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Identifying Equitable Screening Mammography Strategies for Black Women in the United States Using Simulation Modeling

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Data: Output data from the models are available from Dr. Chapman (email: christinachap@gmail.com)

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Abstract

Background: Screening mammography guidelines do not explicitly consider racial differences in breast cancer epidemiology, treatment, and survival.

Objective: To compare tradeoffs of screening strategies in Black women to those of White women screened under current guidelines.

Design: An established Cancer Intervention and Surveillance Modeling Network model simulated screening outcomes using race-specific inputs for subtype distribution, breast density, mammogram performance, age-, stage-, and subtype-specific treatment effects, and non-breast cancer mortality.

Setting: United States.

Participants: 1980 US birth cohort of Black and White women.

Intervention: Screening strategies until age 74 with varying initiation ages and intervals.

Measurements: Outcomes included benefits (life-years gained, breast cancer deaths averted, and mortality reduction), harms (mammograms, false positives, and overdiagnoses), and benefits-to-harm ratios (tradeoffs) by race. We evaluated efficiency (resources per unit benefit), mortality disparity reduction, and equity in tradeoffs. Equitable strategies for Black women were defined as those with tradeoffs closest to benchmark values for screening White women biennially from 50–74.

Results: Biennial screening from 45–74 was the most efficient for Black women, while biennial screening from 40–74 was the most equitable. Initiating screening ten-years earlier in Black vs. White women reduced Black-White mortality disparities by 57% with comparable life-years gained/mammogram for both populations. Selection of the most equitable strategy was sensitive to assumptions about disparities in real world treatment effectiveness: the less effective treatment was for Black women, the more intensively Black women could be screened before tradeoffs fell short of those experienced by White women.

Limitations: Single model.

Conclusion: Initiating biennial screening in Black women at age 40 yields reduces breast cancer mortality disparities and yields benefit-to-harm ratios that are comparable to tradeoffs of White women screened biennially from 50–74.

Keywords

breast cancer; race; equity; disparities; screening mammography; decision analysis; simulation modeling; Black/African American

Introduction

Screening mammography guidelines provide recommendations for the overall US population(1, 2) but do not explicitly consider racial disparities in breast cancer epidemiology, screening, and treatment. Compared to White women, Black women in the US have a younger age at breast cancer diagnosis (58 v. 62 years),(3) are diagnosed more often with adverse features, including triple-negative(4) and advanced stage disease,(3) and have higher age-standardized breast cancer mortality rates (28.2 vs. 20.3 per 100,000).(3, 5)

These disparities are partially mediated through and further complicated by racism, particularly the institutionalized(6)/structural(7) and interpersonal(6) forms. Structural racism drives breast cancer disparities by influencing upstream healthcare factors (e.g. insurance access(8)) and broader societal constructs (e.g. poverty(9)), which influence stage and treatment receipt. Structural and interpersonal racism may also explain point-of-care disparities that drive screening and treatment differences.(10–13). Finally, all three forms of racism (institutionalized, interpersonal, and individualized(6)) racism influence competing mortality,(14, 15) which modifies screening outcomes. These complexities suggest that Black women may need different screening schedules to achieve similar screening outcomes as White women.

Unfortunately, no randomized trial data exist to optimize screening by race since few Black women were included in early trials(16, 17). Ideally, new trials would test screening schedules by race, but are not feasible due to the large sample sizes required. In these situations, simulation modeling can synthesize race-specific data and test a range of screening strategies. The Cancer Intervention and Surveillance Modeling Network (CISNET) models were previously used to inform breast cancer screening guidelines, but guideline-focused studies lacked race-specific modeling.(18, 19) Separate race-specific modeling studies lacked current knowledge about molecular subtypes and modern therapy. (20, 21)

In this study, we used an updated, race-specific CISNET model to identify equitable screening strategies, defined as strategies for Black women that yielded benefit-to-harm tradeoffs similar to those of White women screened according to the United States Preventive Services Task Force (USPSTF) guidelines.(1) The results are intended to inform discussions about health equity, given that race-neutral screening guidelines can do harm if they yield unequal outcomes and are applied instead of more equitable alternatives that retain acceptable tradeoffs.

