Comparison of recommendations for screening mammography using CISNET models

Running title: Screening mammography recommendations

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Condensed Abstract: The purpose of this study was to use the CISNET breast cancer models to compare the three most widely discussed current recommendations for screening mammography, including: (1) annual screening ages 40-84; (2) annual screening ages 45-54, followed by biennial screening ages 55-79; and (3) biennial screening ages 50-74. The principal finding is that mean mortality reduction is greatest with the first recommendation of annual screening starting at 40 (39.6%), compared with the second (30.8%) and third (23.2% based on 2009 CISNET, 26.6% based on 2016 CISNET) recommendations.

ABSTRACT

Background: Currently, there are several different recommendations for screening mammography from major national healthcare organizations, including: (1) annual screening ages 40-84; (2) screening annually ages 45-54, then biennially ages 55-79; and (3) biennial screening ages 50-74.

Methods: Mean values of six Cancer Intervention and Surveillance Modeling Network (CISNET) models were used to compare these three screening mammography recommendations in terms of benefits and risks.

Results: Mean mortality reduction was greatest with the recommendation of annual screening ages 40-84 (39.6%), compared with the hybrid recommendation of screening annually ages 45-54, then biennially ages 55-79 (30.8%), and the recommendation of biennial screening ages 50-74 (23.2%). For a single-year cohort of U.S. women age 40 years old, assuming 100% compliance, more breast cancers deaths would be averted over their lifetime with annual screening starting at age 40 (29,369) than with the hybrid recommendation (22,829) or biennial screening ages 50-74 (17,153 based on 2009 CISNET estimates, 15,599 based on 2016 CISNET estimates). To achieve the greatest mortality benefit, this single-year cohort of women would have the greatest total number of screening mammograms, benign recalls, and benign biopsies performed over the course of screening by following annual screening starting at 40 (90.2 million; 6.8 million; 481,269, respectively) than by following the hybrid recommendation (49.0 million; 4.1 million; 286,288) or biennial screening from ages 50-74 (27.3 million; 2.3 million; 162,885).

Conclusion: CISNET models demonstrate that the greatest mortality reduction is achieved with annual screening of women starting at age 40.

INTRODUCTION

Breast cancer deaths are prevented by routine screening mammography, as evidenced by randomized controlled trials (RCTs), mortality data from organized population-based screening programs, and international service screening experience (1). According to a meta-analysis of RCT data, the relative risk of dying from breast cancer was 20% less in women invited to screening mammography compared with women who were not (2). National data from the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute (NCI) indicate that after the widespread introduction of screening mammography in the late 1980s, the breast cancer death rate in the United States subsequently decreased by 37% (3), although this decline in death rate cannot entirely be attributed to screening. Among women who actually underwent screening mammography, incidence-based mortality studies based on service screening data from Europe and Canada have demonstrated a 38% to 40% decrease in breast cancer deaths (4, 5) , and case-control studies based on service screening data from Europe and Australia have demonstrated a 48% to 49% decrease in breast cancer deaths (4, 6).

These RCTs, U.S. population-based data, and international service screening data are not without their limitations, however, including the use of older mammography technology and the issues of non-compliance and contamination, both of which underestimate the benefit of current practice on women undergoing screening (RCTs), lack of information about which women were actually screened (SEER population-based data), and differences in screening intervals and starting ages (service screening) (2, 4, 7-9). Computer models, although also not without limitations, attempt to rectify some of the shortcomings of the data previously mentioned by applying consistent starting ages and screening intervals both within and across various models.

Under the auspices of the National Institutes of Health, which is part of the U.S. Department of Health and Human Services, the National Cancer Institute (NCI) has funded the Cancer Intervention and Surveillance Modeling Network (CISNET) to develop such models (10-12). In 2009 and 2016, the United States Preventive Services Task Force (USPSTF) issued recommendations on screening for breast cancer, informed by reports from CISNET (13, 14).

