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Multilevel Factors Associated With Time to Biopsy After Abnormal Screening Mammography Results by Race and Ethnicity

Marissa B. Lawson, MD; Michael C. S. Bissell, PhD; Diana L. Miglioretti, PhD; Joanna Eavey, MSPH; Christina H. Chapman, MD, MS; Jeanne S. Mandelblatt, MD, MPH; Tracy Onega, PhD; Louise M. Henderson, PhD; Garth H. Rauscher, PhD, MPH; Karla Kerlikowske, MD, MS; Brian L. Sprague, PhD; Erin J. A. Bowles, MPH; Charlotte C. Gard, PhD; Sana Parsian, MD; Christoph I. Lee, MD, MS

IMPORTANCE Diagnostic delays in breast cancer detection may be associated with later-stage disease and higher anxiety, but data on multilevel factors associated with diagnostic delay are limited.

OBJECTIVE To evaluate individual-, neighborhood-, and health care–level factors associated with differences in time from abnormal screening to biopsy among racial and ethnic groups.

DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study used data from women aged 40 to 79 years who had abnormal results in screening mammograms conducted in 109 imaging facilities across 6 US states between 2009 and 2019. Data were analyzed from February 21 to November 4, 2021.

EXPOSURES Individual-level factors included self-reported race and ethnicity, age, family history of breast cancer, breast density, previous breast biopsy, and time since last mammogram; neighborhood-level factors included geocoded education and income based on residential zip codes and rurality; and health care–level factors included mammogram modality, screening facility academic affiliation, and facility onsite biopsy service availability. Data were also assessed by examination year.

MAIN OUTCOME AND MEASURES The main outcome was unadjusted and adjusted relative risk (RR) of no biopsy within 30, 60, and 90 days using sequential log-binomial regression models. A secondary outcome was unadjusted and adjusted median time to biopsy using accelerated failure time models.

RESULTS A total of 45 186 women (median [IQR] age at screening, 56 [48-65] years) with 46 185 screening mammograms with abnormal results were included. Of screening mammograms with abnormal results recommended for biopsy, 15 969 (34.6%) were not resolved within 30 days, 7493 (16.2%) were not resolved within 60 days, and 5634 (12.2%) were not resolved within 90 days. Compared with White women, there was increased risk of no biopsy within 30 and 60 days for Asian (30 days: RR, 1.66; 95% CI, 1.31-2.10; 60 days: RR, 1.58; 95% CI, 1.15-2.18), Black (30 days: RR, 1.52; 95% CI, 1.30-1.78; 60 days: 1.39; 95% CI, 1.22-1.60), and Hispanic (30 days: RR, 1.50; 95% CI, 1.24-1.81; 60 days: 1.38; 95% CI, 1.11-1.71) women; however, the unadjusted risk of no biopsy within 90 days only persisted significantly for Black women (RR, 1.28; 95% CI, 1.11-1.47). Sequential adjustment for selected individual-, neighborhood-, and health care–level factors, exclusive of screening facility, did not substantially change the risk of no biopsy within 90 days for Black women (RR, 1.27; 95% CI, 1.12-1.44). After additionally adjusting for screening facility, the increased risk for Black women persisted but showed a modest decrease (RR, 1.20; 95% CI, 1.08-1.34).

CONCLUSIONS AND RELEVANCE In this cohort study involving a diverse cohort of US women recommended for biopsy after abnormal results on screening mammography, Black women were the most likely to experience delays to diagnostic resolution after adjusting for multilevel factors. These results suggest that adjustment for multilevel factors did not entirely account for differences in time to breast biopsy, but unmeasured factors, such as systemic racism and other health care system factors, may impact timely diagnosis.

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Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Marissa B. Lawson, MD, Department of Radiology, University of Washington School of Medicine, 825 Eastlake Ave East, LG-200, Seattle, WA 98109 (mblawson@uw.edu).

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Screening mammography can contribute to improved outcomes by identifying localized breast cancers when they can be treated with curative intent.[1-3] However, diagnostic delays of 90 days or longer after a suspicious screening mammogram can reduce the benefits of early detection and are associated with greater proportion of late-stage disease, greater morbidity from more aggressive treatment, fewer life-years gained, larger tumor size, and positive lymph node status.[4-6] Even with delays shorter than 90 days, women can experience clinically significant psychological distress while awaiting breast biopsy.[7-9]

Previous studies have shown that individual-level factors, such as race and ethnicity, insurance status, and education, are associated with diagnostic and treatment delay after abnormal mammography results.[10-18] Several studies have reported that women from racial and ethnic minority groups, such as Asian, Black, and Hispanic women, are more likely to experience longer times to diagnosis or treatment.[10,11,14-18] However, few studies approach these disparities using a framework like the one promoted by the National Institute of Minority Health and Health Disparities (NIMHD), which emphasizes that multiple levels of influence, such as neighborhood socioeconomic status and health care factors, can impact health outcomes.[19] Prior studies that account for neighborhood- and health care–level factors in assessing diagnostic delays after mammography have been limited by relatively homogenous patient populations,[20-23] only including Medicare patients,[20] or assessing only 1 geographic region.[21-23]

We assessed differences in time from abnormal screening mammography test result to biopsy among racial and ethnic groups in the Breast Cancer Surveillance Consortium (BCSC), a large, geographically and racially and ethnically diverse national cohort, broadly representative of the US population.[24] We assessed the risk of having no biopsy performed within 30, 60, and 90 days of abnormal screening results by racial and ethnic group and evaluated how individual-, neighborhood-, and health care–level factors affect the relationship between racial and ethnic group and delay.

Key Points

Question Are individual-, neighborhood-, and health care–level factors associated with differences by race and ethnicity in time to diagnostic resolution following abnormal screening mammography results?

Findings In this cohort study of 45 186 women with recommendation for biopsy after abnormal screening results, Black women had an increased risk of no biopsy within 30, 60, and 90 days after screening, adjusting for multilevel factors. The screening facility accounted for the greatest attenuation of Black women's increased risk of no biopsy.

Meaning These findings suggest interventions are needed to reduce systemic racism and health care system barriers to timely diagnosis after abnormal mammography results.