Methods

We used CISNET Model GE (Georgetown University Medical Center, Washington, DC, and Albert Einstein College of Medicine, Bronx, NY) for this study.^{12–14} The study was considered human subjects exempt by the Georgetown University Institutional Review Board due to public de-identified data use.

Screening Strategies and Population

We evaluated nine strategies that varied by starting age (40, 45, and 50 years) and interval (annual, biennial and hybrids: annual 40–49 and biennial thereafter; biennial 40–49 and annual thereafter; and the American Cancer Society recommendation: annual 45–54 and biennial thereafter(2)); with cessation at 74. The nine strategies were compared to biennial screening of White women from 50–74 since this is the implicit benchmark for outcomes and benefit-to-harm ratios based on US Preventive Service Task Force guidelines(1). In secondary analyses, we evaluated two additional strategies: initiation of annual screening at 30 or 35 through 39, followed by biennial screening from 40 to 74 (Appendix Figure 4a & 4b).

We modeled the cohort of US women born in 1980, who turn 40 in 2020, followed for their lifetimes starting from age 25 (because breast cancer is rare before then). As in prior modeling studies,(18) we assumed 100% of Black and White women used screening to focus on screening efficacy. This assumption was considered reasonable since contemporary studies show minimal to no difference in screening mammography use between Black and White women.(22)

Model Overview

The model has been described in detail elsewhere (schematic, Appendix Figure 1).(23–25) Additional information is available upon request. The model is available for use via collaboration. Briefly, model GE is a parallel-universe population simulation model that begins with estimates of breast cancer incidence and estrogen receptor /HER-2-specific survival trends in the absence of screening or adjuvant treatment.(24–27) Breast cancer is modeled to have a molecular sub-type specific distribution of preclinical screen-detectable periods (sojourn time) and clinical detection times. The model assumes one-third of ductal carcinoma in-situ cases do not progress to invasive cancer. Molecular subtype- and stage-specific treatment reduces the hazard of breast cancer death. Women can die of breast cancer or other causes.

Model Input Parameters

The model parameters(24, 27) were updated with race-specific inputs (Table 1). Race was typically defined by self-report. Breast cancer incidence was modeled based on an age-period-cohort model.(26) Race-specific rates were obtained by applying an age-specific relative risk of breast cancer for Black vs. White women using Surveillance, Epidemiology, and End Results (SEER) data.(28)

Race-specific breast density was modeled using BIRADS categories(29) and assigned from ages 25–40. Density could decrease by one category or remain the same at age 50–64 and again at 65 based on prevalence observed in the Breast Cancer Surveillance Consortium database.(30, 31) We assumed density affected mammogram performance characteristics and incidence.

Screening sensitivity and specificity by age-, race- and density group were calibrated to Breast Cancer Surveillance Consortium data for invasive cancers and ductal carcinoma in-situ combined on initial vs. subsequent mammography.(31)

Stage was defined based on American Joint Committee on Cancer v.6, and dependent on age group (<50, 50+), density, molecular subtype and screen vs. clinical detection.(32) Stage- and molecular subtype-specific chemotherapy included anthracycline-based regimens with taxanes; estrogen receptor+ tumors included five years of endocrine therapy and HER-2/ ErbB-2+ tumors included trastuzumab.

We model treatment effects by considering treatment efficacy and dissemination. Treatment efficacy was based on clinical trials(33) and was modeled as a reduction in the hazard of breast cancer death. We used data from pooled analyses of National Surgical Adjuvant Breast and Bowel Project (NSABP) trials to estimate race-specific treatment efficacy(34). That analysis demonstrated similar or slightly lower systemic therapy efficacy for Black relative to White women with treated on the same trials and considering age, stage, comorbidities, and estrogen receptor status.(34, 35) We therefore conservatively assumed equal efficacy by race.