The purpose of this study is to use CISNET breast cancer models to compare the three most widely discussed current screening mammography recommendations for women of average breast cancer risk: (1) annual screening ages 40-84 (hereafter referred to as annual screening starting at 40); (2) annual screening ages 45-54, followed by biennial screening ages 55-79; and (3) biennial screening ages 50-74. While CISNET itself has compared screening strategies (12), it is precisely because the most recent CISNET analysis involved only one of the three most widely discussed strategies that the current study was performed.

METHODS

We use the 2009 and 2015-16 CISNET breast cancer specific models (hereafter referred to as 2009 CISNET and 2016 CISNET, respectively) to analyze the implications of different screening recommendations, including: (1) annual screening starting at 40; (2) annual screening ages 45-54, followed by biennial screening ages 55-79; and (3) and biennial screening ages 50-74. Table 1 outlines the screening recommendations of various organizations. The methods CISNET used to develop their models are detailed in a technical report published by the Agency for Healthcare Quality and Research (11). In brief, CISNET had six groups at different institutions develop independent computer models with multiple input parameters including estimates of breast cancer incidence, survival trends with and without screening or adjuvant

therapy, mammography performance data from the Breast Cancer Surveillance Consortium (BCSC), and breast cancer-specific mortality data from the SEER Program. However, the models are each different, and while estimates of outcomes are somewhat similar, there are significant differences among the six models, as well as inherent imprecision in models in general. For more details, the specific model parameters and inputs can be found on the CISNET website (15) . All CISNET models assume 100% adherence to screening and treatment. A factor that cannot be controlled is the quality of diagnostic studies and treatment; although high quality is assumed given mammography requirements under the Mammography Quality Standards Act and surgical and oncological standards, realistic variations might be expected.

CISNET quantified benefits in terms of breast cancer deaths averted and life-years gained by screening per 1000 women based on a single-year cohort of U.S. women: those born in 1960 for 2009 CISNET and those born in 1970 for 2016 CISNET. Benefits in terms of lives saved, life-years gained, and estimates of number needed to screen to avert a breast cancer death assume follow-up over each woman's lifetime. We have extended 2009 CISNET to obtain absolute numbers of women who would both benefit and experience risk from screening over the full age range specified for the single birth-year cohort of U.S. women born in 1960 and alive in the year 2000 (2.468 million based on year 2000 U.S. census data (16)). A woman born in 1960 and alive in 2000 would be 40 years old and enter the age range that screening begins for the first of the three screening strategies. In our comparison of screening strategies, some women begin screening at age 40, some at age 45, and some at age 50, and all attend annually or biennially, or a combination of the two, until screening ends. Benefits are also stated in terms of numbers needed to screen (NNS) to avert one breast cancer death and to gain one life-year for each strategy. Use and risks of screening are quantified in terms of numbers of mammograms, benign

recalls (women recalled from screening with no significant or nonmalignant findings), and benign biopsies performed, both per 1000 women screened and in absolute numbers for that single birth-year cohort. Since both CISNET modelers and the USPSTF acknowledge that "methods for estimating overdiagnosis at a population level are not well established" (12, 14, 17) and "Existing science does not allow for the ability to determine precisely what proportion of cancer diagnosed by mammography today reflects overdiagnosis, and estimates vary widely depending on the data source and method of calculation used" (11), the decision was made not to include overdiagnosis in this study's risk assessment. However, unless breast cancers actually can regress and disappear (which no one has ever observed for an invasive cancer found by mammography), delaying the age at which screening is started and extending the time between screens will have no effect on "overdiagnosis", since "overdiagnosed" cancers still will be present at the age of 45 or 50 and still will be present whether screening is annual or biennial.

CISNET estimates in 2009 considered annual and biennial screening for a variety of starting and ending ages (extending to age 84). For both annual and biennial screening, by taking differences between 2009 CISNET estimates over wider age ranges, we estimate benefits and risks over a variety of age ranges, including those of the three major models, including the hybrid recommendation of screening annually ages 45-54, then biennially ages 55-79.

