JNCI Cancer Spectrum (2022) 6(2): pkac016

https://doi.org/10.1093/jncics/pkac016
First published online February 18, 2022
Article

Breast Cancer Incidence, Hormone Receptor Status, Historical Redlining, and Current Neighborhood Characteristics in Massachusetts, 2005-2015

Emily Wright, BA *, Pamela D. Waterman, MPH, Christian Testa, BS, Jarvis T. Chen, ScD, and Nancy Krieger, PhD

Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, MA, USA

*Correspondence to: Emily Wright, BA, PhD(c), Department of Social and Behavioral Sciences, Kresge 7th floor, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA 02115, USA (e-mail: e.wright@g.harvard.edu).

Abstract

Background: Scant research has analyzed contemporary US cancer incidence rates in relation to historical redlining (ie, 1930s US federally imposed residential segregation), implemented via the color-coded federal Home Owners' Loan Corporation (HOLC) maps. **Methods:** We analyzed Massachusetts Cancer Registry data for all patients with primary invasive breast cancer (BC) diagnosed in 2005-2015 among women in the 28 Massachusetts municipalities with digitized 1930s HOLC maps. Multilevel Poisson regression estimated BC incidence rate ratios (IRR), overall and by tumor estrogen receptor (ER-positive, ER-negative) and progesterone receptor (PR-positive, PR-negative) status, in relation to HOLC grade and contemporary census tract (CT) social characteristics. **Results:** Net of age and racialized group, the extremes of BC incidence were detected by combinations of HOLC grade and contemporary CT racialized economic segregation. Compared with CTs with the best HOLC grade (A + B) and most privileged contemporary characteristics (T1), for all, ER-positive and PR-positive BC, incidence was highest in T1 and mixed HOLC grade CTs (eg, $IRR_{ER+;\ Mixed\text{-}T1} = 1.10$, 95% confidence interval [CI] = 1.01 to 1.21) and lowest in CTs with most concentrated racialized economic deprivation (T3) and no HOLC grade (eg, $IRR_{ER+;\ No\ Grade\text{-}T3} = 0.85$, 95% CI = 0.75 to 0.95). For ER-negative and PR-negative BC, incidence was highest in CTs with the most contemporary deprivation, but the best HOLC grade (eg, $IRR_{ER-;\ A+B\text{-}T3} = 1.27$, 95% CI = 0.93 to 1.75) and lowest in T1 and worst HOLC-graded CTs (eg, $IRR_{ER-;\ D\text{-}T1} = 0.84$, 95% CI = 0.56 to 1.25). **Conclusion:** Breast cancer risk may be shaped by combined histories of redlining and present-day CT characteristics.

Despite growing interest in the social determinants of cancer (1,2), including contemporary residential segregation, scant research has explored how cancer risk is shaped by historical redlining (ie, 1930s US federally imposed residential segregation), implemented via the color-coded federal Home Owners' Loan Corporation (HOLC) maps. These maps, produced for more than 200 cities, graded areas by assessors' evaluations of their mortgage credit worthiness, using 4 categories: A (HOLC designation "best" = green), B (HOLC designation "still desirable" = blue), C (HOLC designation "definitely declining" = yellow), and D (HOLC designation "hazardous" = red) (3,4). These maps nationalized US residential segregation, simultaneously encouraging mortgage lending in predominantly White and affluent neighborhoods (A, B) and discouraging investment in neighborhoods whose residents were disproportionately low income, foreign born, or people of color (C, D) (3,4).