However, outside of clinical trials, treatment effectiveness depends on differences in treatment dissemination, including access, delays, dose reductions, and discontinuation. Sub-optimal treatment dissemination occurs more often in Black than White women.(21, 36–38) In previous policy-oriented work,(18) we assumed full dissemination (i.e. all women receive the most effective therapy) to identify a pure effect of screening under optimal treatment conditions. However, given the differences in treatment dissemination by race, we used published data(36) to estimate the impact of disparities in dissemination. The best available evidence we identified showed that after accounting for mediators contained in our model, (e.g. stage and subtype), a residual Black-White disparity in breast cancer death remains (hazard ratio 1.24, Table 3, Model 3 from citation(36)). We converted this hazard ratio to a percentage (80.6%) and incorporated it into the dissemination parameter to account for decreased treatment effects in Black women.

We used existing US race- and age-specific non-breast cancer mortality rates.(26, 39) These mortality rates implicitly capture the net effect of racism, downstream disparities (e.g. comorbidities, social determinants of health, access to care) and other factors that differentially influence survival by race.

Analysis

We simulated 100 million life histories from birth to death, or age 120, to account for the entire potential life history in the absence of screening and treatment. Simulations strategies

Results

Benefits

Among the strategies tested in Black women, benefits generally increased as the number of mammograms increased due to initiating screening earlier than age 50 and/or screening more frequently (Table 2). Efficient strategies for Black women always included the biennial strategies and the most intensive strategy, A40–74. Biennial screening from 45–74 was the most efficient for LYG/mammogram (Figure 1&2). Annual strategies starting at 45 or 50 and the American Cancer Society hybrid strategy were dominated (Figure 1 and Appendix Figure 3a–c). Efficient strategies were similar considering other metrics (Appendix Figure 3a–c). Marginal benefits for initiating biennial screening at age 40, 45, or 50 v. no screening and B50–74 are shown in Appendix Figure 5.

Equity in Benefit-to-Harm Ratios

The strategy that yielded the LYG per mammogram ratio closest to the benchmark (B50–74 for White women) was biennial 40–74, (15.0 vs. benchmark: 14.5 LYG per mammogram, respectively) (Table 2). Among the three strategies that yielded benefit-to-harm ratios that met or exceeded the benchmark, B40–74 resulted in the largest mortality reduction for black women (Figure 1 & Table 2). B40–74 resulted in 32% more LYG and 19% more breast cancer deaths averted than screening Black women biennially from ages 50–74 but required 45% more mammograms and resulted in 52% more false positives (calculated from Table 2). For secondary metrics, B40–74 remained the most equitable strategy (Appendix Figure 2a–c), with the exception that B45–74 was slightly more equitable when considering breast cancer deaths averted/false positive.

Impact on Mortality Disparities

If Black and White women were screened biennially from 50–74, there would be an excess of 3.29 deaths among Black women (17.62 vs. 14.33 per 1,000 for Black v. White women, respectively, calculated from Table 2). In contrast, if biennial screening was initiated in Black women beginning at 40, deaths would drop by 1.88 (from 17.62 to 15.74) per 1,000 women, removing 57% of the racial disparity (Table 2) in mortality expected under current guideline screening (1.88 of 3.29 excess deaths).

Sensitivity Analysis

The results were sensitive to assumptions about treatment disparities. As treatment dissemination decreased, relative benefits of screening increased, permitting use of progressively more intensive strategies before tradeoffs fell below benchmarks (Figure 2). If treatment were equally disseminated for Black and White women (but current levels of competing mortality disparities persisted), screening Black women biennially from 50–74 would yield similar benefit-to-harm ratios as the benchmark values for White women (Figure 2 and Appendix Table 1a–d). If disparities in treatment resulted in Black women experiencing 90% or less of treatment effectiveness experienced by Whites, biennial screening would need to start at 40 or 45 in Black women to achieve benefit-to-harm ratios comparable to benchmark values.

Discussion

To our knowledge, this is the first study to use simulation modeling to consider whether race-neutral breast cancer screening guidelines lead to unequal outcomes. Our results suggest that in self-identified Black women, initiation of earlier screening than is presently recommended for the overall US population by the US Preventive Services Task Force(1) or the American Cancer Society(2) can reduce mortality disparities and maintain acceptable benefit-to-harm tradeoffs. This highlights an important concept in health equity: equivalent interventions may yield inequitable outcomes(43).