CISNET estimates in 2009 used 6 models to estimate benefit, while only one model, their "exemplar" Stanford model, was used to provide quantitative estimates of risks. We report mean benefits across all 6 models, weighing each model equally. The first and second recommendations, (1) annual screening starting at 40 and (2) annual screening ages 45-54 followed by biennial screening ages 55-79, recommend that a healthy woman continue screening

until her life expectancy is less than 10 years (second recommendation) or less than 5-7 years (first recommendation). Based on 2010 life expectancy tables (18), the average U.S. woman's life expectancy drops below 10 years at age 80-81 years and below 7 years at age 85-86 years. Based on these life expectancies, we estimate benefits and risks using 2009 CISNET taking age 79 as the final screening age for the average woman following the second recommendation, and age 84 as the final screening age for the average woman following the first recommendation.

2016 CISNET included 6 models to provide quantitative estimates of benefits and risks. Estimates of benefits and risks in 2016 CISNET were based on the single birth-year cohort of U.S. women born in 1970 and alive in the year 2010 (2.197 million based on 2010 U.S. census data (16)). Compared to 2009 CISNET estimates, 2016 CISNET estimates involved a smaller number of annual, biennial, and hybrid screening scenarios, with all scenarios ending screening at age 74 years. Specifically, 2016 CISNET assessed only one of the three currently considered screening recommendations (the third), since all screening scenarios considered by 2016 CISNET ended screening at age 74, and since the only hybrid strategies 2016 CISNET considered transitioned from annual to biennial screening at age 50, rather than the second hybrid recommendation of transitioning from annual to biennial screening at age 55. Since neither the second hybrid nor the first recommendation is modeled by 2016 CISNET, we use 2009 CISNET models to compare the three current recommendations for screening mammography. We also compare CISNET 2009 and 2016 estimates of benefits and risks for the third screening recommendation of biennial screening of women ages 50-74. 2009 CISNET was based largely on screen-film mammography performance, while 2016 CISNET was based primarily on digital mammography performance. As of June 1, 2016, 98% of the 16,042 mammography units in the U.S. were digital mammography units(19).

Statistical analyses were not performed because assessing for statistical significance of differences was not the objective of this paper; rather, the goal was to quantify the benefits and risks estimated by CISNET models and our extension of CISNET models for the three major screening recommendations.

RESULTS

Table 2 shows the benefits of screening mammography over a lifetime of compliance with each of the three major screening recommendations based on 2009 CISNET modeling (10). Table 2 demonstrates that the largest mean mortality reduction is achieved with the first recommendation of annual screening starting at age 40 (39.6%, compared to 30.8% for the second recommendation and 23.2% for the third). Similarly, following the first recommendation averts the most breast cancer deaths (11.9 per 1000 women screened, 29% more than the hybrid recommendation and 71% more than the third recommendation) and gains the most life-years (189 per 1000 women screened compared to 149 for the hybrid recommendation and 110 for the third recommendation).

Table 2 also demonstrates that the NNS per death averted and the NNS per life year gained was smallest – and therefore most efficacious – with the first recommendation (NNS per death averted of 84 for the first compared to 108 for the hybrid and 144 for the third recommendation; NNS per life-year gained (LYG) of 5.3 for the first, 6.7 for the hybrid, 9.1 for the third recommendation, respectively).

Table 3 shows the benefits of screening mammography for the single-year cohort of women who turned 40 years old in the year 2000 and who followed each recommendation. If none of these women underwent screening mammography, then 2009 CISNET estimates that

from age 40 on, 3% (10), or approximately 74,000 women in this single-year cohort of 2,468,000 women would die due to breast cancer. Alternatively, if this cohort of women followed the first recommendation of annual screening ages 40-84 with 100% compliance, then 29,369 breast cancer deaths could be averted, a 39.6% mortality reduction. This is 29% more deaths averted than by the same group of women following the hybrid recommendation (22,829 deaths averted, a 30.8% mortality reduction, and 71% more deaths averted than by the same group following the third recommendation (17,153 deaths averted, a 23.2% mortality reduction). Likewise, the largest number of life-years would be gained if this single-year cohort followed the first recommendation (466,452 LYG), 27% more than if they followed the hybrid recommendation (367,732 LYG), and 72% more than if they followed the third recommendation (271,480 LYG).