Methods

Study Setting, Data Sources, and Participants

We performed an observational cohort study using prospectively collected data from 2009 to 2019 across 7 BCSC registries[25]: Carolina Mammography Registry, Kaiser Permanente Washington Registry, Metro Chicago Breast Cancer Registry, New Hampshire Mammography Network, Sacramento Area Breast Imaging Registry, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System. BCSC registries collect demographics, risk factors, screening history, pathologic characteristics of breast lesions, and mammography indication and results. Data are pooled at a central Statistical Coordinating Center. All registries and the Statistical Coordinating Center received institutional review board approval from all participating registries and the statistical coordinating center for active or passive consenting processes or a waiver of consent to enroll participants, link data, and perform analysis. All procedures were Health Insurance Portability and Accountability Act adherent, and the identities of women, physicians, and facilities are protected by a Federal Certificate of Confidentiality and other protections.[26,27] This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Our study included screening mammograms with abnormal results that were subsequently assigned a Breast Imaging Reporting and Data System (BI-RADS) final assessment category 4 or 5, indicating findings that were suspicious or highly suggestive of malignant neoplasms and recommended for breast biopsy.[28] We excluded mammograms from women with a personal history of breast cancer or symptoms at the time of the examination.[29] Mammograms were also excluded from the cohort if (1) the screening facility had less than 75% capture of biopsy results after abnormal screening results, (2) they were from women younger than 40 years or older than 79 years at the time of screening, or (3) self-reported race or ethnicity was missing. The screening modalities included screen-film mammography, digital mammography (2-dimensional mammography only), and digital breast tomosynthesis (3-dimensional mammography).

Measures, Definitions, and Outcomes

Exposure variables included individual-, neighborhood-, and health care–level factors. Individual- and examination-level factors were obtained at the time of screening from health history questionnaires or the electronic health records and included self-reported race and ethnicity, age, first-degree family history of breast cancer, BI-RADS breast density as assessed on the screening examination, history of prior breast biopsy (yes or no), and time since prior mammogram. Women's residential zip codes were geocoded based on 2007 to 2011 American Community Survey data for neighborhood-level factors, including educational attainment, median household income, and residential rurality. We separated individual- and neighborhood-level factors into nonmodifiable (ie, age, family history of breast cancer, breast density, and history of previous breast biopsy) and modifiable factors (ie, time since last

mammogram, geocoded education, geocoded income, and rurality), in which modifiable factors represent factors amenable to intervention. Health care–level factors obtained from the BCSC registries included mammogram modality, screening facility's academic affiliation, and availability of onsite biopsy services at the screening facility.

Our primary outcome was no breast biopsy within 30, 60, and 90 days after abnormal screening results. Our secondary outcome was days to first biopsy after abnormal screening results.

Statistical Analysis

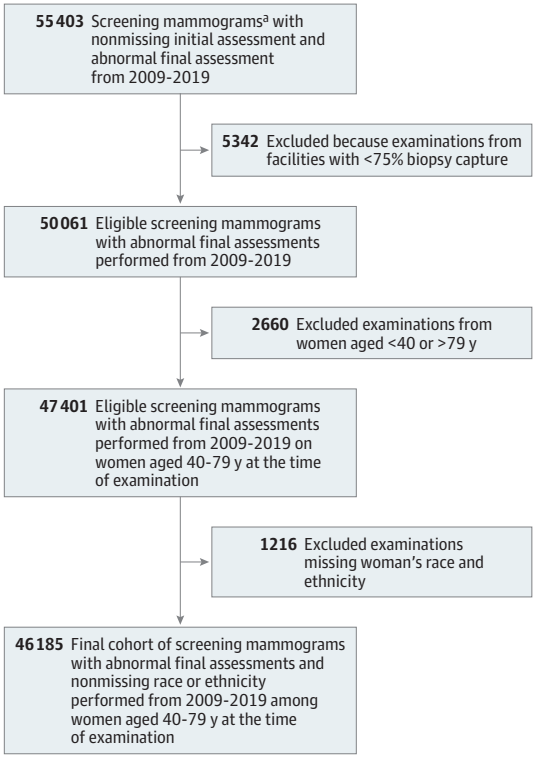
We estimated the proportion of women who had not yet undergone biopsy within 30, 60, and 90 days after screening and median time to biopsy separately for each exposure variable. We plotted time-to-biopsy curves for each racial and ethnic group and calculated *P* values using a log-rank test. We fit sequential log-binomial regression models to identify factors associated with increased relative risk (RR) of no biopsy within 30, 60, and 90 days. Models used a complete-case approach, excluding observations with missing covariates to ensure a consistent study population across models. Model 1 was an unadjusted model including race and ethnicity; model 2 adjusted for nonmodifiable individual-level factors; model 3 additionally adjusted for modifiable individual- and neighborhood-level factors; and model 4 additionally adjusted for health care–level factors. This model ordering was chosen to demonstrate risk of delay after sequentially adjusting for factors at progressive levels of influence in our multilevel disparities framework.[19]

To account for confounders within BCSC registries and individual facilities, we fit 3 additional models: model 5 included factors from model 4 directly adjusted for BCSC registry (to account for potential regional practice variations); model 6 included factors from model 4 directly adjusted for the individual facility within BCSC registries; and model 7 included factors from model 2 directly adjusted for the individual facility within BCSC registries.[30,31] Models 2 through 7 adjusted for examination year as a continuous linear covariate to account for changes in practice patterns over time. We estimated 95% CIs for RRs using robust SEs, assuming an independent working covariance structure to account for clustering within screening facility for models 1 through 5 and clustering within women for models 6 and 7, which directly adjusted for facility. We estimated the relative contributions of each group of factors by calculating the percentage of excess risk attenuation for each model ([*unadjusted RR* − *adjusted RR*] / [*unadjusted RR* − 1]).[32] We performed a subanalysis to further evaluate the association of health care–level factors with the RR of no biopsy by adjusting for each health care–level factor separately, clustered on screening facility.

We fit accelerated failure time models using a log-logistic distribution to estimate median days to biopsy, sequentially adjusting for the covariates using the analytic sample of complete cases, as described above. Women who did not undergo biopsy were censored at 180 days after abnormal screening results to increase the likelihood that biopsies were related to the initial screening. CIs for median days to biopsy were estimated using a nonparametric bootstrap[33] of 10 000 iterations and showed good convergence.

Statistical analyses were performed using SAS STAT version 14.2 (SAS Institute), R version 4.0.2, and RStudio version 1.3.1056 (R Project for Statistical Computing). Tests of statistical significance used a 2-sided α = .05. Data were analyzed from February 21 to November 4, 2021.

Figure 1. Flowchart of Study Cohort Selection



[a] Screening mammograms were excluded if the woman was symptomatic at the time of the examination or had a personal history of breast cancer.

