

The Recent US Preventive Services Task Force Guidelines Are Not Supported by the Scientific Evidence and Should Be Rescinded

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The recent US Preventive Services Task Force (USPSTF) guidelines on mammographic screening ignore the scientific evidence and should be rescinded. There are no data to support the age of 50 years as a threshold for screening. There are no data to support screening women aged 40 to 49 years on the basis of risk. The USPSTF failed to understand the randomized controlled trials and used the lowest possible benefit in its calculations. The death rate from breast cancer has decreased by 30%, primarily because of screening. The agency ignored direct data with regard to decreasing deaths in real populations in favor of computer models. The USPSTF admits that its guidelines will result in unnecessary deaths from breast cancer that could be avoided by screening annually beginning at the age of 40 years.

Key Words: Breast cancer, mammography screening, screening guidelines

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In November 2009, the US Preventive Services Task Force (USPSTF) [1] withdrew its support for mammographic screening for women aged 40 to 49 years and recommended that women aged 50 to 74 years be screened every 2 years. It is unclear why the USPSTF decided to drop its support, considering that the only important new data that have become available since 1997 (when the National Cancer Institute once again supported screening beginning at the age of 40 years) are national statistics showing that as more women participate in mammographic screening, the death rate from breast cancer continues to decrease. The USPSTF, incongruously, agreed that screening is saving lives but decided that it would make the decision for women in their 40s because the members felt that the “harms” of screening (anxiety from having the test, breast compression, false-positive results, needle biopsies, and possible overtreatment) were worse than allowing women to die from breast cancer. These guidelines will likely result in women being advised by their doctors, who rely on the advice of the USPSTF, to forgo mammography screen-

ing. Perhaps an even greater risk is that insurance companies, citing these guidelines, may no longer pay for screening before age 50 and only every 2 years from 50 to 74, essentially denying access to screening for many women. The medical community has made cogent arguments in support of providing patients with information so that they can make “informed decisions,” but the USPSTF has taken the decision to participate in mammographic screening away from women.

It is clear that the USPSTF did not think through the consequences of its guidelines. In addition to denying women in their 40s access to mammographic screening, the agency also told women in their 40s that they should not perform breast self-examinations and should not allow trained health care professionals to perform clinical breast examinations. What does this leave for women in their 40s? The USPSTF is telling women to wait until their cancers are so large that they can no longer ignore them and then bring them to their doctors’ attention, when there is no longer a chance for cure. Is this what we should advise our patients?

Furthermore, the USPSTF is withdrawing support for screening women aged 50 to 74 years annually, advising instead that they can wait 2 years between mammograms, essentially saying that it is fine to allow their cancers to grow for an additional year before they are diagnosed. The USPSTF even acknowledges in its discussion that screening every 2 years, instead of annually,

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will result in unnecessary deaths that could be avoided with annual screening, but the agency found this to be reasonable because it reduces the false-positive rate.

The USPSTF has misled American women and their physicians by suggesting that they have reviewed all of the pertinent literature and data on breast cancer screening and that their guidelines are “evidence based.” In fact, the USPSTF has selected the information that suits its agenda. The death rate from breast cancer has decreased by 30% since 1990 [2]. This is directly linked to the onset of annual mammographic screening for women aged ≥ 40 years in the mid-1980s [3]. Before mammographic screening, nothing had influenced the death rate since 1940.

Studies in Sweden and the Netherlands have clearly shown that when mammographic screening is introduced into the general population, the vast majority of the subsequent decrease in deaths is due to mammographic screening, not to new therapies [4-6]. Completely ignoring these direct measures, the USPSTF has chosen to rely on its own computer models, not even mentioning that other computer models disagree with its conclusions [7]. What the agency has done is comparable to stating that because sophisticated financial computer models predicted that the economy was sound in the fall of 2008, the financial collapse must not have happened. There is no justification for relying on computer models when there are direct data that bear on the question.

By relying on the number of screening studies needed to save one life, the USPSTF is clearly sending the message that it does not think that it is worth saving women in their 40s, but the agency does not have the honesty to state this directly. If cost is the issue, then the USPSTF needs to factor in the cost of allowing breast cancers to be advanced before they are treated (necessitating more morbid and expensive therapy), not to mention the costs to their families and society of losing these women. The agency needs to allow women to decide what is a reasonable cost and not deny them access to screening simply because it does not feel that it is worth saving women from dying of breast cancer. True cost-benefit analysis was performed in 1994, when the National Cancer Institute promulgated the exact same guidelines. At that time, screening beginning at the age of 40 years was well within the agreed-on cost-benefit limits [8].

The marked decrease in deaths that accompanies mammographic screening has been a major advance for women’s health. This is a remarkable achievement, and now, the USPSTF, deciding that women should be allowed to die from their breast cancers, is trying to turn back the clock 20 years. The following material is a summary of the data the USPSTF ignored. The agency clearly failed to understand randomized controlled trials (RCTs) of screening, and its negligent exclusion of data

that do not support its agenda is unconscionable. Women should be informed of the “harms” of screening, but they should be provided a clear explanation of the proven benefits so that they can make “informed decisions” for themselves.