Our results were highly sensitive to assumptions about disparities in treatment dissemination. Consistent with previous modeling studies(44), relative benefits of screening increased as treatment effectiveness decreased (i.e. Black-to-White disparities widened). This explains why more intensive screening strategies can be employed as disparities widen without compromising tradeoffs (relative to benchmark values). Although our previous policy-oriented studies(18) estimated screening benefits under ideal treatment conditions, this assumption ignores the impact of racism and other causes of disparities. Racism increases disparities in treatment and competing mortality, but these two inputs have opposing effects (i.e. competing mortality decreases relative screening benefits). Therefore, ignoring decades-old treatment disparities would have underestimated relative screening benefits for Black women.

Similar to conclusions from our past modeling analyses(18, 19), most annual screening strategies for Black women were inefficient; they had fewer benefits and more harms than biennial strategies. One explanation is that although higher age-specific breast cancer incidence in the 40s in Black vs. White women provides sufficient benefit to outweigh harms of starting screening at age 40, there may not be sufficient differences in the parameters we used to model tumor biology to warrant annual vs. biennial screening. We will reassess as knowledge about breast cancer biology evolves.

Comorbidities also vary in a complex, race-specific manner. For example, obesity decreases treatment effectiveness (due to suboptimal completion and other factors), but has mixed effects on breast cancer incidence. Obesity decreases breast cancer incidence pre-menopausally, but increases incidence post-menopausally. Unfortunately, the barriers that preclude equitable breast cancer treatment often prevent equitable treatment of comorbidities.(45) Our group previously modeled the impact of obesity on racial disparities in breast cancer and found that obesity had no net effect on disparities due to opposing pre- and post-menopausal effects(20). In the current study, the net impact of comorbidities on breast cancer incidence and treatment is already implicitly considered, given that our inputs are derived from real-world datasets that contain women with comorbidities. However, specific comorbidities may sufficiently alter screening outcomes for subsets of women. In future analyses, we will model screening recommendations for groups of women by race with specific comorbidities.

The role of screening in reducing disparities represents a dynamic interplay between tumor growth, early detection, and molecular-targeted therapy. This is illustrated by our finding

that when disparities in treatment dissemination were eliminated, similar screening could yield similar outcomes for Black and White women, but if treatment disparities persist or widen, then Black women might benefit from more intensive screening than White women. Although earlier screening may partially mitigate the impact of treatment disparities, it should not supersede efforts to achieve treatment equity. Indeed, CISNET(21) and others(36) have shown that disparities in treatment represent one of the largest modifiable mediators of breast cancer survival disparities. Addressing treatment disparities therefore remains a high priority. However, aspects of treatment disparities are attributable to systemic racism, which is difficult to change and won't be resolved in the near term. We therefore reduce harm by compensating for this with enhanced screening. Implementation of equitable screening represents a practical, sustainable, high-impact solution for reducing disparities that could be implemented in the short term.

However, elimination of breast cancer racial disparities goes beyond screening and treatment. Racial disparities in insurance and stage at diagnosis reflect the larger and longstanding issue of structural racism (employment, educational opportunity, etc.), (7, 8). Well-placed efforts within healthcare may, therefore, fall short of eliminating cancer inequity.

This study used a well-established CISNET model and followed best modeling practices. (18, 27) However, there are several caveats to consider. First, we used a single model. All models make structural assumptions about non-observable aspects of breast cancer, including the proportion of ductal carcinoma in-situ cases that progress to invasive cancer. We plan to expand these analyses with several CISNET models to test the impact of structural uncertainty on conclusions about race-specific screening schedules. There is also parameter uncertainty in any simulation model, but we used the model previously and calibrated to US trends using multiple real-world data sources.(27)