Table 3 also shows the risks of screening mammography in terms of recalls and benign biopsies for the single-year cohort of women who turned 40 years old in the year 2000 and who followed each recommendation. The largest number of screening mammograms, benign recalls, and benign biopsies would occur under the first recommendation, the smallest number under the third recommendation, and an intermediate number under the second (hybrid) recommendation. Based on these 2009 CISNET estimates, on average a woman getting annual screening starting at age 40 could expect to be recalled from screening for a benign diagnostic work-up once every 13 years, and could expect to undergo a benign biopsy once every 187 years. Benefit compared to risk is shown in the last column of Table 3 in terms of LYG per benign biopsy for each screening regimen. A woman getting annual screening starting at age 40 could expect 1 LYG for every benign biopsy.

Table 4 compares 2009 and 2016 CISNET estimates of benefit and risk for the third recommendation of biennial screening ages 50-74. While 2016 benefit estimates are slightly

higher than 2009 estimates per 1000 women screened (9% higher for deaths averted, 10% higher for LYG), and benign recalls are 1% higher, benign biopsies are estimated to be 121% higher based on 2016 CISNET than 2009 CISNET. One possible explanation is that 2009 estimates were based on BCSC data for the more clinically relevant outcome of biopsies actually performed, while 2016 estimates were based on BCSC data for radiologists' recommendations for biopsy (10-12); in other words, more biopsies are recommended than are actually performed. Breast cancers deaths averted for a single-year cohort by biennial screening ages 50-74 are 17,153 based on 2009 CISNET, which used the cohort of women born in 1960, and 15,599 based on 2016 CISNET, which used the cohort of women born in 1970 (10, 12).

The number of women in the single-year cohort of women born in 1960 who would still die from breast cancer given 100% compliance with screening, based on 2009 CISNET mean estimates, is 44,671 for strategy 1, 51,211 for strategy 2, and 56,887 for strategy 3.

DISCUSSION

The purpose of this study was to use CISNET breast cancer models to compare the three most widely discussed current recommendations for screening mammography: (1) annual screening starting at 40; (2) screening annually ages 45-54 and biennially ages 55-79; and (3) biennial screening ages 50-74. The principal finding is that mean mortality reduction is greatest with the first recommendation of annual screening starting at 40 (39.6%), compared with the hybrid (30.8%) and third (23.2% based on 2009 CISNET, 26.6% based on 2016 CISNET) recommendations.

The primary value of analyzing 2016 CISNET results is to compare these new results with 2009 CISNET results to determine how CISNET estimates have changed. There are three

main differences between 2009 and 2016 CISNET. First, 2016 CISNET modeled only one of the three major screening recommendations (biennial screening ages 50-74). The second (hybrid) recommendation has women transitioning from annual to biennial screening at age 55 rather than 50, and in our comparison, on average ends at age 79 rather than age 74; in our comparison, the first recommendation on average ends annual screening at age 84 rather than age 74. Hence, 2016 CISNET does not model benefits or risks for either the first or second recommendation. It is important to point out that just because the six 2016 CISNET models ended all screening strategies at age 74 does not mean that women ages 75 and older do not continue to accrue benefits from screening mammography. In fact, CISNET results demonstrate that, as CISNET itself reports, "for women with no comorbidity who have an average of a 17-year remaining life expectancy, screening would be efficient through age 78 to 80 years"(11), and that benefits exceed risks up to age 90 years (20).

Second, CISNET changed its manner of calculating benign biopsies between 2009 and 2016. 2009 CISNET used BCSC data on the number of women actually undergoing benign biopsies, with positive predictive value (PPV) based on biopsies performed (PPV_3), while 2016 CISNET switched their definition to the number of women recommended to undergo biopsy based on radiology findings (PPV_2) (21),. It is important to understand that PPV_3 (CISNET 2009) is based on biopsies actually performed, which reflects actual health care delivery. As a result of this change in their definition of "negative biopsies", 2016 CISNET may substantially overestimate the risk of benign biopsy. For example, using 2009 CISNET, biennial screening from ages 50-74 years was estimated to yield 66 benign biopsies per 1000 women screened, while 2016 CISNET estimated this number to be 146 (Table 4), 121% greater than the 2009 estimate. One can only speculate on why CISNET changed its method of estimating the number

of benign biopsies. The number of women biopsied is the clinically relevant number, reflecting actual health care delivery, not the number of women recommended for biopsy.