FACTS

Data From the “Age Trial”

The USPSTF suggested that its analysis was warranted because of the new data available from the Age trial, which screened women beginning at ages 40 and 41. The USPSTF clearly did not understand that the Age trial made huge compromises. After prevalence screening, the investigators used single-view mammography, which they knew missed 20% to 25% of cancers [9]. Furthermore, they admitted that they failed to biopsy clustered calcifications, causing them to miss additional small cancers [10]. None of these problems are mentioned by the USPSTF.

Data From the Canadian National Breast Screening Study

The USPSTF continued to use the results from the Canadian National Breast Screening Study-1 (CNBSS1), despite the fact that this trial was clearly compromised by its failure to adhere to the requirement for blinded randomization [11]. Ignoring the rules requiring blinded randomization for an RCT, each woman in the CNBSS1 had a clinical breast examination before being assigned to the screened group or the control group. This identified women who had palpable cancers and positive axillary nodes. Then the allocation process took place on open lists, so that a line could be skipped to ensure that these women, with advanced breast cancers, were placed in the mammography group. This resulted in a significant excess number of women with advanced, incurable breast cancer who were placed in the screening group at the start of the trial [12], biasing it from the start. This is a major breach that invalidates the results of the trial, yet the USPSTF continued to use the results of the CNBSS1 to lower the benefit found in the other trials, which, by design, underestimate the benefit (see below).

The Age of 50 Years As a Screening Threshold

The USPSTF singled out women aged 40 to 49 years as if there were some scientific justification for this. There are no ungrouped data, none at all, supporting the idea that any of the parameters of screening change abruptly at age 50 or any other age, so there is no scientific support for using the age of 50 years as any but an arbitrary threshold [13].

The detection rate of breast cancer parallels the prior probability of breast cancer in the population, increasing

steadily with increasing age but with no abrupt change at any age [14]. The myth that the parameters of screening change suddenly at the age of 50 years is due to data grouping to make it seem as if there is a sudden change at 50, when in fact there is none [15]. The USPSTF, without any justification, continues to promulgate this falsehood by grouping data by decades to make it seem as if there is a sudden jump at the age of 50 years. The age of 50 originated as a surrogate for menopause. There are no data showing that any of the parameters of screening change with menopause.

There is no scientific justification for using the age of 50 years as a threshold for screening. If the USPSTF chose this threshold arbitrarily, it failed to alert women and their physicians. This is purely data manipulation, and the USPSTF has used it to try to deny women in their 40s access to screening.

Benefits of Screening at Ages 40 to 49

The RCTs of mammographic screening have always demonstrated a statistically significant mortality reduction for screening women aged 40 to 74 years [16,17]. Although the RCTs were not designed to permit retrospective subgroup analyses [18] of women aged 40 to 49 years, with longer follow-up, the mortality reduction is significant and as high as 44% [19]. Even the USPSTF agrees that there is a benefit to screening women aged 40 to 49; the agency decided, however, to use the smallest benefit (15%) it could find for its analysis and ignored statistically significant benefits that were at least double those.

The Methodology of Screening RCTs

The USPSTF clearly did not understand the methodology used in the RCTs of screening. In these trials, women are “invited” to be screened. This means that women who are allocated to the screening arms who refuse the invitation to be screened (noncompliance) and die of breast cancer are still counted as deaths in the screened groups, while women allocated to be unscreened control groups whose lives are saved by mammography they undergo outside the trial (contamination) are still counted as unscreened controls. If the members of the USPSTF actually understood that the trials underestimate the benefit, they neglected to mention it.

Benefits of Screening Compared With Improved Therapies

In its calculations, the USPSTF chose the lowest possible estimate of benefit (15%). In fact, in the United States, the death rate from breast cancer is down by 30% [2], and in Sweden, it is down by >40% [20]. The USPSTF used computer modeling showing that 23% to 65% of the decrease in deaths in the United States is due to

mammographic screening, choosing to believe, however, that most of the benefit is due to improved therapies while ignoring the direct evidence from Sweden and the Netherlands showing that the vast majority of the decrease in deaths is due to mammographic screening [4-6].

Mortality Reductions in Women Aged < 50 Years

Even though the RCTs were not designed to evaluate women aged 40 to 49 years, breaking women aged 40 to 49 out as a separate subgroup reveals that the Gothenburg Breast Cancer Screening Trial had a 44% statistically significant mortality reduction for women aged < 50 years [21], and the Malmo Mammographic Screening Program had a 35% statistically significant mortality reduction for women aged < 50 years [22]. The Swedish trials combined had a 29% statistically significant mortality reduction for women aged < 50 years [19]. The population-based trials had a 26% statistically significant mortality reduction [19] for women aged < 50 years. It is only when the compromised CNBSS1 is added that the benefit drops to 15%.