Results

Cohort Description

Our cohort included 46 185 screening examinations with abnormal results from 109 facilities performed on 45 186 women (median [IQR] age, 56 [48-65] years) (**Figure 1**). Women self-identified as Asian (5644 women [12.2%]), Black non-Hispanic (hereafter, *Black*) (6227 women [13.5%]), Hispanic (3055 women [6.6%]), and White non-Hispanic (hereafter, *White*) (30 053 women [65.1%]) (**Table 1**). Women who identified as Alaska Native, American Indian, Native Hawaiian, Pacific Islander, mixed (≥2 races or ethnicities), or other were included in the category *other or mixed* (1206 women [2.6%]). Only 16.2% of White women lived in neighborhoods with median household income in the third quintile or below nationally, compared with 18.2% of Asian women, 65.2% of Black women, and 29.3% of Hispanic women (*P* < .001). Only 2.6% of White women lived in neighborhoods where no more than

Table 1. Characteristics of Screening Examinations and Women by Race and Ethnicity[a]

Characteristic	No. (%) (N = 45 186)[b]					
	Overall	Asian	Black, non-Hispanic	Hispanic	Other or mixed[c]	White, non-Hispanic
Examinations						
All observations, No.	46 185	5644	6227	3055	1206	30 053
Days to biopsy following abnormal results, median (IQR)	23.3 (12.0-45.4)	30.3 (15.7-58.5)	29.3 (15.2-56.5)	26.9 (14.0-52.0)	24.8 (12.8-47.7)	20.7 (10.8-40.0)
No biopsy following abnormal results						
Within 30 d	15 969 (34.6)	2709 (48.0)	2699 (43.3)	1309 (42.8)	468 (38.8)	8784 (29.2)
Within 60 d	7493 (16.2)	1226 (21.7)	1192 (19.1)	574 (18.8)	235 (19.5)	4266 (14.2)
Within 90 d	5634 (12.2)	771 (13.7)	879 (14.1)	370 (12.1)	162 (13.4)	3452 (11.5)
Individual level						
Age at screening, y						
40-49	13 035 (28.2)	1962 (34.8)	1522 (24.4)	1213 (39.7)	396 (32.8)	7942 (26.4)
50-59	14 768 (32.0)	1972 (34.9)	2050 (32.9)	952 (31.2)	413 (34.2)	9381 (31.2)
60-69	12 324 (26.7)	1254 (22.2)	1720 (27.6)	626 (20.5)	280 (23.2)	8444 (28.1)
70-79	6058 (13.1)	456 (8.1)	935 (15.0)	264 (8.6)	117 (9.7)	4286 (14.3)
First-degree family history of breast cancer						
No	34 876 (81.0)	4578 (88.4)	4722 (82.2)	2405 (86.4)	918 (83.2)	22 253 (78.8)
Yes	8175 (19.0)	599 (11.6)	1024 (17.8)	378 (13.6)	185 (16.8)	5989 (21.2)
Missing	3134 (6.8)	467 (8.3)	481 (7.7)	272 (8.9)	103 (8.5)	1811 (6.0)
Breast density						
Almost entirely fatty	3317 (7.7)	177 (3.4)	547 (9.1)	263 (9.4)	108 (9.6)	2222 (7.9)
Scattered fibroglandular	17 104 (39.5)	1394 (26.9)	2917 (48.5)	1077 (38.4)	429 (38.1)	11 287 (40.1)
Heterogeneously dense	19 155 (44.3)	2662 (51.5)	2371 (39.4)	1287 (45.9)	489 (43.5)	12 346 (43.9)
Extremely dense	3688 (8.5)	940 (18.2)	184 (3.1)	175 (6.2)	99 (8.8)	2290 (8.1)
Missing	2921 (6.3)	471 (8.3)	208 (3.3)	253 (8.3)	81 (6.7)	1908 (6.3)
Prior breast biopsy						
No	33 999 (73.6)	4528 (80.2)	4604 (73.9)	2393 (78.3)	931 (77.2)	21 543 (71.7)
Yes	12 186 (26.4)	1116 (19.8)	1623 (26.1)	662 (21.7)	275 (22.8)	8510 (28.3)
BCSC v2 5-y risk score, %						
0 to <1.00 (low)	12 005 (29.1)	2482 (49.1)	1686 (29.7)	1573 (57.6)	343 (31.5)	5921 (22.2)
1.00 to <1.67 (average)	15 419 (37.4)	2049 (40.6)	2260 (39.8)	864 (31.7)	442 (40.6)	9804 (36.7)
1.67 to <2.50 (intermediate)	8851 (21.5)	437 (8.7)	1249 (22.0)	226 (8.3)	213 (19.5)	6726 (25.2)
2.50 to <4.00 (high)	4233 (10.3)	79 (1.6)	423 (7.5)	60 (2.2)	83 (7.6)	3588 (13.4)
≥4.00 (very high)	717 (1.7)	5 (0.1)	55 (1.0)	6 (0.2)	9 (0.8)	642 (2.4)
Missing	4960 (10.7)	592 (10.5)	554 (8.9)	326 (10.7)	116 (9.6)	3372 (11.2)
Time since last mammogram, y						
None (baseline)	6085 (14.0)	1175 (22.0)	818 (14.9)	608 (21.3)	228 (20.0)	3256 (11.4)
≤2	28 834 (66.4)	3179 (59.5)	3563 (65.0)	1624 (57.0)	628 (55.2)	19 840 (69.4)
>2	8491 (19.6)	989 (18.5)	1101 (20.1)	618 (21.7)	282 (24.8)	5501 (19.2)
Missing	2775 (6.0)	301 (5.3)	745 (12.0)	205 (6.7)	68 (5.6)	1456 (4.8)
Neighborhood level						
Probability of high school education, %						
≤75	3184 (7.0)	1104 (19.6)	640 (10.4)	596 (19.7)	83 (7.0)	761 (2.6)
>75	42 539 (93.0)	4517 (80.4)	5541 (89.6)	2434 (80.3)	1100 (93.0)	28 947 (97.4)
Missing	462 (1.0)	23 (0.4)	46 (0.7)	25 (0.8)	23 (1.9)	345 (1.1)
Probability of college education, %						
≤50	6128 (13.4)	1023 (18.2)	1457 (23.6)	891 (29.4)	132 (11.2)	2625 (8.8)
51-75	26 206 (57.3)	2847 (50.6)	4101 (66.3)	1513 (49.9)	651 (55.0)	17 094 (57.5)
>75	13 389 (29.3)	1751 (31.2)	623 (10.1)	626 (20.7)	400 (33.8)	9989 (33.6)
Missing	462 (1.0)	23 (0.4)	46 (0.7)	25 (0.8)	23 (1.9)	345 (1.1)

(continued)

Table 1. Characteristics of Screening Examinations and Women by Race and Ethnicity[a] (continued)