Second, our purpose was to establish whether there was a scientific rationale for recommending different screening strategies by race assuming full screening efficacy (i.e., 100% use). However, patterns of use may vary by age and race, affecting screening outcomes. For example, if younger Black women are less likely to complete biannual screening exams than older Black women, the benefits of starting screening at 40 vs. 50 would decrease. If there are differences in return to screening after a false positive by race(46) (or age(47)), then relative benefit-to-harm ratios for Black and white women might shift. We will address the age and race patterns in future analyses. We will account for the fact that tomosynthesis may decrease false positives(48) and that culturally competent coping strategies(49) and physician counseling(50) can reduce mammography avoidance after false positives. Our findings are likely to be relevant into the future until there are major changes in early detection technology or treatment paradigms. The models consider survival after local and systemic therapy, but do not model types of surgery. We did not model cost, but plan to in subsequent analyses. Earlier screening initiation may increase patient, payer, and societal costs, but earlier detection may reduce treatment costs and save more lives. Screening harms (e.g. false positives, benign biopsies, and overdiagnoses) can affect quality of life, but there are no current data to suggest that the quality of life effects differ by race. Additionally, our study is designed inform to population-level guidelines,

and cannot fully capture nuances that may alter the risks and benefits for individual women whose characteristics differ substantially from those in our study.

Finally, race and racism (whether structural, interpersonal, or internalized (6)) are complex constructs. Many, including members of our own team, have published on race and recognize that associations between race and health or societal outcomes are often rooted in racism as opposed to biology. (51) (20, 21, 52–54) (55) (56, 57)

Our modeling used nationally representative data for US women that self-report as Black. Our choice of approach was guided by modeling best practices (23, 58), guidelines on presenting research on racial inequities(59), and consideration of the practicalities of making recommendations for screening in clinical practice. We use self-reported race because it is strongly associated with breast cancer mortality,(3) breast cancer molecular subtype distribution,(3) observed treatment effectiveness,(36) and competing mortality.(14) These associations persist even after socioeconomic status is considered(14, 36), suggesting that replacing socioeconomic status for race would not be methodologically appropriate in our study. These data also informed our modeling of treatment effects in Black women: Black women with different molecular sub-types of breast cancer derive equal benefits from equal treatment in clinical trials,(34) but treatment remains unequal in practice.(4, 57)

We acknowledge that racism and not race, is likely the primary driver of many of the disparities in inputs in our study. However, few datasets contain validated measures of racism, so self-reported race remains the best available variable at the present time. Racial disparities in breast cancer mortality are complex, and can persist after partial efforts to control for socioeconomic status. We are exploring data sources that could better capture the effects of lifetime socioeconomic status and racism in future studies. Until then, the majority of our model inputs are derived from U.S. population-based data. The results capture the heterogeneity in Black women and are generalizable to self-identify as such. Compared to screening guidelines for the overall US population, our results suggest that alternative screening guidelines provide an opportunity to reduce racial disparities in breast cancer mortality without increasing harms. Failing to consider race in this context may represent a missed opportunity to reduce breast cancer disparities while allowing Black women to derive the same screening tradeoffs as White women.

Overall, despite some improvements, (28, 60) Black-White breast cancer disparities persist. Our results suggest that Black women consider initiating biennial screening at age 40 instead of 50. Given that this screening strategy falls within the “individual decision making” category for the US Preventive Services Task Force, this represents a practical, evidence-based opportunity to advance equity.

