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OPINION

Breast cancer screening guidelines: discrepancies raise concerns about validity

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Various medical organizations throughout the world have issued breast cancer screening guidelines that differ with respect to the age at which screening should begin, the screening intervals, and the age at which screening should stop. Even within the United States (US), there are considerable differences with respect to breast cancer screening guidelines among numerous medical organizations and task forces [1–3]. After reviewing the same body of evidence, why have expert panels throughout the world issued such conflicting guidelines? The discrepancies among the various guidelines raise concerns that specialty bias and fee for service conflicts of interest may threaten their validity.

Breast cancer screening has the potential for both benefit and harm. It is estimated that 10,000 screening mammograms prevent three-to-four breast cancer deaths [4]. Thus, most women who undergo screening will derive no benefit from it and many might even be harmed. These harms include false-positives, radiation exposure, cost, and overdiagnosis, which refers to the detection of cancers that pose no threat to life and that in the absence of screening would never have been detected. The validity of breast cancer screening guidelines is therefore of paramount importance, as these guidelines are issued after weighing the benefits and harms of screening and should serve as a trusted resource for clinical decision-making.

However, physicians who serve on guideline panels might be inclined to recommend services from which they derive a substantial portion of their income (i.e., fee for service conflicts of interest) and recommend procedures and treatments that they have been trained to provide (i.e., specialty bias) [5]. Fee for service conflicts of interest and specialty bias may, therefore, unconsciously influence physicians who serve on panels that issue guidelines for mammography screening [5]. Specialty organizations might, therefore, be inclined toward recommending more screening partly due to specialty bias and fee for service conflicts of interest among the members of their guideline panels.

When issuing recommendations for breast cancer screening, it is important to discern the evidence that forms the basis for these guidelines. In non-randomized studies, there are biases that skew the results in favor of screening, particularly lead-time, length, and selection biases [4]. Such biases are mitigated in randomized-controlled trials and meta-analyses of those trials, which ultimately provide the highest levels of evidence. Nine randomized trials have been undertaken to assess the efficacy of mammography screening: Health Insurance Plan (HIP), Malmo, Two-County, Stockholm, Gothenberg, Edinburgh, Canada National Breast Screening Study (CNBSS) I, CNBSS II, and the United Kingdom Age trial [4]. A meta-analysis of those trials shows that screening reduces breast cancer-specific mortality by 25% in women who initiate screening after age 50, and that benefit emerges 7–9 years after the initiation of screening. However, when screening is initiated for women in their 40s, the benefit of screening takes longer to emerge (i.e., 12–14 years), and the reduction in mortality is 19% [4]. The discrepancy in the effect of screening between younger and older women has been attributed to "age-creep" bias: women who start screening at age 40 may see a benefit if they continue screening after age 50, but there is no inherent benefit in starting screening before that age [4].

In recent years, the US Preventive Services Task Force (USPSTF) and National Health Service (NHS) breast cancer screening guidelines have largely been derived from evidence gathered from randomized trials. These organizations have placed very little emphasis on observational studies [3, 6]. The USPSTF has recommended mammography screening for women aged 50–74 undertaken every 2 years [3], while the NHS recommends screening for women aged 50–70 every 3 years [6]. However, recently, the USPSTF

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has proposed a change in their guidelines, and issued a draft recommending mammography screening for women aged 40–74 [7]. The underlying reason for this change is perplexing, as there are no new randomized clinical trials demonstrating any benefit for mammography screening under the age of 50 since the publication of their previous guideline. In fact, the UK Age Trial, specifically designed to assess the benefit for mammography screening under the age of 50, reported its results in 2020, and found no mortality benefit for screening women in this age group after more than 10 years of follow-up (RR 0.98 [0.79–1.22]; $p = 0.86$) [8].

Physician organizations, such as the American College of Obstetricians and Gynecologists (ACOG) and the American College of Radiology (ACR), recommend that women should start annual screening between the age of 40–45, and transition to biennially after the age of 55 [1, 2]. These organizations propose that after age 75, the decision to stop screening should be a shared decision-making process between the patient and their physician. Both organizations incorporate observational studies in addition to the randomized trials as a basis for their guidelines [1, 2] (Table 1).

Breast cancer mortality rates started to decline in 1990 in various industrialized countries around the world, and this is often attributed to screening and advancements in treatment. However, screening recommendations differ between countries such as the United Kingdom (UK), where organized screening is conducted, and the US where opportunistic screening is conducted and is dependent on the insurance policy of each individual. Yet, the declines in mortality in the US mirror those of the UK and other industrialized countries, even though mammography screening in the US is generally initiated at an earlier age, with shorter intervals between screens, and often continued past the age of 70, when compared to those other countries. For instance, the US has seen a 39% decline in breast cancer mortality rates between 1988 and 2015 [4] and the United Kingdom (UK) has seen a 42% decline in the same time period [6]. Therefore, the more aggressive screening strategies in the US have had no demonstrable effect in further lowering breast cancer mortality rates.

There is an important distinction between "clinical practice guidelines" and "position statements". Clinical practice guidelines should be developed on the basis of the highest levels of evidence and establish standards of care [9]. On the other hand, position statements may articulate an approach to a clinical problem on the basis of physician experiences and observational studies [9]. Variations in position statements are expected, particularly when one considers differences in physician backgrounds and expertise. Thus, specialty groups could issue position statements. These position statements may provide their perspective on issues for which there is no evidence from randomized trials, such as the potential benefit of screening with respect to quality-of-life parameters. However, variations in clinical practice guidelines should raise concerns about the validity of those guidelines.

Specialty physician organizations with potential specialty bias and fee for service conflicts of interest should refrain from issuing clinical practice guidelines. Moreover, national task forces and independent research associations tasked with creating clinical practice guidelines should consider potential fee for service conflicts of interest and specialty bias when determining which physicians to include in their guideline panels. Finally, adopting one national set of guidelines in breast cancer screening based on evidence from randomized trials and meta-analysis of those trials may ultimately prove to be the most optimal for

Table 1 Overview of breast cancer screening guidelines by organization [1–3, 6, 7]

Organization	Type of organization	Age to start screening	Age to stop screening	Screening interval	Modalities used
US preventive services task force (USPSTF) 2023 draft recommendation	United States national organization	40	74	Once every 2 years	Mammography
US preventive services task force (USPSTF) (2016)	United States national organization	50	74	Once every 2 years	Mammography
National health service (NHS)	United Kingdom national organization	50	70	Once every 3 years	Mammography
American college of obstetricians and gynecologists (ACOG)	United States physician association	40	> 75 no stated year to stop	Once every 1–2 years	Mammography and clinical breast exams
American college of radiology (ACR)	United States physician association	40	> 75 no stated year to stop	Once a year	Mammography, MRI for women with dense breasts

clinical decision-making and would strengthen confidence in the validity of those guidelines.

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Declarations

Conflict of interest The authors have no conflicts of interest to declare.

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