Characteristic	No. (%) (N = 45 186)[b] Overall	Asian	Black, non-Hispanic	Hispanic	Other or mixed[c]	White, non-Hispanic
Household income level, quintile						
≤Third	10 974 (24.0)	1025 (18.2)	4030 (65.2)	886 (29.3)	233 (19.7)	4800 (16.2)
Fourth	23 538 (51.5)	3256 (57.9)	1818 (29.4)	1628 (53.7)	657 (55.6)	16 179 (54.5)
Fifth (highest)	11 190 (24.5)	1340 (23.8)	333 (5.4)	515 (17.0)	292 (24.7)	8710 (29.3)
Missing	483 (1.0)	23 (0.4)	46 (0.7)	26 (0.9)	24 (2.0)	364 (1.2)
Residence						
Urban	40 499 (87.7)	5602 (99.3)	5881 (94.4)	2967 (97.1)	1118 (92.7)	24 931 (83.0)
Large rural	3028 (6.6)	22 (0.4)	274 (4.4)	50 (1.6)	45 (3.7)	2637 (8.8)
Small rural	1028 (2.2)	10 (0.2)	33 (0.5)	20 (0.7)	22 (1.8)	943 (3.1)
Isolated rural	1630 (3.5)	10 (0.2)	39 (0.6)	18 (0.6)	21 (1.7)	1542 (5.1)
Health care level						
Type of screening mammogram obtained						
Film	1560 (3.4)	140 (2.5)	142 (2.3)	125 (4.1)	67 (5.6)	1086 (3.6)
Digital (2D only)	37 154 (80.6)	4995 (88.5)	5381 (86.6)	2513 (82.3)	984 (81.7)	23 281 (77.6)
Tomosynthesis	7403 (16.1)	508 (9.0)	689 (11.1)	417 (13.6)	153 (12.7)	5636 (18.8)
Missing	68 (0.1)	1 (<0.1)	15 (0.2)	0	2 (0.2)	50 (0.2)
Facility with academic affiliation						
No	38 341 (83.1)	4528 (80.3)	5795 (93.1)	2376 (77.8)	917 (76.0)	24 725 (82.3)
Yes	7817 (16.9)	1114 (19.7)	431 (6.9)	677 (22.2)	289 (24.0)	5306 (17.7)
Missing	27 (0.1)	2 (<0.1)	1 (<0.1)	2 (0.1)	0	22 (0.1)
Facility with onsite biopsy services						
No	10 925 (24.0)	562 (10.0)	2236 (36.7)	507 (16.6)	218 (18.2)	7402 (25.0)
Yes	34 677 (76.0)	5052 (90.0)	3849 (63.3)	2540 (83.4)	981 (81.8)	22 255 (75.0)
Missing	583 (1.3)	30 (0.5)	142 (2.3)	8 (0.3)	7 (0.6)	396 (1.3)
Examination year						
2009-2014	31 983 (69.2)	4176 (74.0)	4374 (70.2)	2074 (67.9)	838 (69.5)	20 521 (68.3)
2015-2019	14 202 (30.8)	1468 (26.0)	1853 (29.8)	981 (32.1)	368 (30.5)	9532 (31.7)

Abbreviations: 2D, 2-dimensional; BSCS v2, Breast Cancer Surveillance Consortium risk calculator version 2.

[a] *P* values for χ^2 tests of independence between each covariate and race/ethnicity and χ^2 tests of equal proportions within race/ethnicity category were all $P < .001$.

[b] Column percentage among nonmissing, excluding those with missing data, which is percentage of total.

[c] Includes women who identified as Alaska Native, American Indian, Native Hawaiian, Pacific Islander, mixed (≥2 races or ethnicities), or other.

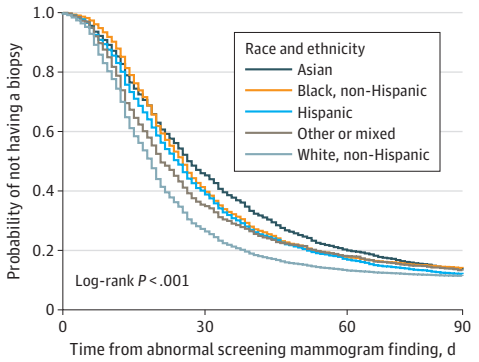
75% of adults had completed high school, compared with 19.6% of Asian women, 10.4% of Black women, and 19.7% of Hispanic women ($P < .001$).

Among 46 185 mammograms with abnormal results, 15 969 (34.6%) were not resolved through biopsy or aspiration within 30 days, 7493 (16.2%) were not resolved within 60 days, and 5634 (12.2%) were not resolved within 90 days. The median (IQR) time to biopsy for the entire cohort was 23.3 (12.0-45.4) days. The unadjusted median (IQR) time to biopsy for White women was 20.7 (10.8-40.0), compared with 30.3 (15.7-58.5) days for Asian women, 29.3 (15.2-56.5) days for Black women, and 26.9 (14.0-52.0) days for Hispanic women (Table 1; eTable 1 in the Supplement). χ^2 tests of independence between each covariate and race and ethnicity and χ^2 tests of equal proportions within race and ethnicity were all statistically significant. Kaplan-Meier curves for time to biopsy by racial and ethnic groups are provided in **Figure 2**. The difference in curves was largest at 30 days and narrowed over time, with the smallest differences at 90 days ($P < .001$).

Primary Outcome

Among the 38 068 complete cases in the analytic sample (eTable 2 in the Supplement), racial and ethnic minority women were at increased risk of no biopsy within 30 days of abnormal screening compared with White women (Asian women: RR, 1.66; 95% CI, 1.31-2.10; Black women: RR, 1.52; 95% CI, 1.30-1.78; Hispanic women: RR, 1.50; 95% CI, 1.24-1.81) (**Table 2**). The increased risk was essentially unchanged after accounting for nonmodifiable individual-level factors. All individual- and neighborhood-level factors together accounted for approximately 16.7% to 20.0% of the excess risk of no biopsy among racial and ethnic minority women within 30 days. Additionally adjusting for the health care-level factors did not result in substantial change in women's risk of no biopsy, with the excess risk of no biopsy changing by less than 2% for all racial and ethnic groups. A subanalysis adjusting for individual- and neighborhood-level factors and the selected health care-level factors individually produced similar RRs as adjusting for individual- and

Figure 2. Time to Biopsy Curves Following Abnormal Screening Mammogram Results by Race and Ethnicity



No. at risk

Asian	5644	2739	1232	779
Black, non-Hispanic	6227	2759	1201	879
Hispanic	3055	1302	570	371
Other or mixed	1206	453	232	161
White, non-Hispanic	30053	8749	4235	3444

neighborhood-level factors and all health care–level factors simultaneously (ie, model 4).

The largest attenuation of risk was observed after adjusting for facility (models 6-7). For example, adjusting for screening facility reduced the risk of no biopsy within 30 days among Black women (RR, 1.22; 95% CI, 1.16-1.29), accounting for 57.7% excess risk of no biopsy compared with the unadjusted risk. This observed impact on risk of no biopsy within 30 days after accounting for sequential multilevel factors was similar for Asian and Hispanic women.