Supplementary Material

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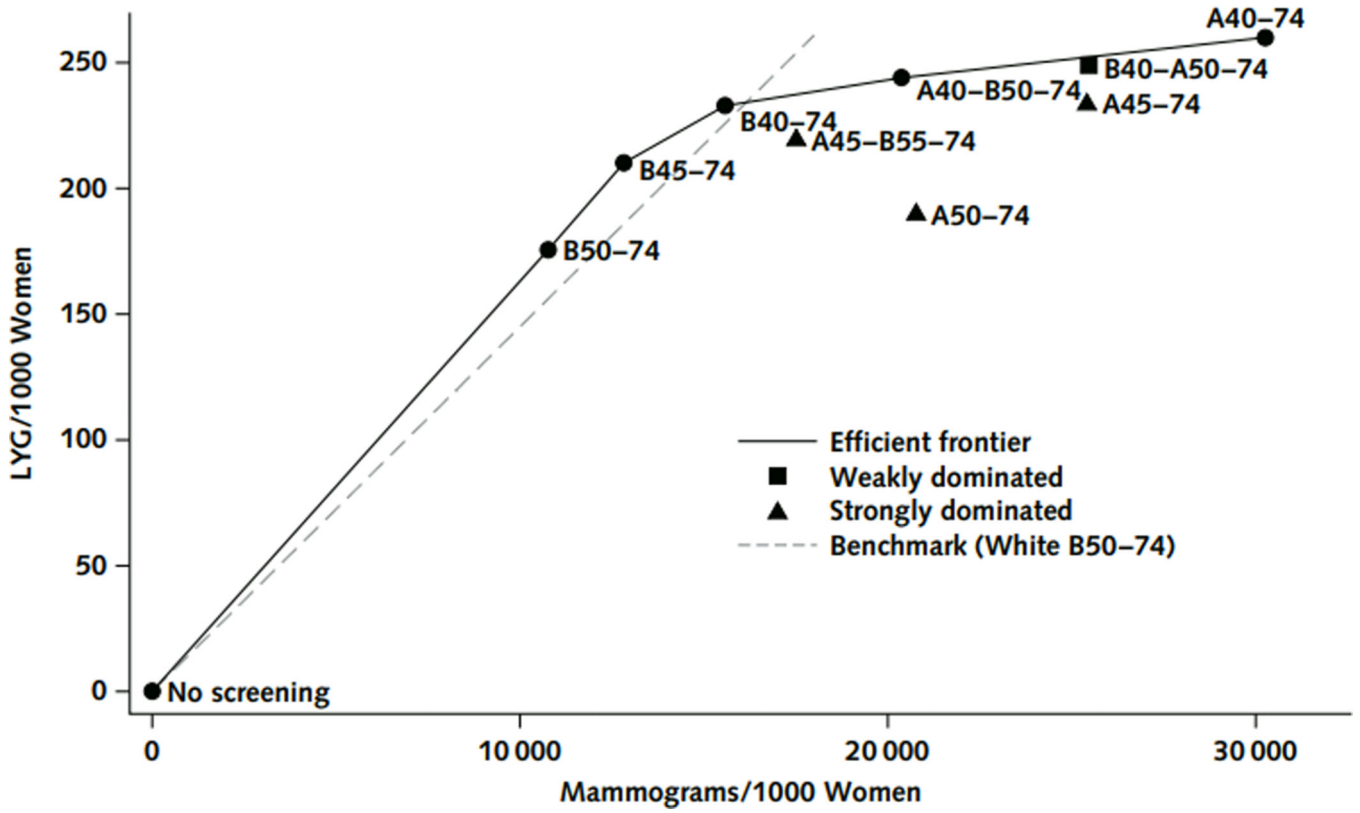


Figure 1: Efficiency frontier for the base case (80% treatment effects for Black women) for life-years gained per mammogram (LYG/M). Treatment effects are described as “dissemination” here to clarify the assumptions made: efficacy was assumed to be equal for black and white women, but dissemination differed due to disparities in treatment receipt that impacted breast cancer survival. Efficient (blue circles and line), weakly dominated (green squares) and strongly dominated (red triangle) strategies are shown. The dashed line shows life-years gained per mammogram benchmark (B50-74 in White women). Strategies for Black women that fall above the line yield greater LYG/M than then benchmark and those that fall below the line yield fewer LYG/M than the benchmark.