A third difference between 2009 and 2016 CISNET involves estimate of the number of women ages 40 and over who would die from breast cancer in the absence of screening mammography. The 2009 CISNET estimated median value for all 6 models was 3%, while the 2016 median value was 2.5% (range 1.5-3.2%) (11); CISNET's rationale for this change is not fully explained. Effectively, CISNET substantially increased their estimate of the number of women who would benefit from treatment (adjuvant therapy and surgery) alone. This recalls the persistent conjecture in the literature that adjuvant therapy has eclipsed the importance of early detection, despite the fact that numerous recent studies published demonstrate decreased breast cancer specific deaths associated with invitation or exposure to screening mammography compared with women not invited or not attending screening (4, 5, 22-28) . Evaluations of service screening programs have shown substantial mortality reductions in women exposed to screening compared to those not exposed to screening, with some studies going to great lengths to show that access to and quality of treatment was homogeneous across the comparison groups (23) . For example, Tabar et al compared mortality reductions over time in exposed and unexposed women, showing that there was some improvement in deaths avoided due to modern therapy, but it was substantially less than deaths avoided by exposure to screening in combination with modern therapy; these estimates included interval cancers in the group exposed to screening who did not have their breast cancer diagnosed by screening (28). This study was unique in that it compared mortality reductions in unexposed women over the time period before and after the introduction of adjuvant therapy (28). In these observational studies where women had access to the same therapies, there were fewer deaths among women who had access to

screening, and even fewer among women who participated in screening, despite access to the same therapies. A recent CISNET analysis estimates that annual screening would account for the great majority (69% to 74%) of breast cancer mortality reduction in the United States at full compliance (29).

Estimates of the number of women in the single-year cohort who would still die from breast cancer given 100% implementation of each of the three screening guidelines (44,671 with screening strategy 1, 51,211 with strategy 2, and 56,887 with strategy 3) highlight the need to improve breast screening, whether with mammography or another modality.

It is also of value to consider 2009 CISNET risk data from the individual woman's perspective and to highlight how frequently she is likely to experience "risks". Specifically, data in Table 3 show that if a woman born in 1960 and alive in the year 2000 underwent annual screening starting at age 40, then on average she could expect to be recalled for a benign diagnostic work-up once every 13.3 screening exams or approximately once every 13 years. Following that same screening recommendation, she could expect on average to undergo a benign biopsy once every 187 screening exams, and therefore be unlikely to undergo a benign biopsy during an entire lifetime of annual screening. These risks are considerably lower than most women have expressed willingness to accept. For example, in an attitudinal study of 479 U.S. women, Schwartz et al found that "women were highly tolerant of false positives: 63% thought that 500 or more false positives per life saved was reasonable and 37% would tolerate 10,000 or more" (30). On a related note, "false-positive mammograms were associated with increased short-term anxiety but not long-term anxiety, and there was no measurable health utility decrement," according to a study by Tosteson et al. That study also found that false-positive mammograms actually increased a woman's intention to undergo future screening and

that most women would not drive any extra distance for screening with a lower likelihood of false positives (31). Additionally, Table 3 shows that for the annual screening starting at age 40, CISNET models estimated that one life-year would be saved for each benign biopsy experienced. One does not need an attitudinal survey to conclude that almost all women would be willing to undergo a benign biopsy to extend their life by a year.