Although considerable social science research has documented the long-lasting social impacts of redlining, a practice not outlawed until the late 1960s (3-7), fewer than 15 studies have investigated the contemporary health impacts of historical redlining (8-15) of which only one has focused on cancer (12). Two considerations suggest such research is warranted. First, historical redlining has been shown to shape contemporary patterns of racial segregation (3-7), which, in turn, is a well-documented determinant of health, including cancer risk, across the life course (2,16,17). Second, conceptually clarifying and modeling these related, yet distinct, forms of structural

Received: June 4, 2021; **Revised:** October 2, 2021; **Accepted:** November 29, 2021

racism—explicitly unjust policies (ie, redlining) and area-based measures of their legacies (ie, contemporary residential segregation)—and how they are interactively embodied is crucial for understanding etiology, agency, and accountability related to contemporary health inequities (18). For example, our recent multicity study in Massachusetts, the first to examine HOLC maps in relation to cancer, documented increased risk of late-stage (vs early) breast cancer (BC) for women living in previously redlined and yellow areas, overall and partially mediated by present-day residential census tract (CT) segregation at the time of diagnosis (12).

In this study, we examined the implications of historical redlining for contemporary inequities in breast cancer incidence, overall and by hormone receptor status, using population-based cancer registry data. We examined tumor estrogen receptor (ER) and progesterone receptor (PR) status separately because the expression of these biomarkers is relevant to BC treatment, predictive of prognosis, and varies by racialized group and socioeconomic position (19-22). Informed by ecosocial theory (18,23,24), we hypothesized that potential pathways linking historical redlining, contemporary CT characteristics, and BC incidence by hormone receptor status could include social exposures relevant to etiology and access to and quality of medical treatment (25-31).

Methods

Study Population

The study base comprised all residents of Massachusetts living in the 28 municipalities with HOLC maps who were diagnosed with incident primary invasive BC (32) between January 1, 2005, and December 31, 2015, and categorized by the cancer registry as "female" (n = 60 173) (33) and the corresponding total population of female residents of Massachusetts. We linearly interpolated population denominators for 2005-2009 using 2000 (34) and 2010 decennial census data (35) and additionally used 2010 decennial data and annual American Community Survey (ACS) 5-year estimates for 2011 to 2015 (eg, 2009-2013 centered in 2011) (36). This study was approved as exempt by the institutional review boards of the Massachusetts Cancer Registry (MCR), Harvard T.H. Chan School of Public Health (Protocol IRB16-1325), and Massachusetts Institute of Technology (Protocol 946302-3).

Individual Covariates

We obtained MCR data on patients' age at diagnosis, racialized group, tumor characteristics, country of birth, and residential address at the time of diagnosis. Because CT-level, census-defined, age-specific population denominator data on racialized groups needed for estimating incidence rates (IRs) are available only for selected, nonmutually exclusive groups (American Indian or Alaska Native; Asian or Pacific Islander; Black; Hispanic; White; White non-Hispanic; and a group the census categorized as "Other"), we constructed matching categories among patients and used White non-Hispanic as the referent group (34,35). "Other" racialized group was defined in the MCR as "some other known race" (information regarding a patient's racialized group could be abstracted from their medical records but could not be assigned to one of the other available codes) and in the census data as "some other race alone" (individuals selected this category and none of the other available racial categories). We categorized ductal or lobular (*International Classification of Diseases for Oncology* 3 codes 8500-8543) vs other histology (32); early (localized) vs late (regional or distant) stage at diagnosis; and grade I, II, or III-IV. We employed data on country of birth, by subregion (36), only in the descriptive tables, because of its high missingness (45.0%). Per our data use agreement with MCR, one author (PDW) geocoded residential addresses using ArcGIS (version 10.4.1) while on-site at the MCR (37) and appended solely the 2010 CT geocodes to our dataset, which we used to link to HOLC grade and CT characteristics. Only 1472 patients (2.4%) could not be geocoded to this level.

