings for the state of Washington. Based on 542,000 women screened, as sited in the	*Please see comment above regarding the unpublished nature of this study. However, we must also point out that this study assumed a uniform cost of recall for <u>all</u> women, including the*

	Comment	Response
	draft, the results represented below show an annual savings of $355,466; not including treatment costs.	*cost of biopsy for women so referred. This in essence ignores the **higher** biopsy rate seen with DBT in the Friedewald study as well as in the recent studies from Greenberg and McCarthy. While a higher biopsy rate may be clinically indicated for DBT (i.e., because of a greater targeting of recall and higher positive predictive value), this also represents an increase in cost that is not accounted for in the cited analysis.*
Pooja Voria, MD, MBA, Vice President, Washington State Radiological Society & Swedish Breast Centers, Radia, Inc., PS		
1	Since 50% of all adult women have dense breasts, the inclusion of breast density in a lay letter could cause a significant and sudden demand for supplemental services that are either not available in all areas or insufficient to handle the additional capacity. In addition, this information is only useful if referring providers or radiologists can provide guidance for next steps such as a supplemental screening test. Therefore, the decision to notify patients of their breast density needs to be cautiously addressed. Screening tests are most effective if they are widely accessible, cost effective, safe, and have high sensitivities and specificities. Several states have enacted breast density notification laws, but do not provide guidance for patients for supplemental screening or ensure that insurance plans cover the costs of these tests.	*Thank you for these comments. No changes to the evidence review.*
2	Given the available data today as provided in the HTA Appropriate Imaging for Breast Cancer Screening in Special Populations Draft Evidence Report as well as the attached WSRS Digital Breast Tomosynthesis (DBT) position statement, the radiologists in Washington State would highly encourage women with dense breasts to obtain digital breast tomosynthesis 3D mammograms as a supplement to the digital 2D mammogram.	*No changes to the evidence review.*
3	We would recommend reserving adjunct screening with MRI for women with a lifetime risk of breast cancer that exceeds 20% based on the recommendations of the American Cancer Society. Although supplemental screening ultrasound has received widespread attention in the news, it is not the ideal supplemental screening tool based on the available data. Our position may be proactively modified as new data become available.	*No changes to the evidence review.*

	Comment	Response
4	Dr. Christoph Lee's article in Radiology, "Comparative Effectiveness of Combined Digital Mammography and Tomosynthesis Screening for Women with Dense Breasts," was published after the HTA draft evidence report was released. We would encourage the research team to incorporate information from this article into the report.	*Please see our response to comment #4 on page 4. We have included this study in the final report.*
5	In addition, CMS has already valuated tomosynthesis at $57 in addition to the digital screening 2D mammogram beginning January 1, 2015. This too should be reflected in the analysis.	*Please see our response to comment #8 on page 6. We have included this payment estimate in the report and model.*
6	The cohort model only looks at the impact of the screening costs and does not look at the downstream costs including call backs, ultrasounds, biopsies generated by false positives, and time away from work. It is these added downstream costs that can significantly burden a patient and the healthcare system.	*Please see our response to comment #4 on page 7. Costs included in our model included those of screening, imaging and biopsy after recall, and detection of interval cancers over a 12-month period. We did not include lost productivity and note this as a limitation in our report.*