CEPAC Voting and Policy Implications Summary
Supplemental Screening for Women with Dense Breast Tissue
December 13, 2013

The last CEPAC meeting addressed the comparative clinical effectiveness and value of supplemental screening tests following negative mammography in women with dense breast tissue. During CEPAC public meetings, the Council deliberates and votes on key questions related to the systematic review of the evidence and the supplementary information presented. At the December 13, 2013 meeting, CEPAC discussed issues regarding the application of the available evidence to help patients, providers, and payers address the important questions of the benefits from supplemental screening for breast cancer in women with dense breast tissue and to support dialogue needed for successful action to improve the quality and value of health care in this population. The key questions are developed by the research team for each appraisal, with input from the CEPAC Advisory Board to ensure that the questions are framed to address the issues that are most important in applying the evidence to support clinical practice and medical policy decisions. Ex-officio CEPAC members participate fully in the discussion of the evidence but do not vote.

Following CEPAC's deliberation on the evidence and subsequent voting, the Council engaged in a moderated discussion with a Roundtable composed of clinical experts, a patient advocate, regional health insurers, and provider group participants. The participants in the Roundtable discussion are shown in the Appendix. The Roundtable discussion explored the implications of CEPAC's votes for clinical practice and medical policy, considered real life issues critical for developing best practice recommendations in this area, and identified potential avenues for applying the evidence to improve patient care. The main themes and recommended best practices from the conversation are summarized in the sections below.

10.2 Summary of the Votes and Considerations for Policy

Following the evidence presentation and public comments, CEPAC voted on questions concerning the comparative clinical effectiveness and comparative value of supplemental

breast cancer screening options for women with dense breast tissue. We present below the voting results along with comments reflecting the most important considerations mentioned by CEPAC members during the voting process.

Comparative Clinical Effectiveness

1. For women with dense breast tissue, is the evidence adequate to demonstrate that digital mammography offers superior diagnostic performance compared with film mammography?

   CEPAC Vote: **15 Yes** 0 No

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?

   CEPAC Vote: **15 Yes** 0 No

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?

   CEPAC Vote: 5 Yes **10 No**

   Comments: CEPAC members who voted "no" cited the lack of direct studies in women with dense breasts and insufficient data on long-term patient outcomes, especially in women with lower levels of risk. In particular, CEPAC members emphasized their concern that supplemental screening among women with a lower prevalence of cancer would lead to a substantial increase in false positive results and unnecessary biopsies, which would in turn greatly increase patient anxiety and put women at risk of complications. Members also commented on the possibility of overdiagnosis in this population, as perhaps as many as 10%-30% of the cancers that could be detected by supplemental screening might never advance to threaten a woman's health and therefore would be unnecessarily treated as a result of supplemental detection.

   CEPAC members who voted "yes" pointed to the data on additional cancers detected and felt that the benefit of finding additional cancers outweighs the harms of false positive findings.

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?

   CEPAC Vote: **9 Yes** 6 No

   Comments: The trend toward more "yes" votes by CEPAC members reflects the shift in balance between benefits (additional cancers detected) and harms (anxiety and risk from false positive findings, and overdiagnosis and overtreatment). As the underlying risk of cancer increases, Council members were more likely to believe that the net health benefits of supplemental screening were positive for most women. Council members who voted "yes," however, stressed that the overall poor quality of evidence on patient outcomes made it difficult to determine precisely at what risk threshold supplemental screening would be expected to have a positive net benefit.

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?

   CEPAC Vote: **14 Yes** 0 No 1 Abstain

   Comments: In describing the rationale for their votes, CEPAC members noted the more robust data available from studies of supplemental screening among women with overall high risk of breast cancer, and commented again on the balance of benefits and harms being more likely to be positive among populations at high risk.

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 highest to lowest preference, 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 test results that miss critically

significant cancers; false positive test results with their impact of unnecessary biopsies and anxiety; and overdiagnosis.

CEPAC vote:

- **13 of 15 voting CEPAC members listed MRI as their first choice recommendation, and the remaining 2 members listed DBT as their first choice.**
- **9 of 15 voting CEPAC members listed ABUS as their least-preferred choice, and the remaining listed HHUS (4/15) and DBT (2/15) as their least-preferred choice.**

Comments: CEPAC members voting for MRI noted that there was more direct evidence for the use of HHUS as a supplemental screening test, but that the evidence on MRI as a screening test among women at high risk of breast cancer suggested strongly that it would identify as many, if not more, additional cancers while producing far fewer false positive results. Though ABUS addresses many of the practical concerns related to HHUS, CEPAC members who voted for it as their least preferred option concluded that the evidence to support its use in high risk patients is much more limited, and findings to date have been largely inconsistent. The Council also noted that though the evidence for DBT is promising as a first-line screening option, there is no evidence examining its use as a supplemental screening test among women with dense breast tissue.