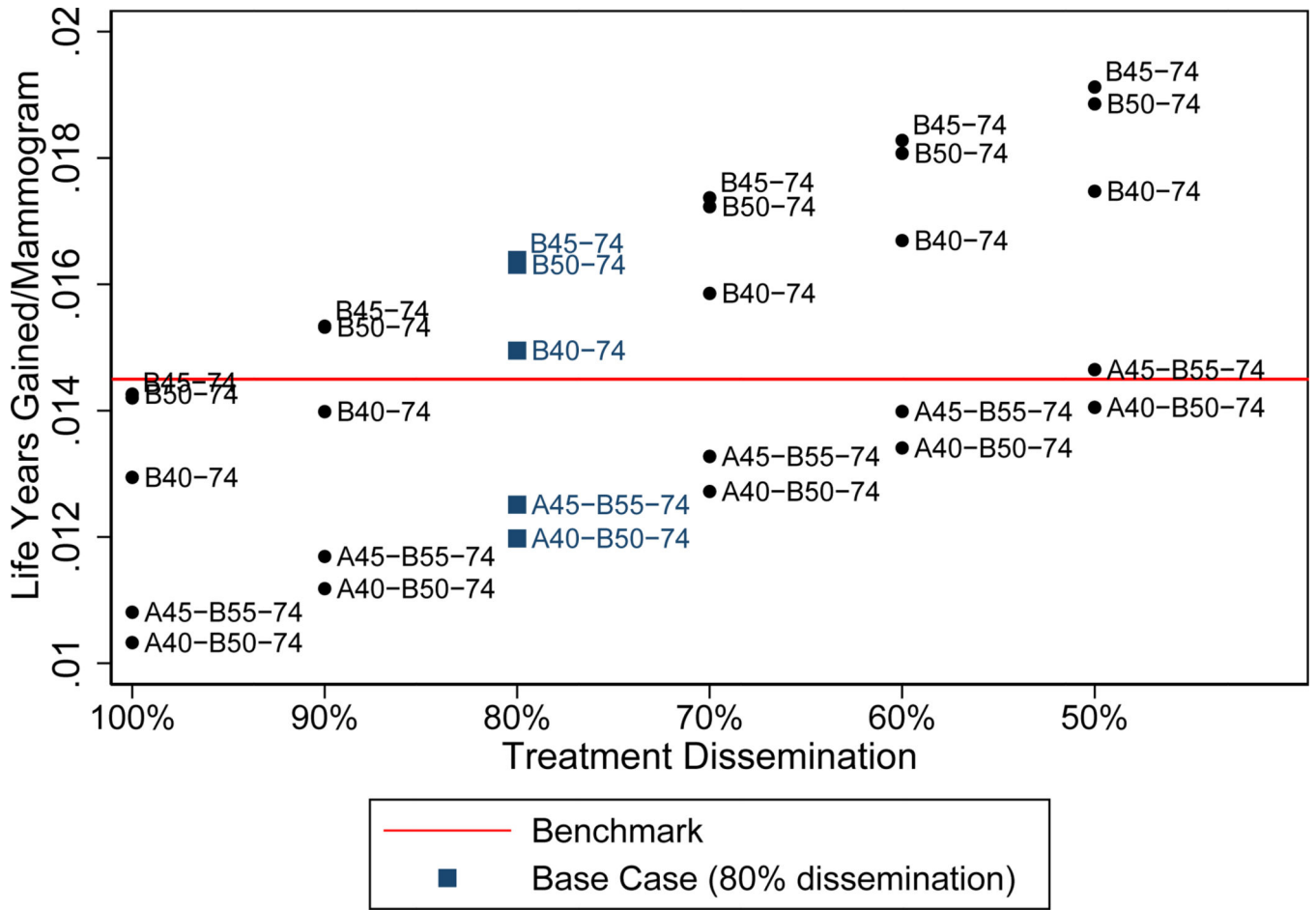


Figure 2: Life years gained/mammogram sensitivity analysis. The Black/White ratio of treatment effects is varied from 50–100%, with 80% representing the base case (blue squares). Treatment effects are described as “dissemination” here to clarify the assumptions made: efficacy was assumed to be equal for black and white women, but dissemination differed due to disparities in treatment receipt that impacted breast cancer survival. Strategies above and below the red line yield greater and lesser LYG/M than the benchmark (B50–74 in White women), respectively.