HOLC Grade

As described in detail in our recent article (12), we assigned each of the 474 CTs in the 28 Massachusetts municipalities included in 1930s HOLC maps (4) a HOLC grade (A, B, C, D, mixed, no grade) based on the percentage of the CT's land area included in the 4 HOLC areas: A, B, C, or D for 297 CTs with at least 50% and less than or equal to 100% land area contained in that HOLC area; mixed for 39 CTs with no HOLC area accounting for at least 50% land area; no grade for 138 CTs with less than 50% land area in HOLC-graded areas. Because only 5 CTs had an A HOLC grade, we used the combination of the 2 most creditworthy grades (A and B; n = 43 CTs) as the referent group, referred to as A + B. Reflecting the racialized and particularly anti-Black content of HOLC grades, HOLC notes for D-rated areas in Massachusetts included such derogatory statements as "Section south of the railroad is a slum area. Negro is concentrated around the West St. Station. The bulk of the two-family houses are converted singles" (Everett, D3) (4).

CT Characteristics

To construct CT-level covariates for the 2005-2015 period (2010 normalized boundaries), we used 2000 decennial census data (34) and ACS 5-year estimates centered in 2008-2015 to interpolate values for the years 2005-2007 (35). 2000 census data were analyzed in SAS, version 9.4 (38). We constructed variables reflecting the percentage of persons below the US federal poverty line, percentage born outside the United States, and Index of Concentration at the Extremes (ICE) measures for 1) economic, 2) racial, 3) racialized economic, and 4) home ownership polarization (39,40). ICE quantifies spatial social polarization and ranges from -1 (everyone in the most deprived group) to 1 (everyone in the most privileged group) (Supplementary Table 1, available online). The groups selected to reflect extreme privilege and deprivation for these 4 measures, which we have used in previous studies for cancer and other health outcomes (11,12,28,40,41), were, respectively, 1) high- vs low-income households, 2) persons categorized as White non-Hispanic vs Black non-Hispanic, 3) White non-Hispanic persons in high-income households vs Black persons (any ethnicity) in low-income households, and 4) owner- vs renter-occupied housing.

Outcomes

We obtained data on patients' hormone receptor status, coded as ER- or PR-positive, ER or PR-negative, or borderline (42). Since 2010, tumors were coded as positive if at least 1% of cells stained and negative if less than 1% of cells stained, with no allowance for a borderline result. Before 2010, uniform cut points were not employed, and tumors could be coded as borderline

(eg, <5%: negative; 5%-19%: borderline; ≥20%: positive) (42,43). We opted not to analyze data on human epidermal growth factor receptor 2 (HER2) because it was only available since 2010 (44). No data were available on molecular subtypes (45-47).

Statistical Analyses

We used R version 4.0.4 (48) to conduct all analyses, with all tests of statistical significance being 2-sided. We descriptively quantified the distribution of all variables, for patients and residents, including regarding missingness. Given evidence of collinearity between the contemporary CT measures (Supplementary Methods, Supplementary Table 2, available online), as expected, we included these variables in separate regression models. We used multiple imputation using chained equations to create 10 imputed cancer case datasets under the missing-at-random assumption, including in the imputation model of all variables in Table 1 except birthplace (49). We grouped patients categorized as ER or PR borderline as missing for imputation. Because results indicated nonlinear, nonmonotonic associations between the continuous CT variables and incidence of each outcome, we employed 1) terciles for the ICE measures (T1 = most concentrated privilege, T3 = most concentrated deprivation), based on the overall distribution (all Massachusetts CTs, 2005-2015) for each measure; 2) cut points closely mirroring quartiles of the overall distribution of the percent foreign-born measure (<10%, 10%-19.9%, 20%-29.9%, ≥30%); and 3) established poverty cut points (<5%, 5%-9.9%, 10%-19.9%, ≥20%) (50-52).

We computed directly age-standardized incidence rates (IR) (per 100 000), using the US 2000 standard million population to ensure comparability with other cancer registry data (53), with analyses singly stratified by individual and CT characteristics. We constructed 95% confidence intervals (CI) using the Dobson method (54,55). We then used multilevel Poisson regression models (random intercept for municipality) to estimate indirectly age-standardized incidence rate ratios (IRR) and corresponding 95% confidence intervals, using Massachusetts-wide, age-specific reference IRs of each outcome (Supplementary Table 3, available online).

