



New England Comparative Effectiveness Public Advisory Council

Public Meeting – Boston, Massachusetts

Supplemental Breast Cancer Screening for Women with Dense Breast Tissue

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QUESTIONS FOR DELIBERATION

Introduction

Each public meeting of CEPAC will involve deliberation and voting on key questions related to the systematic review of the evidence and supplementary information presented by ICER. Members of CEPAC will discuss issues regarding the application of the available evidence to guide clinical decision-making and payer policies. The key questions are developed by ICER with significant input from members of the CEPAC Advisory Board to ensure that the questions are framed to address the issues that are most important in applying the evidence to practice and medical policy decisions.

About the Questions

Comparative Clinical Effectiveness

The general framework within which CEPAC discusses and votes on the evidence is shown below:

Given a health care “intervention A” for “patients with condition X,” we will compare its clinical effectiveness for these patients to that of a “comparator B” by voting on the following question:

Is the evidence “adequate” to demonstrate that “intervention A” is equivalent or superior to “comparator B” for “patients with condition X”?

Discussion and voting will highlight the following issues:

1. The evidence on risks and benefits to determine the *comparative* clinical effectiveness of management options for specific patient populations. In judging comparative clinical effectiveness, there are two interrelated questions: the relative magnitude of differences in risks and benefits; and the relative confidence that the body of evidence can provide in the accuracy of estimates of risks and benefits. Considering these two issues together is required in order to make a judgment of whether the evidence is “adequate” to demonstrate that one intervention is equivalent to or superior than another.
2. Issues related to individual patient preferences and values, provider training, volume, or other factors that should be considered in judging the evidence on clinical effectiveness and value.
3. Weighing the evidence on cost-effectiveness and projected budgetary impact to determine the comparative value of various management options for key patient populations.
4. Comments or recommendations related to broader considerations of public health, equity, disparities, and access.

Comparative Value

When a majority of CEPAC votes that the evidence is adequate to demonstrate that an intervention produces patient outcomes as good as or better than a comparator, the Panel will also be asked to vote on whether the intervention represents a “high,” “reasonable,” or “low” value. The value “perspective” that CEPAC will be asked to assume is that of a state Medicaid program that must make resource decisions within a fixed budget for care. While information about hypothetical budget tradeoffs will be provided, CEPAC will not be given prescribed boundaries or thresholds for budget impact or incremental cost-effectiveness ratios to guide its judgment of high, reasonable, or low value.

For each vote, Council members will be asked to identify which element of the information provided to them on “value” was most influential in their judgment: 1) information on the incremental cost for an additional benefit (or for reduction in risk); or 2) information on the budget impact of different care/payment scenarios. Council members will also be asked to describe briefly the rationale for their rating of comparative value.

Questions for Supplemental Breast Cancer Screening for Women with Dense Breast Tissue

Background

In 2009, the state of Connecticut enacted into law a requirement that health care facilities conducting mammographies include the following language in reports to women who have dense breast tissue, defined as heterogeneously dense or extremely dense breasts using the Breast Imaging Reporting and Data System (BI-RADS) established by the American College of Radiology:

If your mammogram demonstrated that you have dense breast tissue, which could hide small abnormalities, you might benefit from supplementary screening tests, which can include a breast ultrasound screening or a breast MRI examination, or both, depending on your individual risk factors. A report of your mammography results, which contains information about your breast density, has been sent to your physician's office and you should contact your physician if you have any questions or concerns about this report .¹

The legislation also requires that health insurers provide coverage for supplemental screening with ultrasound if a mammogram indicates heterogeneous or dense breast tissue.

The passage of this legislation was driven by two factors: dense breast tissue has been found to be an independent risk factor for the development of breast cancer, and also may obscure the presence of cancers on mammography.^{2,3} The “masking” issue is controversial, however, as some reports suggest that masking may be more pronounced with film mammography than with digital mammography, which has become the screening standard in the U.S.⁴

Massachusetts is also pursuing breast density notification legislation, and similar laws have been passed elsewhere in the country, including Alabama, California, Illinois, Indiana, Maryland, New York, Texas, and Virginia.^{5,6} Legislation in Illinois and Indiana also includes a mandate for insurance coverage of supplemental screening.

Multiple technologies for supplemental screening of women with dense breast tissue exist, including both handheld and automated breast ultrasound, MRI and digital breast tomosynthesis (DBT), a three-dimensional version of digital mammography.⁷ A number of questions have not yet been addressed, however, including the potential for false-positive results and overdiagnosis as well as the full impact of supplemental screening on patient morbidity and mortality for women at varying levels of breast cancer risk.

To address these concerns, a systematic literature review was undertaken on behalf of the California Technology Assessment Forum (CTAF) to examine the evidence on supplemental screening with the modalities of interest. Outcomes of interest included performance characteristics (e.g., diagnostic accuracy, diagnostic yield, AUC), downstream testing, biopsies performed, changes in follow-up interval,

cancers detected, breast cancer-specific and overall mortality, overdiagnosis, and other potential harms of testing, and test costs. The CTAF review will be presented in its entirety in this report, and will be supplemented with new evidence published since the completion of the review.

A simulation model was also developed to explore the clinical and economic impact of various supplemental screening strategies among adult women with dense breast tissue. The original model was focused on screening-eligible women in California, and will be adapted to represent all women eligible for screening in New England. Specifically, the population of interest will be adult women (ages 40-74) in New England who are mammography-negative and have received notification that their breast tissue is heterogeneously dense (BI-RADS mammographic density category 3) or extremely dense (BI-RADS mammographic density category 4). The timeframe of interest will be 1 year. Outcomes will include performance characteristics (e.g., sensitivity/specificity), total positive and negative biopsies performed, cancers detected, cancers missed, and screening strategy costs.