The second screening strategy, in which women screen annually for ages 45-54 and transition to biennial screening at age 55, is a hybrid of the first and third recommendations with respect to frequency and starting age. Of note, the current ACR/SBI (first) recommendation is the former ACS guideline, with the exception of a shorter estimated longevity as a stopping age. While one might suggest that this new (second) hybrid recommendation has outcomes very similar to the first recommendation, but with risks much closer to those of third screening recommendation, our analysis based on 2009 CISNET demonstrates otherwise. Specifically, the benefits of mortality reduction and life-years gained for the (second) hybrid recommendation are approximately halfway between those of the first and third recommendations (Tables 2 and 3). Similarly, the estimated risks of benign recalls and benign biopsies for the (second) hybrid recommendation are approximately halfway between those of the first and third recommendations (Table 3). Although the second strategy models the ACS “strong" recommendation of annual screening ages 45-54 and biennial screening ages 55-79, an ACS "qualified" recommendation states that “women should have the opportunity to begin annual screening between the ages of 40 and 44 years”(1). Based on 2009 CISNET, starting annual screening at age 40 instead of age 45 would increase mean mortality reduction from 30.8% to 32.7%, mean life-years gained from 149 to 163 per 1,000 women screened, and mean lives saved in the single-year cohort born in 1960 from 22,829 to 24,063. Another ACS "qualified"

recommendation is that women 55 years and older should have the opportunity to continue screening annually. Annual screening from ages 55-79 instead of biennial screening would increase mean mortality reduction from 23.5% to 28.3%, increase mean life-years gained from 97 to 118 per 1,000 women screened, and mean lives saved in the single-year cohort from 17,399 to 20,978. Annual screening from ages 40-79 would result in both benefits and risks much closer to those of the first recommendation. We modeled the strongly recommended ACS hybrid strategy because it is widely discussed both in the medical and lay press. The "qualified" ACS recommendation supports more frequent and earlier onset screening that closely matches the ACR, ACOG, NCCN and SBI recommendations. It is important to note that the ACS recommendations include the possibility of starting annual screening at age 40 and undergoing annual rather than biennial screening after age 54, and that many women will likely choose to go beyond their minimum recommendation.

Just as RCTs, U.S. population-based trends, and international service screening studies have their limitations, computer models have their own limitations. Models are a way to try to predict what might happen, but their outcomes depend heavily on their assumptions. If assumptions are incorrect or uncertain, then the validity of the results is less certain. Two CISNET models make the assumption that invasive breast cancers may fail to progress (11); however, extremely few cases of non-progressive invasive breast cancer have been reported in the literature. One of the 6 models did not include DCIS at all, which is known to be a non-obligate precursor to invasive cancer (11). Additionally, BCSC data used by CISNET considered screening within 9 and 18 months of a prior screening exam as "annual", while screening between 18 and 30 months of a prior screening exam was considered "biennial" screening; therefore, biennial encompasses 3 more months than annual (32), potentially biasing "biennial"

screening to detect more cancers. Other limitations include the assumption that all women adhere to each stated screening and treatment, rather than the variable adherence occurring in the real world.

We did not model overdiagnosis because of the wide range of frequency estimates reported in the literature and low level of reliability given to those estimates (17). However, our (EA, MH, ES) extensive clinical experience with modern mammography indicates that screen-detected cancers (including overdiagnosed cancers), if not removed and left untreated, remain visible and suspicious for malignancy at next screening exam, so that a strategy involving less screening simply delays overdiagnosis but does not reduce it. Therefore, the frequency of both overdiagnosis and overtreatment likely are unaffected by the age at which screening starts (40 versus 45 versus 50) or by screening frequency.

In their concluding summary, CISNET authors close with "Choices about optimal ages of initiation and cessation will ultimately depend on program goals, ..." (11). If the screening program goal is to perform as few mammograms as possible to achieve limited benefit and fewer risks, with number of mammograms as a surrogate for cost, then the optimal age of initiation may be 50 with an optimal frequency of biennial screening, ending at age 74. On the other hand, if the goal is to avert the most breast cancer deaths and gain the most life-years, CISNET modeling shows that the optimal age of initiation for screening mammography is 40 years, the optimal screening frequency is annual, and the optimal stopping age is when a woman's life expectancy is less than 5-7 years. Individual women should continue to have the choice to reduce their risk of dying from breast cancer as much as possible, and as CISNET models show, annual mammography starting at age 40 years is the best way to do so.