We first fit univariate models. We then fit models including racialized group membership and, singly, HOLC grade or ICE for racialized economic polarization (terciles), as this CT variable showed the steepest univariate BC incidence gradients. Finally, we fit models with interaction terms for HOLC grade by ICE tercile. We presented IRRs for all combinations of HOLC grade and ICE tercile in relation to a common referent group: best HOLC grade (A + B) and most privileged ICE tercile (T1). We examined interaction on multiplicative and additive scales, using the relative excess risk because of interaction for the latter (56,57). All analytic results were pooled using Rubin's rules (58). We ran 3 sensitivity analyses using "ER-positive or PR-positive" vs "ER-negative and PR-negative" as an outcome, excluding small groups (aged younger than 15 years, American Indian or Alaska Native), and subdividing no vs any A or B land area mixed CTs. Results were similar to those reported here (available on request).

Results

The 28 Massachusetts municipalities with digitized HOLC maps contained 44.4% of Massachusetts total population in 1940 and 29.6% in 2005-2015 (Supplementary Table 4, available online) and were clustered around the Greater Boston area (Figure 1). The 474 CTs in these 28 municipalities comprised 32% of Massachusetts' 1478 CTs (2010 boundaries) and had more adverse contemporary characteristics than Massachusetts CTs in areas without HOLC maps (Supplementary Table 4, available online). Among these 474 CTs, contemporary characteristics exhibited a HOLC gradient with mixed and ungraded CTs in the middle range (Figure 2).

Regarding the individual characteristics of women residents and BC patients in the HOLC catchment area, 11.0% (14.1% of residents) were categorized as Black (any ethnicity), 5.1% of patients (13.2% of residents) as Hispanic, and 79.4% of patients (64.2% of residents) as White non-Hispanic (Table 1). Of the patients, 16.2% and 26.2% were categorized as ER-negative or PR-negative, respectively. The proportion categorized as ER-negative or PR-negative was highest among Black (27.6% ER-negative; 37.7% PR-negative), followed by Hispanic patients (20.0% ER-negative; 29.6% PR-negative), with 14.3% and 24.2% of White non-Hispanic patients categorized as ER-negative and PR-negative, respectively.

Patients and residents were unevenly distributed across CT contexts (Table 1). Of the patients, 10.9% (14.2% of residents) lived, at the time of diagnosis, in historically redlined areas; 21.5% of Black, 23.0% of Hispanic, and 8.6% of White non-Hispanic patients resided in redlined areas; and 34.6% of patients (42.9% of residents) lived in CTs with the most concentrated present-day racialized economic deprivation (ICE T3), with 79.0% of Black, 70.6% of Hispanic, and 26.1% of White non-Hispanic patients living in these T3 CTs. Compared with patients living in CTs without HOLC maps, patients in HOLC-graded areas were more often people of color and living in CTs with more adverse characteristics (Table 2).

When analyzed singly in relation to BC incidence, directly age-standardized IRs for all, ER-positive, and PR-positive BC exhibited expected contemporary CT characteristic gradients: highest IRs in most privileged CTs, lowest in most deprived CTs (Table 3). IRs for PR-negative and ER-negative BC exhibited weaker gradients and, in some cases for ER-negative BC, gradients weakly in the opposite direction (eg, for ICE for racialized economic polarization, $IR_{ER+;\ T1} = 128.40$, 95% CI = 124.69 to 132.19, and $IR_{ER+;\ T3} = 96.26$, 95% CI = 93.40 to 99.19; $IR_{ER-;\ T1} = 21.15$, 95% CI = 19.63 to 22.76, and $IR_{ER-;\ T3} = 22.68$, 95% CI = 21.28 to 24.14). When stratified singly by HOLC grade, the highest IRs for all BC outcomes occurred in mixed-grade CTs and the lowest occurred in D-grade (redlined) CTs (eg, $IR_{all\ BC;\ mixed} = 147.23$, 95% CI = 140.34 to 154.36; $IR_{all\ BC;\ D} = 118.48$, 95% CI = 112.89 to 124.27) (Table 3). In indirectly age-standardized multilevel Poisson models that newly adjusted for racialized group membership, similar results were observed, with the highest IRs for all outcomes occurring in mixed CTs and the lowest IRs occurring in D-grade (all, ER-negative, PR-negative BC) or C- and D-grade CTs (ER-positive, PR-positive BC) (Table 4).