The increased risk of no biopsy within 60 days for racial or ethnic minority women compared with White women was smaller but remained statistically significant (Asian women: RR, 1.58; 95% CI, 1.15-2.18; Black women: 1.39; 95% CI, 1.22-1.60; Hispanic women: 1.38; 95% CI, 1.11-1.71). These risk levels demonstrated a similar pattern of change after adjusting for multilevel factors compared with the risk of no biopsy within 30 days.

The unadjusted risk of no biopsy within 90 days of abnormal screening was not statistically significant for Asian and Hispanic women but remained statistically significant for Black women (RR, 1.28; 95% CI, 1.11-1.47). This increased risk for Black women was minimally changed with adjustment for multilevel factors (excess risk attenuation, 3.6%). However, additionally adjusting for registry or facility had the greatest impact on the risk for Black women. For example, the adjusted risk accounting for registry was attenuated by 35.7% (RR, 1.18; 95% CI, 1.08-1.30) compared with the unadjusted model.

Although Asian women's risk of no biopsy within 90 days of an abnormal screening finding was not statistically significant in models 1 through 4, Asian women were at statistically significantly increased risk after adjusting for multilevel factors and registry (RR, 1.18; 95% CI, 1.07-1.29) and multilevel factors and facility (RR, 1.15; 95% CI, 1.05-1.27). Full models including all covariates are included in eTable 3 in the Supplement.

Secondary Outcome

Unadjusted and adjusted estimated median time to biopsy for all racial and ethnic groups was less than 30 days (**Table 3**). After adjusting for multilevel factors and facility (model 6), the estimated median days to biopsy was 26.5 (95% CI, 25.7-27.2) days for Asian women, 27.3 (95% CI, 26.4-28.3) for Black women, 25.6 (95% CI, 24.7-26.6) days for Hispanic women and 23.0 (95% CI, 22.6-23.3) days for White women.

Discussion

In this large national cohort study of women who had a screening mammogram and BI-RADS category 4 or 5 final assessment, racial and ethnic minority women were at increased risk of not having a timely biopsy compared with White women. This difference was greatest when comparing the rates of biopsy within 30 days of an abnormal screening finding. Although this disparity diminished with increased time from abnormal screening finding, Black women continued to experience statistically significantly increased risk of not having a biopsy within 90 days of screening. Asian women also had statistically significantly increased risk of not having a biopsy within 90 days of screening after adjusting for registry and screening facility. Adjusting for screening facility accounted for nearly 30% of the excess risk of no biopsy within 90 days, suggesting that structural health care system factors may have a considerable impact on observed differences in time to biopsy among racial and ethnic groups. Such factors not captured in our analysis may include variation in communication methods to patients, ease of biopsy scheduling, or availability of translators.[34]

Our results extend and confirm results in smaller studies describing racial and ethnic disparities in time to diagnosis.[20-23] Although almost 90% of women in our cohort received a biopsy within 90 days of screening, the increased adjusted risk of no biopsy at 90 days for Black and Asian women is of particular importance in light of the Cancer Intervention and Surveillance Modeling Network study showing a decline in life-years gained with screening mammography after a 3-month delay in diagnostic testing.[4] Together, these findings suggest that racial and ethnic disparities in time to diagnosis may exacerbate disparities in breast cancer outcomes.

Although the health care–level covariates we included were not associated with risk of not receiving a timely biopsy, we found that the screening facility was an important risk factor for delay. In our study, adjusting for screening facility was associated with the largest sequential decrease in risk of not having a biopsy within 30, 60, and 90 days. This suggests that health care–level factors, in part, drive differences in time to biopsy.

While screening facility was associated with time to biopsy, persistent increased risk of no biopsy within 90 days following an abnormal screening finding after adjusting for included multilevel factors among Asian and Black women suggests other unmeasured factors may also contribute to diagnostic delay. Although there are several possible contributors, structural racism—both in and outside of health

Table 2. Relative Risk of No Biopsy Within 30, 60, and 90 Days of Abnormal Screening Results and Excess Risk Attenuation by Race and Ethnicity

Race and ethnicity	Relative risk (95% CI) [excess risk attenuation, %][a]						
	Model 1[b]	Model 2[c]	Model 3[d]	Model 4[e]	Model 5[f]	Model 6[g]	Model 7[h]
No biopsy within 30 d							
Asian	1.66 (1.31-2.10)	1.64 (1.29-2.09) [3.0]	1.55 (1.27-1.89) [16.7]	1.54 (1.27-1.86) [18.2]	1.40 (1.34-1.45) [39.4]	1.23 (1.17-1.28) [65.2]	1.25 (1.20-1.31) [62.1]
Black, non-Hispanic	1.52 (1.30-1.78)	1.51 (1.29-1.76) [1.9]	1.42 (1.24-1.63) [19.2]	1.43 (1.24-1.64) [17.3]	1.35 (1.29-1.41) [32.7]	1.22 (1.16-1.29) [57.7]	1.24 (1.18-1.30) [53.8]
Hispanic	1.50 (1.24-1.81)	1.51 (1.25-1.83) [−2.0]	1.40 (1.19-1.65) [20.0]	1.40 (1.20-1.62) [20.0]	1.29 (1.23-1.36) [42.0]	1.16 (1.10-1.23) [68.0]	1.18 (1.12-1.24) [64.0]
Other or mixed[i]	1.35 (1.21-1.50)	1.35 (1.21-1.50) [0.0]	1.29 (1.17-1.43) [17.1]	1.29 (1.17-1.41) [17.1]	1.23 (1.14-1.34) [34.3]	1.21 (1.12-1.31) [40.0]	1.24 (1.15-1.35) [31.4]
White, non-Hispanic	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
No biopsy within 60 d							
Asian	1.58 (1.15-2.18)	1.57 (1.14-2.16) [1.7]	1.50 (1.16-1.95) [13.8]	1.47 (1.15-1.88) [19.0]	1.36 (1.26-1.46) [37.9]	1.20 (1.11-1.30) [65.5]	1.23 (1.14-1.33) [60.3]
Black, non-Hispanic	1.39 (1.22-1.60)	1.38 (1.21-1.58) [2.6]	1.32 (1.18-1.49) [17.9]	1.34 (1.18-1.52) [12.8]	1.23 (1.14-1.33) [41.0]	1.25 (1.14-1.36) [35.9]	1.28 (1.17-1.40) [28.2]
Hispanic	1.38 (1.11-1.71)	1.38 (1.11-1.71) [0.0]	1.29 (1.06-1.58) [23.7]	1.28 (1.06-1.53) [26.3]	1.19 (1.08-1.30) [50.0]	1.12 (1.01-1.23) [68.4]	1.14 (1.04-1.25) [63.2]
Other or mixed[i]	1.44 (1.24-1.68)	1.43 (1.23-1.67) [2.3]	1.38 (1.20-1.59) [13.6]	1.36 (1.20-1.55) [18.2]	1.36 (1.19-1.55) [18.2]	1.38 (1.21-1.57) [13.6]	1.42 (1.25-1.62) [4.5]
White, non-Hispanic	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
No biopsy within 90 d							
Asian	1.21 (0.96-1.52)	1.21 (0.96-1.53) [0.0]	1.21 (1.00-1.46) [0.0]	1.19 (0.99-1.43) [9.5]	1.18 (1.07-1.29) [14.3]	1.15 (1.05-1.27) [28.6]	1.17 (1.06-1.29) [19.0]
Black, non-Hispanic	1.28 (1.11-1.47)	1.27 (1.10-1.46) [3.6]	1.27 (1.13-1.42) [3.6]	1.27 (1.12-1.44) [3.6]	1.18 (1.08-1.30) [35.7]	1.20 (1.08-1.34) [28.6]	1.21 (1.09-1.35) [25.0]
Hispanic	1.12 (0.95-1.33)	1.13 (0.95-1.34) [−8.3]	1.11 (0.94-1.30) [8.3]	1.09 (0.94-1.27) [25.0]	1.05 (0.94-1.18) [58.3]	1.05 (0.93-1.19) [58.3]	1.06 (0.95-1.20) [50.0]
Other or mixed[i]	1.18 (0.98-1.43)	1.18 (0.97-1.44) [0.0]	1.17 (0.97-1.41) [5.6]	1.16 (0.96-1.39) [11.1]	1.19 (1.01-1.41) [−5.6]	1.23 (1.04-1.45) [−27.8]	1.25 (1.06-1.48) [−38.9]
White, non-Hispanic	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]