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TABLES

Recommending Organizations	Screening Frequency	Starting Age (y)	Stopping Age (y)
ACR*, ACOG, NCBC, NCCN, SBI*	Annual	40	Life expectancy less than 5-7 y*
ACS, ASBS, ASCO	Annual to age 54, Biennial 55+, with option for annual	45, with option to start at 40	Life expectancy less than 10 y
USPSTF, AAFP, ACP	Biennial	50	74

ACR = American College of Radiology, ACOG = American College of Obstetricians and Gynecologists, NCBC = National Consortium of Breast Centers, NCCN = National Comprehensive Cancer Center Network, SBI = Society of Breast Imaging, ACS = American Cancer Society, ASBS = American Society of Breast Surgeons, ASCO = American Society of Surgical Oncology, USPSTF = United States Preventive Services Task Force, AAFP = American Academy of Family Physicians, ACP = American College of Physicians

* ACR and SBI recommend stopping screening when life expectancy is less than 5-7 years; the other three organizations recommending annual screening starting at age 40 do not specify a screening stopping point

Table 1. Mammography screening recommendations of various national organizations.

Screening Strategy	# of Exams per 1000 W	Percent Mortality Reduction	BC Deaths Averted per 1000W	LYG per 1000 W Screened	NNS per Death Averted	NNS per LYG
1) A40-84	36,550	39.6%	11.9	189	84	5.3
2) Hybrid, A45-54, B55-79	19,846	30.8%	9.25	149	108	6.7
3) B50-74	11,066	23.2%	6.95	110	144	9.1

Table 2. Comparison of mammography use and benefits of the three major screening mammography strategies based on mean values of the six 2009 CISNET models. Number of exams, breast cancer deaths averted, and life-years gained (LYG) are per 1,000 women screened over each regimen. A40-84 stands for annual screening mammography ages 40-84 years; H45-79 stands for a hybrid strategy consisting of annual screening ages 45-54, then biennial screening ages 55-79; B50-74 stands for biennial screening ages 50-74 years.

Screening Strategy	Total # of Mammo Exams	Total Deaths Averted	Total LYG	Total # of Negative Recalls	Total # of Benign Biopsies
1) A40-84	90.2 million	29,369	466,452	6.8 million	481,260
2) Hybrid, A45-54, B55-79	49.0 million	22,829	367,732	4.1 million	286,288
3) B50-74	27.3 million	17,153	271,480	2.3 million	162,888

Table 3. Total number of mammography exams, breast cancer deaths averted, life-years gained, negative recalls, benign breast biopsies, and LYG per benign breast biopsy if the single-year cohort of women born in 1960 and alive in the year 2000 (2.468 million) followed each screening regimen, based on 2009 CISNET models. A40-84 stands for annual screening mammography ages 40-84 years; H45-79 stands for a hybrid strategy consisting of annual screening ages 45-54, then biennial screening ages 55-79; B50-74 stands for biennial screening ages 50-74 years.

Biennial Screening Ages 50-74	Exams per 1000 Women Screened	Median Mortality Reduction	Median Deaths Averted per 1000 Women Screened	Median LYG per 1000 Women Screened	Negative Recalls per 1000 Women Screened	Benign Biopsies per 1000 Women Screened*
2009 CISNET	11,066	21.5%	6.5	111	940	66
2016 CISNET	11,127	25.8%	7.1	122	953	146

* 2009 CISNET defined benign biopsies as the number of women undergoing benign biopsy, while 2016 CISNET changed their definition to the number of women recommended to undergo biopsy based on radiology findings

Table 4. Comparison of 2009 and 2016 CISNET estimates of benefits and risks of the USPSTF-recommended strategy of biennial screening between the ages of 50 and 74 years. Median values for all 6 models are compared for benefit. Risks of negative recalls and benign biopsies are from the single "exemplar" Stanford model in 2009 and from all 6 models in 2016. Median, rather than mean, values are reported for all parameters because 2016 CISNET did not report deaths averted per 1000 women screened for each of the six individual models.