In models including HOLC by ICE interactions (Table 4 and Figures 3 and 4), the extremes of BC incidence were newly detected by combinations of ICE tercile and HOLC grade, rather than by ICE or HOLC singly. For all BC, ER-positive, and PR-positive BC, the highest IRs occurred in CTs with T1 ICE and mixed HOLC grade (eg, $IRR_{ER+;\ mixed\text{-}T1} = 1.10$, 95% CI = 1.01 to 1.21) (Figure 3) and the lowest (or similarly low, for all BC) occurred in CTs with T3 ICE and no HOLC grade (eg, $IRR_{ER+;\ no\ grade\text{-}T3} = 0.85$, 95% CI = 0.75 to 0.95). For ER-negative and PR-negative BC, IRs were highest (and similar) in CTs with more contemporary deprivation, but the highest HOLC grade (A + B-T3, A + B-T2 for ER-negative and A + B-T3 for PR-negative; eg, $IRR_{ER-;\ A+B\text{-}T3} = 1.27$,

Table 1. Observed individual and residential CT characteristics of all women and women diagnosed with primary invasive breast cancer, 2005-2015, residing in the 28 Massachusetts municipalities with 1930s HOLC grades (n = 474 CTs), total and according to racialized group: Massachusetts Cancer Registry data (n = 15 689 patients) and decennial Census and American Community Survey data (n = 10 765 212 residents)