Comparative Value

When voting on comparative value, CEPAC was asked to assume the perspective of a state Medicaid agency or a provider organization that must make resource decisions within a fixed budget for care. While information about hypothetical budget tradeoffs are provided, CEPAC is not given prescribed boundaries or thresholds for budget impact or incremental cost-effectiveness ratios to guide its judgment of high, reasonable, or low value. For the CEPAC voting questions, comparative value is defined as the incremental cost to a public insurer for each supplemental screening option to achieve *net* health benefits, if any, in comparison to a "referent" screening option, in this case HHUS. The comparative net health benefit requires consideration of all relevant potential benefits and harms as described in the report.

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 MRI vs. HHUS?

   CEPAC Vote: 5 High **9 Reasonable** 1 Low

Comments: CEPAC members who voted that MRI represents "high" or "reasonable" value compared to HHUS maintained that MRI's superior balance of additional cancers detected vs. false positive results justified its higher costs and represented a reasonable use of healthcare resources if limited to the relatively small subpopulation of women at overall high risk of breast cancer. Some CEPAC members cautioned that without direct evidence on the effects of supplemental screening specifically among women with dense breast tissue or on the impact of supplemental screening on patient morbidity and mortality, the Council could be mistaken in its estimation of the value of additional testing, but that their judgment is based on the best evidence available on the effectiveness of supplemental screening with MRI for high risk women. The CEPAC member who voted that MRI represents "low" value stated that supplemental screening with MRI, even if limited to high risk women, represents a 25 percent increase in breast cancer spending with a relatively low yield in terms of demonstrated clinical benefit, and that those dollars could be better spent elsewhere in the health system.

Note: The Council abstained from voting on the relative value of DBT and ABUS compared to HHUS due to insufficient evidence to demonstrate comparative clinical benefit between the various options.

Broader Considerations for Equity

8. Are there any considerations related to public health, equity, disparities in access or outcomes for specific patient populations, or other social values that should also be considered in medical policies related to the use of hand-held ultrasound (HHUS), automated breast ultrasound (ABUS), breast magnetic resonance imaging (MRI), or digital breast tomosynthesis (DBT)?

Comments:

- Consideration of the economic impact of supplemental screening should be broadened to consider the societal perspective, including considerations for missed work, transportation, and other costs.
- The policy community should be cautious when legislating in the area of supplemental screening, as it may have the unintended consequence of driving differential access to services and variation in practice. Some states in New England lack the capacity to sustain increased demand for public health screening, particularly in northern parts of the region.

10. 3 Roundtable Discussion and Key Policy Implications

1) Consideration of supplemental screening for women with dense breast tissue should be integrated within systems that assess their overall breast cancer risk and engage them in shared decision-making.

The Roundtable participants and CEPAC discussed the range of concerns regarding the issue of appropriate screening strategies for women based on their overall risk for breast cancer. Experts on the Roundtable noted that it is important for clinicians and women to understand that dense breast tissue conveys some increased risk for breast cancer but by itself is not a reason to consider a woman at "high risk" of developing the disease. CEPAC members highlighted the need for more concerted efforts to develop standards or systems for clinical pathways to appropriately refer women for supplemental screening, and determine how breast density factors into those considerations. Roundtable experts from Connecticut, the only state in New England to enact a breast density notification law and mandate coverage for screening ultrasound in women with dense breasts, noted that practices vary in how they handle referrals for supplemental screening. In some practices, particularly in community settings, primary care physicians refer women with dense breast tissue for secondary screening automatically, regardless of overall risk status. In other practices, the decision to undergo additional screening is driven primarily by the patient; Roundtable participants reported that the proportion of patients requesting supplemental screening approximated 20% in some practices. Other experience at academic health centers in New England suggests that patients are not routinely sent for supplemental screening but rather are invited to consult with their primary care doctor about future screening options and help determine next steps. In these settings, women with certain risk factors are referred to a specialized breast cancer center and/or genetic counseling specialty department for further consultation.

CEPAC members stressed the importance of building systems in multi-disciplinary clinics that would be able to integrate the management of patients' questions arising from dense breast tissue notification with a reliable, efficient method for assessing their overall risk for breast cancer, and to share this information with patients. Systems should also support dialogue between patients and physicians regarding the various screening modalities available, and the patient's preference for additional screening. The ultimate goal of these systems should be to embody the principle of shared decision-making within mechanisms that would prove feasible across different practice settings.

2) Specialty societies, review groups, and others should seek to use consistent risk thresholds and assessment tools to capture overall breast cancer risk in order to avoid confusion among clinicians and patients.