[a] Percentages of excess risk attenuation in adjusted models are calculated relative to unadjusted model 1.

[b] Unadjusted model.

[c] Adjusted for nonmodifiable factors (age, family history of breast cancer, breast density, and history of previous breast biopsy).

[d] Includes factors from model 2 and additionally adjusted for modifiable factors (time since last mammogram, geocoded education, geocoded income, and rurality).

[e] Includes factors from model 3 and additionally adjusted for health care and facility factors (mammogram modality, screening facility's academic affiliation, and availability of onsite biopsy services at the screening facility).

[f] Includes factors from model 4 and additionally adjusted for registry.

[g] Includes factors from model 4 and additionally adjusted for facility.

[h] Includes factors from model 2 and additionally adjusted for facility (Poisson).

[i] Includes women who identified as Alaska Native, American Indian, Native Hawaiian, Pacific Islander, mixed (≥2 races or ethnicities), or other.

Table 3. Accelerated Failure Time Model Estimates of Median Time to Biopsy

Factor	Time to biopsy (95% CI), d						
	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]	Model 6[f]	Model 7[g]
Race and ethnicity							
Asian	29.5 (22.7-37.5)	29.6 (23.3-37.5)	29.2 (23.4-35.8)	29.1 (23.5-35.9)	27.4 (26.6-28.3)	26.5 (25.7-27.2)	26.7 (25.9-27.5)
Black, non-Hispanic	28.8 (24.8-31.9)	29.1 (25.1-32.2)	28.6 (25.0-31.4)	27.9 (24.2-31.2)	28.3 (27.5-29.1)	27.3 (26.4-28.3)	27.4 (26.5-28.4)
Hispanic	26.5 (22.3-30.8)	27.0 (22.8-31.2)	26.4 (22.5-30.2)	26.4 (22.7-30.0)	26.1 (25.1-27.1)	25.6 (24.7-26.6)	25.8 (24.8-26.8)
Other or mixed[h]	24.6 (21.1-28.3)	24.9 (21.4-28.5)	24.7 (21.4-28.2)	25.0 (22.0-28.2)	24.9 (23.4-26.4)	26.7 (25.1-28.3)	26.9 (25.4-28.6)
White, non-Hispanic	20.3 (18.3-22.5)	20.5 (18.4-22.7)	20.9 (18.8-23.1)	21.1 (19.1-23.3)	21.4 (21.1-21.7)	23.0 (22.6-23.3)	22.7 (22.4-23.0)
Age at screening, y							
40-49	NA	22.7 (19.9-25.5)	22.2 (19.5-25.0)	22.4 (19.8-25.0)	22.2 (21.8-22.7)	23.3 (22.8-23.8)	23.8 (23.3-24.3)
50-59	NA	23.8 (21.2-26.4)	24.0 (21.4-26.7)	24.1 (21.6-26.8)	24.2 (23.8-24.6)	24.8 (24.4-25.3)	24.7 (24.2-25.1)
60-69	NA	23.2 (20.7-25.8)	23.7 (21.1-26.4)	23.7 (21.1-26.4)	23.8 (23.4-24.3)	24.7 (24.2-25.2)	24.3 (23.8-24.7)
70-79	NA	23.4 (20.8-26.1)	24.1 (21.4-26.9)	24.0 (21.3-26.9)	24.2 (23.6-24.8)	25.0 (24.3-25.6)	24.4 (23.8-25.0)
First-degree family history of breast cancer							
No	NA	23.5 (20.9-26.2)	23.6 (21.0-26.2)	23.7 (21.1-26.3)	23.7 (23.5-24.0)	24.6 (24.2-24.8)	24.5 (24.2-24.8)
Yes	NA	22.3 (19.8-24.8)	22.8 (20.3-25.3)	22.8 (20.4-25.3)	22.6 (22.2-23.1)	23.5 (23.0-24.0)	23.2 (22.7-23.7)
Breast density							
Almost entirely fatty	NA	25.3 (21.6-29.1)	24.9 (21.5-28.5)	25.6 (22.7-28.5)	25.2 (24.3-26.1)	25.8 (25.0-26.8)	26.3 (25.3-27.2)
Scattered fibroglandular	NA	22.9 (20.5-25.4)	23.0 (20.5-25.5)	23.2 (20.8-25.6)	23.2 (22.8-23.5)	24.0 (23.6-24.4)	24.0 (23.6-24.4)
Heterogeneously dense	NA	23.0 (20.6-25.7)	23.3 (20.8-25.9)	23.2 (20.7-25.9)	23.3 (23.0-23.6)	24.3 (23.9-24.6)	24.1 (23.7-24.5)
Extremely dense	NA	24.3 (20.6-27.9)	24.9 (21.3-28.5)	24.7 (21.2-28.3)	24.8 (24.0-25.6)	25.1 (24.3-25.9)	24.6 (23.8-25.4)
Prior breast biopsy							
No	NA	22.8 (20.2-25.5)	22.8 (20.2-25.5)	22.9 (20.4-25.5)	23.0 (22.7-23.3)	23.9 (23.5-24.1)	23.9 (23.6-24.2)
Yes	NA	24.4 (21.8-27.0)	25.1 (22.4-27.8)	25.1 (22.5-27.8)	25.0 (24.5-25.5)	25.8 (25.2-26.3)	25.3 (24.8-25.8)
Time since last mammogram, y							
None (baseline)	NA	NA	27.5 (24.1-31.3)	27.5 (24.2-31.2)	27.7 (26.9-28.5)	28.3 (27.4-29.1)	NA
≤2	NA	NA	22.0 (19.6-24.5)	22.1 (19.7-24.5)	22.1 (21.8-22.3)	23.1 (22.8-23.4)	NA
>2	NA	NA	25.6 (22.5-28.6)	25.6 (22.6-28.6)	25.7 (25.1-26.2)	26.1 (25.5-26.7)	NA
Geocoded probability of high school education, %							
≤75	NA	NA	25.8 (20.3-31.2)	26.5 (21.0-32.0)	25.0 (23.8-26.2)	23.7 (22.6-24.8)	NA
>75	NA	NA	23.2 (20.8-25.7)	23.3 (20.9-25.7)	23.4 (23.2-23.7)	24.4 (24.1-24.7)	NA
Geocoded probability of college education							
≤50	NA	NA	23.6 (21.0-26.8)	23.1 (20.4-26.3)	23.4 (22.7-24.2)	25.0 (24.2-25.8)	NA
51-75	NA	NA	23.3 (20.7-26.0)	23.2 (20.6-26.0)	23.4 (23.1-23.7)	24.1 (23.8-24.5)	NA
>75	NA	NA	23.7 (20.1-27.2)	24.5 (21.5-27.3)	23.9 (23.3-24.4)	24.5 (23.9-25.2)	NA

