December 9, 2013

Submitted Electronically

United States Preventive Services Task Force
c/o Dr. Robert Cosby
Agency for Healthcare Research and Quality
540 Gaither Road
Rockville, MD 20850

RE: USPSTF Draft Research Plan on Screening for Breast Cancer

Dear Chairwoman Moyer and Task Force Members:

As an organization with a long history of advocating for quality in mammographic screening, and of encouraging women and their health care providers to utilize proven screening methods to save lives, the American College of Radiology (ACR) —a professional organization representing more than 35,000 radiologists, radiation oncologists, interventional radiologists, nuclear medicine physicians, and medical physicists—appreciates the opportunity to provide input into the USPSTF draft research plan for breast cancer screening. We recognize that this opportunity for public comment was not available in the Task Force's previous consideration of the breast cancer screening recommendations; in addition to providing a venue for public comment, we are hopeful that the Task Force will embrace the input that is received. We believe the processes of the Task Force, the quality of its guidelines, and ultimately the public's trust in its recommendations can be enhanced by maximizing the input of breast imaging specialists and other experts and by ensuring transparency throughout your deliberations. We offer the following general comments relating to the process of the Task Force as well as specific recommendations related to the research plan.

GENERAL COMMENTS

The Task Force Process Should be Fully Open, Balanced and Transparent

Although the Task Force was created for the purpose of providing supplemental guidance to primary care physicians, USPSTF recommendations now have far broader

public policy implications. They are being used to influence national screening program guidelines, federal and private sector coverage policies, as well as direct-to-consumer screening recommendations. With the passage of the Affordable Care Act, the USPSTF was explicitly granted a prominent role in Centers for Medicare and Medicaid Services' coverage decisions and in the establishment of preventive service coverage requirements for private insurers. With such substantive policy issues at stake, the public trust demands that the USPSTF recommendation-development process be entirely transparent, consistent with other federal agencies that create policy and promulgate regulations.

While we understand that the Task Force is not a formal Federal Advisory Committee and is not statutorily bound to abide by the Federal Advisory Committee Act or the Administrative Procedures Act, we believe that the Task Force should embrace the public transparency and accountability protections afforded by these Acts. With millions of lives affected, it is imperative that critical decisions affecting citizens' access to preventive healthcare services not be made behind closed doors without the benefit and protection of well-established federal agency transparency requirements.

In addition to the broad process protections afforded by the APA and FACA, we urge the Task Force to be transparent in its methodology. It should disclose the input received as part of its public comment periods and explain its analysis of public comments, as well as its rationale for accepting or rejecting the input provided by the public. Further, as the Task Force examines evidence and conducts its analysis, it should disclose and clearly explain (1) the evidence it uses to make its recommendations; (2) their rating of the strength of that evidence (SOE) and; (3) the criteria used to make the SOE determination.

In balancing the benefits versus harms of screening mammography, it would be especially misleading to assess benefits in terms of women invited to be screened but harms in terms of women actually screened. Such a clearly biased approach would weaken the task force report and subject it to valid criticism. Although a wider range of literature is to be used in this analysis than in the 2009 report, it is important that all evidence should be used to study harms and benefits. Different types of evidence were used in the last report. Because only randomized controlled trials (RCTs) were used to estimate benefit previously, the report was subject to criticism.

As part of the review that culminated in the 2009 BCS recommendations, the USPSTF commissioned a report from the Oregon Evidence Based Practice Center. However, the Oregon center's report, published at the same time as the Task Force recommendations, reached very different conclusions. The Oregon report said that overdiagnosis is probably around 10%; the Task Force stated that 50% of DCIS will never progress. This disparity left many questioning the rationale for the conclusion of the Task Force which was not explained in the USPSTF report.

The Task Force should engage experts in breast imaging

The Draft Research Plan is foundational to Task Force deliberations in that it establishes the evidence that will be reviewed. It is important that the Task Force not limit its critical analysis of the material only to the thinking of its members. Expert peer review is an important tool in parsing out the strengths and limitations of scientific research and in moving the science of medicine forward. The Task Force should take advantage of the insights provided by expert peer review as it gauges the strength and weakness of the studies it considers.

We would also like to use this opportunity to request, once again, that the Task Force utilize expert consultants in breast imaging throughout their deliberations on the topic. Certainly, the process can only be improved by utilizing experts who are familiar with the research in their field of specialty and who understand its merits and limitations. The absence of such consultations was a source of major criticism of its breast cancer screening guidelines in the past. We believe that this will help the Task Force gain a fair, balanced understanding of the data, and that utilization of these experts helps the perception that the Task Force report reflects this fairness. ACR welcomes the opportunity to recommend such subject member experts to you.

SPECIFIC COMMENTS

Key question 1: *In average-risk women age 40 years and older, what is the effectiveness of routine mammography screening in reducing breast cancer–specific and all-cause mortality (i.e., final health outcomes), and how does it differ by age, risk factor (e.g., family history, dense breast tissue), and screening interval?*

The proposed USPSTF search dates of 2008-2014 would exclude key data from randomized controlled trials (RCTs). The Task Force review should include all the RCTs. It should also be noted that the results of some of these RCTs are more valid/applicable than others. The Edinburgh trial was compromised by economic biases and the Canadian Trial suffered from flawed randomization resulting in a bias against mammography. The Swedish Two County trial, updated over 30 years has shown a consistent 30% mortality benefit.

Although RCTs are the gold standard in proving benefit, they underestimate the magnitude of this benefit due to lack of compliance in the study group and contamination of the control group. There are numerous quality observational, population-based service screening studies which should be included for the review process in addition to the RCTs and CISNET models that are likely to give a better estimate of the magnitude of the benefit.