CEPAC members and Roundtable panelists noted that risk assessment and stratification will never be able to identify 100% of women who will go on to develop breast cancer, and this fact should be communicated to patients. The CEPAC report noted the availability of the Gail model and the Breast Cancer Surveillance Consortium (BCSC) model for calculating breast cancer risk, both of which are sophisticated, computer-based algorithms. The CEPAC report also modeled the patient outcomes of different screening strategies based on categorizing risk according to a simplified, 3-variable version of the BCSC that could be used by primary care clinicians without direct access to computerized risk calculators. Discussion by the Roundtable acknowledged that there is widespread variation in the use of risk assessment models across organizations and practices. Whereas 5-year risk thresholds make conceptual sense in considering supplemental screening, insurance coverage criteria for MRI are focused on determining lifetime risks high enough to warrant annual MRI. There is therefore great need for further efforts to develop robust systems for gathering breast cancer risk and applying that risk consistently to guide practice and policy decisions. Whatever approach is used to calculate risk, the Roundtable emphasized that breast cancer risk information should be readily available to clinicians and patients.

3) Physicians should adopt consistent messaging with their patients about breast density and breast cancer risk to help inform decisions for future screening.

CEPAC members and Roundtable panelists agreed that patients should be notified if they have dense breasts by their physician, but that messaging should promote a dialogue with patients and be consistent and clear in its explanation of the implications of dense breast tissue and options for additional screening. The patient advocate representative on the Roundtable cautioned that notifying a woman of her breast density status without further context can cause significant stress for the patient, but that this anxiety can be reduced through appropriate education. Communication with patients should highlight that, though dense breast tissue confers an increased risk of breast cancer, by itself it is not a reason to consider all such women at “high risk” for developing the disease. Women should also be made aware of the trade-offs involved in supplemental screening, and that though additional screening finds more cancer, it also increases the risk of false positives and unnecessary testing that can cause some women great anxiety and worry.

CEPAC members also stressed that states considering breast density notification policies should be careful to include an education component that helps patients understand the meaning of breast density, their risk, and the potential harms and benefits of supplemental screening.

4) More support is needed to help primary care physicians (PCPs) and other providers engage in discussions with their patients about breast density, risk, and options for supplemental screening.

The Roundtable and CEPAC noted the importance of developing educational materials for clinicians to help them understand the evidence on the various options for supplemental screening and provide a basis for discussions about these choices with women. Clinical experts on the Roundtable indicated that discussion of these issues is appropriate in the primary care setting, but cautioned that many PCPs are already burdened with numerous clinical goals and a range of practice issues, limiting their capacity to have detailed conversations with patients about supplemental screening. CEPAC members agreed, however, that primary care physicians should be able to support patients in their decision-making about supplemental screening, and highlighted that this task can be made easier by coordinated provider education tools, electronic medical records (EMR), and the infrastructure provided by integrated health systems that can capture patient information on health risks at different points of entry in the health system.

In some states confronting a shortage of primary care physicians, other health personnel (e.g., physician assistants, nurse practitioners) are being trained to assume many of the roles currently played by primary care physicians. In these parts of New England, advanced training and education for clinicians on how to discuss with patients the issues around secondary screening and breast cancer risk are needed. The establishment of specialty departments or centers of excellence with automated referral processes from primary care may also be helpful in directing patients to specialists to discuss future screening options. Clinical experts also recommended that screening technologists be trained to identify patients who would benefit from further conversation with a radiologist.

Ensuring that radiologists, other specialists, and primary care clinicians share a common platform of information is critical to make certain that women receive consistent information and can participate with confidence in shared decision-making with their clinicians.

5) Greater guidance is needed to help physicians appropriately manage intervals for supplemental screening and subsequent follow-up for women with dense breast tissue.

Roundtable panelists remarked on the lack of guidance available to providers to help determine the appropriate supplemental screening intervals for women with dense breast tissue. Greater consensus on the best approaches for patient management of women with dense breasts is needed and should be reflected in clinical guidelines.

Evidence Development and Future Research Needs

CEPAC members underscored the importance of further research on supplemental screening among representative populations of women with dense breast tissue. Although data on long-term patient outcomes such as cancer-specific mortality would be ideal, it was recognized that such research would take too many years to be realistic, and that randomized trials or prospective cohort studies that follow all patients out for one year in order to capture interval cancers would be very informative.

CEPAC and Roundtable members agreed that if DBT supplants digital mammography as the primary screening test of choice, that new research will be required to evaluate the comparative benefits and harms of supplemental screening among women with dense breasts with ultrasound or MRI. If possible, studies evaluating DBT as a primary screening test could include an arm in which women with dense breasts who have a negative DBT receive supplemental screening in order to determine the incremental number of cancers detected, false positive rates, etc.