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Table 1:

Model Input Parameters

Parameter	Description and Race-Specificity	Source	Race Definition
Births	Birth Cohorts from 1890–2000 by race	Historical Statistics of the United States, Millennial Edition, Vol. 1. Cambridge University Press, 2006. (61)	Self-report
Incidence	Age-period-cohort model with age-specific relative risk of Black versus White Incidence	SEER (18, 26, 28)	Self-report prioritized if available, otherwise peer SEER standards, used data from medical records
Mammography Use	Assumed equal by race and 100% to isolate the impact of mammography under ideal screening conditions	-	-
Mammography Sensitivity	Age-specific rates for first and subsequent screening exams by race	Unpublished BCSC data, agreement DR285e(31)	Self-report
Breast Density	Prevalence by age and race	Unpublished BCSC data, agreement DR285e(31)	Self-report
ER/HER2	Probability of ER/HER-2 conditional on age, stage, and race	Unpublished BCSC data, agreement DR285e(32)	Self-report
Sojourn time	Calibrated parameters; gamma distributions by age, ER and HER-2 status	Model GE calibration (24)	-
Unscreened Stage Distribution	Clinically-detected cases 2005–2017, by age and race	Unpublished BCSC data, agreement DR285e(32)	Self-report
Screened Stage Distribution	Digital screen and interval-detected cases 2005–2017, by age and race	Unpublished BCSC data, agreement DR285e(32)	Self-report
Survival without treatment	Survival by race from SEER 1975–1979, assumed equal by race	SEER(62)	Self-report prioritized if available, otherwise peer SEER standards, used data from medical records
Treatment efficacy	Reduction in hazard of breast cancer death, Meta-analyses of randomized trial results by ER/HER-2; assumed equal by race(34)	Clinical trial Meta-analyses (33, 34, 63)	-
Treatment dissemination	Assumed 100% for White women per previous modeling studies for USPSTF, Reduced for Black women to account for impact of disparities in treatment receipt; assumed 80% for Black women for base case with sensitivity analysis performed using range of 50%–100%	National Comprehensive Cancer Network data	Self-report
Non-breast cancer (other cause) mortality	Age-, race-, and cohort-specific other-cause mortality rates by year	Modeling performed by University of Wisconsin Breast CISNET group/CDC Wonder (39)	Self-report

Table 1: Abbreviations: BCSC: Breast Cancer Screening Consortium; CISNET: Cancer Intervention and Surveillance Modeling Network; ER: estrogen receptor; SEER: Surveillance, Epidemiology and End Results;

Table 2:

Benefits, Harms, and Benefit to Harm Ratios of Breast Cancer Screening Strategies for Black Women Compared to the Benchmark (B50–74) Strategy for White Women

Strategy	Per 1000 women screened (vs no screening)						Benefit/Harm Ratio		Disparity Reduction
	Mammo-grams	Life-Years Gained	Breast cancer deaths averted*	Percent mortality reduction	False Positives	Over-diagnoses	Life-Years Gained Per Mammo-gram x 10 ⁻³	Life-Years Gained Per Overdiagnosis	
White women									
B50–74	11137	161	8.3	37%	864	8.0	14.5	20.1	-
Black women									
B50–74	10761	176	9.5	35%	829	7.0	16.3	25.1	0%
B45–74	12826	210	10.5	39%	1031	7.3	16.4	28.8	31.4%
B40–74	15576	233	11.3	42%	1264	8.1	15.0	28.8	57.0%
A45-B55–74	17511	219	10.8	40%	1399	7.4	12.5	29.6	42.2%
A40-B50–74	20370	244	11.7	43%	1693	8.2	12.0	29.8	69.3%
A50–74	20660	192	10.4	38%	1522	7.6	9.3	25.3	29.2%
A45–74	25411	234	11.9	44%	1950	8.3	9.2	28.2	74.2%
B40-A50–74	25464	249	12.3	45%	1957	8.7	9.8	28.6	86.0%
A40–74	30257	260	12.7	47%	2385	8.8	8.6	29.5	97.7%

Table 2: A indicates annual; B indicates biennial, numbers after “A” or “B” denote cessation and transition ages. Data shown represent the base case of 80% treatment effects/dissemination.

*Breast cancer deaths per 1,000 women without screening: Black 27.07691 and White: 22.65354.