			Racialized group (US census categories)[b]					
Variable	All residents[a]	All patients[a]	American Indian or Alaska Native	Asian or Pacific Islander	Black	Hispanic	"Other" racialized group	White non-Hispanic
Individual characteristics[c]								
Total number	10 765 212	15 689	17	744	1712	797	80	12 392
Age, No. (%), y								
<5	545 981 (5.1)	0 (0.0)	[d]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
5-14	993 908 (9.2)	0 (0.0)	[d]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
15-24	1 677 909 (15.6)	23 (0.1)	[d]	1 (0.1)	4 (0.2)	5 (0.6)	1 (1.2)	13 (0.1)
25-34	1 944 156 (18.1)	344 (2.2)	[d]	51 (6.9)	45 (2.6)	27 (3.4)	1 (1.2)	218 (1.8)
35-44	1 423 267 (13.2)	1470 (9.4)	[d]	130 (17.5)	221 (12.9)	127 (15.9)	11 (13.8)	987 (8.0)
45-54	1 398 250 (13.0)	3333 (21.2)	[d]	213 (28.6)	391 (22.8)	213 (26.7)	27 (33.8)	2505 (20.2)
55-64	1 171 286 (10.9)	3764 (24.0)	[d]	178 (23.9)	451 (26.3)	215 (27.0)	17 (21.2)	2923 (23.6)
65-74	768 994 (7.1)	3370 (21.5)	[d]	114 (15.3)	342 (20.0)	132 (16.6)	13 (16.2)	2772 (22.4)
75-84	537 468 (5.0)	2404 (15.3)	5 (29.4)	45 (6.0)	191 (11.2)	64 (8.0)	7 (8.8)	2089 (16.9)
≥85	303 994 (2.8)	981 (6.3)	0 (0.0)	12 (1.6)	67 (3.9)	14 (1.8)	[d]	885 (7.1)
Racialized group, No. (%)[b]								
American Indian or Alaska Native	29 511 (0.3)	17 (0.1)	17 (100.0)	0 (0.0)	0 (0.0)	[d]	0 (0.0)	0 (0.0)
Asian or Pacific Islander	1 033 258 (9.6)	744 (4.8)	0 (0.0)	744 (100.0)	0 (0.0)	[d]	0 (0.0)	0 (0.0)
Black	1 518 444 (14.1)	1712 (11.0)	0 (0.0)	0 (0.0)	1712 (100.0)	69 (62.7)	0 (0.0)	0 (0.0)
"Other" racialized group[e]	602 430 (5.6)	80 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	40 (36.4)	80 (100.0)	0 (0.0)
White, non-Hispanic	6 915 150 (64.2)	12 392 (79.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	12 392 (100.0)
Missing[f]	0 (0.0)	84 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	27 (3.4)	0 (0.0)	0 (0.0)
Hispanic ethnicity, No. (%)[b]								
Hispanic	1 416 272 (13.2)	797 (5.1)	[d]	[d]	69 (4.0)	797 (100.0)	40 (50.0)	0 (0.0)
Non-Hispanic	9 348 940 (86.8)	14 892 (94.9)	17 (100.0)	743 (99.9)	1643 (96.0)	0 (0.0)	40 (50.0)	12392 (100.0)
ER status, No. (%)								
Negative	—[g]	2465 (16.2)	1 (6.2)	130 (17.7)	457 (27.6)	155 (20.0)	9 (11.5)	1725 (14.3)
Positive	—	12 767 (83.8)	15 (93.8)	603 (82.3)	1196 (72.4)	619 (80.0)	69 (88.5)	10 306 (85.6)
Borderline	—	9 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (0.1)
Missing[f]	—	448 (2.9)	1 (5.9)	11 (1.5)	59 (3.4)	23 (2.9)	2 (2.5)	352 (2.8)
PR status, No. (%)								
Negative	—	3976 (26.2)	2 (12.5)	215 (29.5)	619 (37.7)	229 (29.6)	21 (26.9)	2908 (24.2)
Positive	—	11 147 (73.4)	14 (87.5)	509 (69.9)	1021 (62.1)	541 (70.0)	56 (71.8)	9040 (75.4)
Borderline	—	56 (0.4)	0 (0.0)	4 (0.5)	3 (0.2)	3 (0.4)	1 (1.3)	46 (0.4)
Missing[f]	—	510 (3.3)	1 (5.9)	16 (2.2)	69 (4.0)	24 (3.0)	2 (2.5)	398 (3.2)
Stage, No. (%)								
Early	—	10 852 (70.5)	11 (64.7)	512 (69.4)	1044 (62.3)	528 (67.3)	50 (63.3)	8743 (72.0)
Late	—	4532 (29.5)	6 (35.3)	226 (30.6)	633 (37.7)	256 (32.7)	29 (36.7)	3402 (28.0)
Missing[f]	—	305 (1.9)	0 (0.0)	6 (0.8)	35 (2.0)	13 (1.6)	1 (1.2)	247 (2.0)
Histologic type, No. (%)								
Ductal or lobular	—	14 548 (92.7)	13 (76.5)	688 (92.5)	1566 (91.5)	754 (94.6)	74 (92.5)	11504 (92.8)
Other	—	1141 (7.3)	4 (23.5)	56 (7.5)	146 (8.5)	43 (5.4)	6 (7.5)	888 (7.2)

(continued)

Table 1. (continued)