These facts were all ignored by the USPSTF. In Sweden, since mammographic screening was introduced into the general population of women in their 40s, the death rate for these women has decreased by >40% [20]. This was also ignored by the USPSTF.

Breast Cancer at Ages 40 to 49

The USPSTF seems to believe that breast cancer is not a major problem for women in their 40s. The agency clearly does not realize that $\geq 40\%$ of the years of life lost to breast cancer are due to cancers diagnosed while women are in their 40s [23].

Benefits of Early Detection

The USPSTF acknowledges [1] that the death rate in the United States has decreased since 1990 “by 2.3% per year overall and by 3.3% for women ages 40 to 50 years” (p 720). This is additive, so that there were 30% fewer deaths in 2005 than would have occurred with no screening. Data from Sweden and the Netherlands clearly show that most of the decrease is due to early detection, with only a small component due to newer therapies [4,6], yet the USPSTF would deny these women access to early detection.

False-Positive Results

There is no test that does not produce false-positive results. The goal of health care is “informed decision making,” but the USPSTF is telling women that it is making the decision about mammographic screening for them.

Overdiagnosis

The USPSTF raised concern about overdiagnosis. There is no direct evidence that this is a major problem. Zahl et al [24] compared two different populations of women at two different points in time with two different prior probabilities of breast cancer. Furthermore, they ignored the baseline increase in breast cancer that has been going on since the 1940s, and they also did not take into account the “prevalence cancers” that occur each year as new women begin screening. Their conclusions are not scientifically supported. A second study by Jørgensen and Gøtzsche [25] also ignored the fact that as women began screening at the age of 50 years, in the countries they reviewed, they brought prevalence cancers with them each year that contributed to a higher apparent “incidence.” What they were looking at is not true incidence, but cancers detected (incidence plus prevalence). As long as new women begin screening each year, the “incidence” will not return to baseline because of the addition of new prevalence cancers. This was a fundamental error in their analysis that voids their conclusions. Analysis of the RCTs, which is the only way to determine if there is overdiagnosis, suggests that it is <10% [26] and likely much lower [27]. There is no evidence that cancers detected by mammography “melt away.”

With regard to ductal carcinoma in situ, there is still debate as to how many of these lesions, detected primarily by mammography, progress and become lethal cancers. Given enough time, many of these lesions, even the most indolent, will progress [28]. The decrease in invasive breast cancer incidence, which has been falsely attributed to reduced hormone use [29,30], is likely due to the removal of the precursor (ductal carcinoma in situ) because of mammographic screening. The bottom line is that overdiagnosis, if it exists, is the fault not of mammography but rather of the inability of pathologists to, as yet, determine the precise lethality of any given lesion.

Overtreatment

It is likely that many breast cancers are “overtreated.” However, this is true for clinically apparent cancers and not simply mammographically detected cancers. Furthermore, overtreatment is not the fault of early detection but rather a therapeutic issue that many investigators are working hard to address. Major efforts are ongoing to try to tailor therapy to each individual and her cancer, but there are few clear answers as yet. Not all bacterial pneumonias need to be treated with antibiotics, but we do not want to risk someone’s life by undertreating. Women should not be deprived of the chance to be cured of breast cancer because a committee decides that they should not have that chance.

Screening Only High-Risk Women Aged 40 to 49 Years

The USPSTF advised that only women at high risk should be screened in their 40s. There is no scientific justification for this recommendation. The USPSTF agrees that the RCTs are the only way to prove a benefit from screening, yet it ignored the fact that none of the RCTs stratified by risk, so there is no scientific evidence that screening only high-risk women will save any lives. Furthermore, most women who develop breast cancer are not at high risk, so screening only high-risk women will miss the 75% to 90% of breast cancers that occur each year among women who are not at elevated risk [31]. The USPSTF’s decision ignores the science and will result in unnecessary deaths.

The USPSTF used the “number of women needed to be screened to save one life” as its measure, estimating that figure at 1,904 for women aged 40 to 49 years, 1,339 for those aged 50 to 59 years, and 337 for those aged 60 to 69 years. The agency decided that 1,904 was too high, but 1,339 was within its threshold to support screening. These estimates, however, were based on a 15% mortality reduction, which, as noted above, is the lowest possible estimate. Using the 30% decrease in deaths that is evident in the United States (in Sweden, it is 40%), the number needed to be screened for women ages 40 to 49 drops to 950, well within the USPSTF’s threshold.

SUMMARY

Mammographic screening has been shown, in the most rigorous scientific studies, to significantly decrease breast cancer deaths for women aged 40 to 74 years. Since screening was introduced into the general population, the death rate has decreased dramatically for American women, and direct data show that most of the decrease in deaths is due to mammographic screening. The USPSTF guidelines ignore the facts and the scientific evidence. The implementation of these guidelines will severely reduce the benefit that has been achieved and, by the agency’s own admission, result in unnecessary deaths from breast cancer that could be avoided by annual screening beginning at age 40. The USPSTF guidelines will set back women’s health by more than 20 years and should be rescinded.

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