In some of the studies that claim little benefit from screening, the source of their underestimate stems from the fact that some women were being screened before the

organized programs began, therefore the death rate did not show a sudden decline. This highlights the great importance of using direct patient data and not registry summaries, since many women who die after the onset of a screening program die from cancers diagnosed before screening was initiated.

The Task Force previously examined the number of women needed to be invited to screening rather than the number needed to be screened. The number needed to be screened provides a more accurate estimate that women and their physicians can understand. The number needed to invite assumes non-compliance by some women, and these noncompliant women could not expect to benefit from screening. It would be especially misleading to assess benefits in terms of women invited to be screened but harms in terms of women actually screened. Such a clearly biased approach would weaken the task force report and subject it to valid criticism.

In addition to mortality reduction, Life Year Gained (LYG) analysis should be considered either as part of this Key Question or as a separate question. Particularly for younger women, LYG will likely be a more meaningful metric than mortality data alone.

Computer modeling should be based on digital mammography and not on film screen technology. These results would be expected to duplicate recently published digital mammography CISNET values for women 40-49 which demonstrated a benefit.

While it may be important to compare younger to older women, it will be important to view specific age brackets in the context of overall changes. The intervals suggested (ages 40–49 vs. 50–59 vs. 60–69 vs. 70–79 years) are arbitrary, and there are no data that show that any of the parameters of screening change abruptly at any age. Grouping younger women together as if they were a uniform group and comparing them, dichotomously, to older women makes changes that occur gradually with increasing age appear to change abruptly at the beginning of each interval.

Although mortality reduction is the major benefit of screening, there are additional benefits of screening. These include a reduced likelihood of requiring chemotherapy, a greater likelihood of surgical treatment options and fewer women requiring mastectomy. Other factors should also be reviewed, such as reduced anxiety and reassurance from either a true negative test result (confirming breast healthy status) or a true positive test result (knowing that cancer was diagnosed and treated earlier with less likelihood of recurrence).

Key question 5*: In average-risk women age 40 years and older, what are the harms of routine mammography screening, and how do they differ by age, risk factor (e.g., family history, dense breast tissue), and screening interval?*

The term “overdiagnosis” has been used to describe malignancies which remain indolent and do not cause death to the patient. The frequency of overdiagnosis, (probably best estimated at less than 10%) varies widely in published reports. In the lay press, it has been wildly overestimated. The Task Force should pay careful attention to the methodology used in published reports, considering whether methods account for

patient risk and lead time bias, absence of which causes gross overestimation of the frequency of overdiagnosis.

But the Task Force should dig deeper and should clearly differentiate the three harms which occur at different levels of the chain of events, from detection to diagnosis to treatment of breast cancer. These include “overdetection”, “overdiagnosis” and “overtreatment.”

The term “overdiagnosis” should be used when a breast tissue sample is sent for pathological review and called histologically malignant, but may in truth be benign. Further advances in the molecular biology and pathology of cancer that might ameliorate this situation are being sought but are not yet available. Thus, treatment of an “overdiagnosed” malignancy may be “overtreatment,” and occurs after biopsy is recommended and tissue is submitted for histological review.

The screening process, whether by clinical exam or by mammography, may lead to “overdetection.” This is inherent in any screening process, whether by imaging or palpation. Although this is considered a screening harm, it is unrealistic to expect the screening process to be able to separate malignancies that have the potential to progress from those that do not, since medical science cannot always do this even at the histologic level.

Registry-based approaches which were previously used for the “harms” data should be given less weight because they do not track individual patient outcomes and are subject to bias.

The anxiety a patient may experience from a screening recall should not be equated with the anxiety associated with dying from metastatic disease.

The harms of not screening should be reviewed and quantified in the same manner as harms of screening if a balanced analysis is to be achieved. Specific harms of not screening include quality of life issues such as pain, suffering, and anxiety from living and ultimately dying from metastatic breast cancer. Also, loss of productivity due to metastatic disease and death, unnecessary chemotherapy and its side effects, unnecessary surgery and testing to document metastatic disease as well as loss of support by either a spouse or parent should be included in the methodology.

Contextual Question 1: *What are the rates of specific adverse effects of current treatment regimens for invasive breast cancer and ductal carcinoma in situ (DCIS) in the United States?*

The Task Force should have a parallel similarly worded Contextual Question concerning the beneficial effects of screening on the quality of life of women. Addition of such a question would help provide a more appropriately balanced assessment of benefits and harms. This would include lower morbidity from cancer treatment, true reassurance if there is no cancer and the screen is negative, and reduced anxiety knowing that cancer was detected and treated earlier, with a lower likelihood of recurrence.

Contextual Question 3: *What are women's values regarding breast cancer screening?*

This presumes that women understand fully the pros and cons of screening. While some scientific value can be quantitated based on scientific evidence, other "values" are based on subjective and personal opinions. Quality of life and the relative importance of non-lethal harms associated with screening fall under the personal and subjectively measured, while the estimated mortality benefit falls under the objective scientifically quantitated. Therefore, the method used to achieve the appropriate balance between such subjective and objective outcomes should be addressed, and should reflect the values of the American public and not merely the individuals serving on the Task Force.

Thank you for your consideration of our comments. Please contact Gloria Romanelli at ACR (703-716-7550) with any questions or to discuss this matter in more detail.

Sincerely,

Harvey L. Neiman, MD, FACR
Chief Executive Officer
American College of Radiology