(continued)

Table 3. Accelerated Failure Time Model Estimates of Median Time to Biopsy (continued)

Factor	Time to biopsy (95% CI), d						
	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	Model 5[e]	Model 6[f]	Model 7[g]
Geocoded household income level, quintile							
≤Third	NA	NA	24.3 (21.2-27.4)	24.5 (21.6-27.5)	25.3 (24.7-25.9)	24.9 (24.3-25.5)	NA
Fourth	NA	NA	23.1 (20.4-25.8)	23.5 (21.0-26.1)	23.4 (23.0-23.7)	24.5 (24.1-24.9)	NA
Fifth (highest)	NA	NA	23.3 (20.2-26.6)	22.5 (19.4-25.8)	22.2 (21.7-22.8)	23.6 (22.9-24.2)	NA
Residence							
Urban	NA	NA	23.4 (20.7-26.1)	23.5 (20.8-26.2)	23.1 (22.9-23.4)	24.3 (24.0-24.6)	NA
Large rural	NA	NA	22.4 (17.9-26.8)	22.4 (18.6-26.2)	26.5 (25.3-27.9)	24.3 (22.8-25.9)	NA
Small rural	NA	NA	24.3 (19.9-28.5)	24.6 (20.9-28.5)	27.9 (26.2-29.8)	24.4 (22.7-26.1)	NA
Isolated rural	NA	NA	25.4 (19.8-31.0)	25.8 (21.3-30.5)	29.6 (27.8-31.5)	25.6 (23.9-27.5)	NA
Type of screening mammogram obtained							
Film	NA	NA	NA	22.4 (17.9-28.4)	21.5 (20.3-22.8)	21.1 (19.9-22.5)	NA
Digital (2D only)	NA	NA	NA	23.7 (21.0-26.4)	23.8 (23.5-24.1)	24.2 (23.8-24.5)	NA
Tomosynthesis	NA	NA	NA	22.9 (19.9-26.8)	22.4 (21.8-23.0)	26.2 (25.4-27.1)	NA
Facility with academic affiliation							
No	NA	NA	NA	24.3 (21.8-26.9)	23.7 (23.5-24.0)	NA	NA
Yes	NA	NA	NA	18.9 (12.1-26.7)	22.3 (21.5-23.0)	NA	NA
Facility with on-site biopsy services							
No	NA	NA	NA	23.3 (20.0-26.4)	23.6 (23.1-24.1)	NA	NA
Yes	NA	NA	NA	23.6 (20.5-26.7)	23.5 (23.2-23.8)	NA	NA

Abbreviations: 2D, 2-dimensional; NA, not applicable.

[a] Unadjusted model.

[b] Adjusted for nonmodifiable factors (age, family history of breast cancer, breast density, and history of previous breast biopsy).

[c] Includes factors from model 2 and additionally adjusted for modifiable factors (time since last mammogram, geocoded education, geocoded income, and rurality).

[d] Includes factors from model 3 and additionally adjusted for health care and facility factors (mammogram modality, screening facility's academic affiliation, and availability of onsite biopsy services at the screening facility).

[e] Includes factors from model 4 and additionally adjusted for registry.

[f] Includes factors from model 4 and additionally adjusted for facility.

[g] Includes factors from model 2 and additionally adjusted for facility (Poisson).

[h] Includes women who identified as Alaska Native, American Indian, Native Hawaiian, Pacific Islander, mixed (≥2 races or ethnicities), or other.

care facilities—may account for these disparities. Structural racism has been associated with the availability of insurance coverage, health insurance reimbursement policies, and health care facility resource allocation.[35] While we were unable to incorporate all of these factors into our analysis, they have a disproportionately negative impact on racial and ethnic minority groups, are associated with worse health care access, and contribute to persistent racial and ethnic disparities in health coutcomes.[35] For example, a study by Molina et al[21] found that, compared with White women, racial and ethnic minority women were more likely to attend facilities not accredited as Breast Imaging Centers of Excellence, and this facility quality characteristic alone accounted for 37% of the observed disparity in diagnostic delays. These results reflect historical racial discrimination and chronic underinvestment in neighborhoods and facilities that serve mostly racial and ethnic minority groups.[36] Continued efforts to allocate facility-level resources, such as patient navigators, translators, and same-day biopsy services, may decrease disparities in diagnostic work-up for breast cancer.[37-39] This need has become even more relevant in the context of rebounding health care system demands after the COVID-19 pandemic shutdowns, which may have disproportionate negative effects on racial and ethnic minority women and the facilities serving them.[40,41]

Our study has several strengths. We evaluated the association of multilevel factors with the risk of women not receiving a timely biopsy in a large, national cohort that is broadly representative of the diverse US population. We have more than a decade's worth of data from 109 BCSC facilities, which covers the full spectrum of breast imaging facilities, from mobile vans to university hospitals, and links women to tumor registries for near-complete capture of breast cancer diagnoses. Moreover, to our knowledge, our study is the largest elucidating racial and ethnic differences in time to biopsy that could potentially lead to more targeted interventions to address breast cancer disparities relying on the multilevel framework set forth by the NIMHD.[19]