Definitions:

1. Heterogeneously dense breasts (BI-RADS category 3): 51-75% of the tissue in a woman's breast is considered to be dense on mammography.⁸
2. Extremely dense breasts (BI-RADS category 4): more than 75% of the tissue in a woman's breast is considered to be dense on mammography.⁸
3. Supplemental screening: screening performed in addition to mammography using a variety of modalities for women considered to be at increased risk of breast cancer, including those with dense breast tissue.
4. Risk categories for breast cancer among women with dense breast tissue:
 - a. "High risk": Women with either heterogeneously or extremely dense breast tissue who are age ≥ 50 and have a family history of breast cancer (i.e., in a first-degree relative), leading to a 5-year cancer incidence generally $>3\%$. More detailed risk algorithms are available, including the Breast Cancer Surveillance Consortium (BCSC) risk calculator (<https://tools.bcsc-scc.org/BC5yearRisk/calculator.htm>).
 - b. "Moderate risk": Either (a) women with either heterogeneously or extremely dense breast tissue who are age ≥ 50 and do not have a family history of breast cancer, or (b) women with heterogeneously or extremely dense breast tissue who are age < 50 with a family history of breast cancer, leading to a 5-year risk of breast cancer of approximately 1.7%-3%. The lower end of this range corresponds with the risk level at which chemoprevention and other measures to reduce breast cancer risk are generally

considered to be appropriate.⁹ More detailed risk algorithms are available, including the Breast Cancer Surveillance Consortium (BCSC) risk calculator (<https://tools.bcsc-scc.org/BC5yearRisk/calculator.htm>).

- c. “Low risk”: Women with either heterogeneously or extremely dense breast tissue who are younger than age 50 and do not have a family history of breast cancer, leading to a 5-year risk of breast cancer of less than 1.7%. More detailed risk algorithms are available, including the Breast Cancer Surveillance Consortium (BCSC) risk calculator (<https://tools.bcsc-scc.org/BC5yearRisk/calculator.htm>).
5. Breast ultrasound: use of sound waves to provide breast images, through two principal technical approaches:
 - a. Handheld: a transducer is manually manipulated over breast tissue by a physician or technologist to produce 2-dimensional images.
 - b. Automated: an automated transducer arm is applied to breast tissue. The technologist selects diagnostic planes to image at a workstation; resulting images are rendered in 3 dimensions.
 6. Breast magnetic resonance imaging (MRI): use of magnetic pulses to generate breast images, which are rendered at a computer workstation to produce images in multiple planes.
 7. Breast tomosynthesis: also known as “3D mammography”; use of digital X-rays to create breast images that are viewed in multiple “slices”. Performed in a fashion similar to mammography, except that the x-ray beam moves in an arc to obtain a volume of data to create the images.

Comparative Clinical Effectiveness: Supplemental Screening vs. No Supplemental Screening

1. For women with dense breast tissue, is the evidence adequate to demonstrate that digital mammography offers superior diagnostic performance compared with film mammography?
2. For women with dense breast tissue, is the evidence adequate to demonstrate that, compared with film mammography, digital mammography substantially reduces the risk of “masking” of breast cancers?
3. For women with dense breast tissue with an overall “low” risk of breast cancer who have a negative screening digital mammogram, is the evidence adequate to demonstrate that supplemental screening with any technology provides more benefit than harm compared with no supplemental screening?
4. For women with dense breast tissue with an overall “moderate” risk of breast cancer who have a negative screening digital mammogram, is the evidence adequate to demonstrate that supplemental screening with any technology provides more benefit than harm compared with no supplemental screening?
5. For women with dense breast tissue with an overall “high” risk of breast cancer who have a negative screening digital mammogram, is the evidence adequate to demonstrate that supplemental screening with any technology provides more benefit than harm compared with no supplemental screening?

Comparative Clinical Effectiveness of Supplemental Screening by Modality

6. There are four options for supplemental screening reviewed in this report: hand-held ultrasound (HHUS), automated breast ultrasound (ABUS), magnetic resonance imaging (MRI), and digital breast tomosynthesis (DBT). Considering both the strength of evidence and the magnitude of potential comparative clinical benefits and harms of these four imaging modalities, if supplemental screening were to be performed for women with dense breast tissue who are at high risk of breast cancer, please rank in order, from first to last, the tests you would recommend to a patient and her clinician. Health benefits and harms considered should include additional cancers detected and the possible impact on patient outcomes; false negative tests that miss clinically significant cancers; false positive test results with their impact of unnecessary biopsies and anxiety; and overdiagnosis.
 - a. HHUS
 - b. ABUS
 - c. MRI
 - d. DBT

Comparative Value of Supplemental Screening by Modality

Comparative value should be viewed as the incremental cost to an insurer for the diagnostic phase of care relative to the comparative *net* health benefits, if any, of the other screening option. Comparative net health benefit includes consideration of all relevant potential benefits and harms.

7. HHUS is the lowest cost test for supplemental screening. If supplemental screening were to be performed for women with dense breast tissue who are at high risk of breast cancer, what is your judgment of the comparative value (high, reasonable, or low) of ABUS vs. HHUS?
8. HHUS is the lowest cost test for supplemental screening. If supplemental screening were to be performed for women with dense breast tissue who are at high risk of breast cancer, what is your judgment of the comparative value (high, reasonable, or low) of MRI vs. HHUS?
9. HHUS is the lowest cost test for supplemental screening. If supplemental screening were to be performed for women with dense breast tissue who are at high risk of breast cancer, what is your judgment of the comparative value (high, reasonable, or low) of DBT vs. HHUS?

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