Limitations

Our study has limitations. Given the observational study design, our selected multilevel factors were limited to available data. Thus, additional factors that may impact delays to biopsy, such as structural racism, were not included in our analysis. Similarly, missing data resulted in exclusion of otherwise eligible women from the statistical models, as we excluded observations with any missing covariate data from all models to ensure the models were fit to the same study population for comparability across models. Exclusion of these incomplete observations and exclusion of facilities with less than 75% biopsy capture may have led to underestimated effects by excluding potentially lower-quality facilities that may screen some racial and ethnic groups at higher proportions compared with other facilities. Additionally, we did not evaluate the type of first biopsy performed (eg, image-guided percutaneous biopsy or open surgical biopsy), which may further impact time to final diagnosis.[42] However, almost all breast biopsies are now performed percutaneously under image guidance as standard of care, including during all years of our study period.[43] We did not adjust for availability of onsite diagnostic services, which may also impact time to biopsy. Additionally, while we demonstrated statistically significant differences in risk of no biopsy at different time points, the clinical significance of short differences in time to biopsy may be limited to increased patient anxiety in the absence of data showing poor clinical outcomes with shorter delays to diagnosis. However, it is possible that these short, earlier delays may compound downstream delays resulting in overall delays to definitive treatment.

Conclusions

In this large, national cohort study of women with abnormal screening mammogram results and a recommendation for biopsy, minority race and ethnicity were significantly associated with increased risk of not receiving a biopsy within 30, 60, or 90 days from abnormal results, with large and persistent differences among Black women. This risk of not having a timely biopsy was substantially attenuated, but not eliminated, after adjusting for screening facility, suggesting that structural racism, within and beyond health care, may contribute to these differences. Future work linking multilevel factors and diagnostic delays to disease stage and other clinically relevant outcomes may allow us to reduce these disparities.

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Author Affiliations: Department of Radiology, University of Washington School of Medicine, Seattle (Lawson); Division of Biostatistics, Department of Public Health Sciences, University of California Davis School of Medicine, Davis (Bissell, Miglioretti); Kaiser Permanente Washington Health Research Institute, Kaiser Permanente Washington, Seattle (Miglioretti, Eavey, Bowles); Department of Radiation Oncology, Michigan Medicine, Ann Arbor (Chapman); University of Wisconsin–Madison School of Medicine and Public Health, Madison (Chapman); Department of Oncology, Cancer Prevention and Control Program, Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington, District of Columbia (Mandelblatt); Department of Population Health Sciences, University of Utah, Huntsman Cancer Institute, Salt Lake City (Onega); Departments of Radiology and Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill (Henderson); Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago (Rauscher); Departments of Medicine and Epidemiology and Biostatistics, University of California, San Francisco (Kerlikowske); General Internal Medicine Section, Department of Veterans Affairs, University of California, San Francisco (Kerlikowske); Departments of Surgery and Radiology, University of Vermont Cancer Center, University of Vermont, Burlington (Sprague); Department of Economics, Applied Statistics, and International Business, New Mexico State University, Las Cruces (Gard); Kaiser Permanente Washington, Seattle (Parsian); Department of Radiology, University of Washington School of Medicine, Seattle (Lee); Department of Health Services, University of Washington School of Public Health, Seattle (Lee).

Author Contributions: Dr Bissell had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Lawson, Bissell, Miglioretti, Chapman, Onega, Kerlikowske, Sprague, Parsian, Lee.

Acquisition, analysis, or interpretation of data: Lawson, Bissell, Miglioretti, Eavey, Chapman, Mandelblatt, Onega, Henderson, Rauscher, Kerlikowske, Sprague, Bowles, Gard, Lee.
Drafting of the manuscript: Lawson, Bissell, Mandelblatt, Parsian, Lee.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Bissell, Miglioretti, Chapman, Gard.
Obtained funding: Miglioretti, Onega, Henderson, Kerlikowske, Lee.
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Supervision: Miglioretti, Parsian, Lee.

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Invited Commentary

Addressing Racial and Ethnic Differences in Diagnostic Resolution of Abnormal Mammographic Findings

Randy C. Miles, MD, MPH

Breast cancer is the most common nonskin cancer and second leading cause of cancer death in US women. Over 280 000 new cases of invasive breast cancer are expected to be diagnosed in 2022, and over 43 000 women are expected to die from the disease during this same period.[1] While early detection though routine screening contributes to improved breast cancer–specific outcomes, delays in diagnostic resolution of abnormal mammographic findings may diminish the benefits of early breast cancer detection resulting in lower disease-specific and overall survival.[2,3]

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In this issue of *JAMA Oncology*, Lawson and colleagues[4] report the results of a prospective cohort study to evaluate multilevel predictors of time to biopsy after abnormal screening mammography by race and ethnicity. The study included 45 186 women between the ages of 40 and 79 years with a recommendation for biopsy following an abnormal screening mammogram between 2009 and 2019 through the Breast Cancer Surveillance Consortium (BCSC), a collaborative network of 6 active breast imaging registries and 2 historic registries. Exposures included woman-, neighborhood-, and health care–level factors. Unadjusted and adjusted relative risk (RR) of a woman not having a biopsy within 30, 60, and 90 days following an abnormal screening mammogram was evaluated using sequential log-binomial regression models, and unadjusted and adjusted median time to biopsy was assessed using accelerated failure time models.

The proportion of abnormal screening mammograms resolved following a biopsy recommendation within 30, 60, and 90 days was 34.6%, 16.2%, and 12.2%, respectively.[4] Compared with White women, Asian, Black, and Hispanic women were all at increased risk of no biopsy within 30 and 60 days following an abnormal screening mammogram (unadjusted RR range, 1.38-1.66). Black women were the only group to experience increased risk of no biopsy at 90 days (RR, 1.28; 95% CI, 1.11-1.47) compared with White women, which persisted after sequential adjustment for woman-, neighborhood-, and health care–level factors (RR, 1.20; 95% CI, 1.08-1.34).

In this large, diverse cohort of women receiving care at 109 breast imaging facilities across the US,[4] a statistically significant difference in diagnostic resolution of abnormal screening findings up to 60 days was demonstrated between White women and women from each racial and ethnic minority group. These findings are consistent with prior studies demonstrating breast cancer diagnostic and treatment delays by race and ethnicity following a positive screening mammogram. Kovar et al[5] found that race was an independent risk factor for delayed breast cancer diagnosis in their evaluation of time from abnormal mammogram to biopsy, surgeon visit, and breast