Variable	All residents[a]	All patients[a]	Racialized group (US census categories)[b]					
			American Indian or Alaska Native	Asian or Pacific Islander	Black	Hispanic	"Other" racialized group	White non-Hispanic
Grade, No. (%)								
Grade I	—	3202 (22.5)	6 (40.0)	117 (17.2)	248 (16.0)	134 (18.6)	14 (19.4)	2690 (23.9)
Grade II	—	6467 (45.4)	4 (26.7)	297 (43.6)	563 (36.4)	306 (42.4)	32 (44.4)	5291 (47.0)
Grade III	—	4545 (31.9)	5 (33.3)	266 (39.1)	734 (47.4)	282 (39.1)	26 (36.1)	3255 (28.9)
Grade IV	—	18 (0.1)	0 (0.0)	1 (0.1)	3 (0.2)	0 (0.0)	0 (0.0)	14 (0.1)
Missing[f]	—	1457 (9.3)	2 (11.8)	63 (8.5)	164 (9.6)	75 (9.4)	8 (10.0)	1142 (9.2)
Place of birth, No. (%)								
United States	—	6260 (72.6)	10 (83.3)	36 (7.6)	603 (52.1)	246 (41.5)	10 (20.4)	5362 (83.6)
Other Northern America	—	90 (1.0)	[d]	[d]	7 (0.6)	[d]	[d]	77 (1.2)
Latin America and Caribbean	—	814 (9.4)	[d]	[d]	420 (36.3)	339 (57.2)	29 (59.2)	93 (1.5)
Europe	—	762 (8.8)	[d]	[d]	35 (3.0)	6 (1.0)	[d]	716 (11.2)
Africa	—	148 (1.7)	[d]	[d]	91 (7.9)	[d]	6 (12.2)	48 (0.7)
Asia	—	548 (6.4)	[d]	429 (90.7)	[d]	[d]	[d]	116 (1.8)
Oceania	—	[d]	[d]	[d]	[d]	[d]	[d]	[d]
Missing[f]	—	7065 (45.0)	5 (29.4)	271 (36.4)	555 (32.4)	204 (25.6)	31 (38.8)	5979 (48.2)
Residential CT characteristics[h]								
No. of patients per CT								
Mean (SD)	—	12.8 (17.5)	1.2 (0.4)	2.8 (2.4)	5.2 (7.3)	2.7 (2.3)	1.1 (0.3)	26.9 (19.7)
Median (min, max)	—	4 (1,97)	1 (1, 2)	2 (1, 16)	2 (1, 58)	2 (1, 13)	1 (1, 2)	23 (1, 97)
Percent of residents foreign-born, No. (%)								
<10%	1 459 966 (13.6)	2451 (15.6)	[d]	44 (5.9)	80 (4.7)	105 (13.2)	4 (5.0)	2211 (17.9)
10%-19%	3 012 125 (28.0)	4972 (31.7)	[d]	169 (22.7)	306 (17.9)	152 (19.1)	14 (17.5)	4326 (34.9)
20%-29%	3 278 925 (30.5)	4705 (30.0)	7 (41.2)	256 (34.5)	538 (31.4)	213 (26.7)	25 (31.2)	3688 (29.8)
≥30%	2 999 651 (27.9)	3549 (22.6)	[d]	274 (36.9)	788 (46.0)	327 (41.0)	37 (46.2)	2156 (17.4)
Percent of residents below poverty, No. (%)								
<5%	2 043 249 (19.0)	4009 (25.6)	[d]	165 (22.2)	78 (4.6)	72 (9.0)	14 (17.5)	3675 (29.7)
5%-9%	2 600 167 (24.2)	4397 (28.0)	[d]	186 (25.0)	225 (13.1)	95 (11.9)	15 (18.8)	3871 (31.3)
10%-19%	3 431 351 (31.9)	4768 (30.4)	[d]	218 (29.3)	617 (36.0)	275 (34.5)	23 (28.8)	3647 (29.5)
≥20%	2 675 755 (24.9)	2503 (16.0)	9 (52.9)	174 (23.4)	792 (46.3)	355 (44.5)	28 (35.0)	1188 (9.6)
ICE for economic segregation, No. (%)								
Tercile 1 (highest concentration high-income households)	3 258 081 (30.3)	5935 (37.9)	[d]	272 (36.6)	173 (10.1)	97 (12.2)	17 (21.2)	5369 (43.4)
Tercile 2	3 425 309 (31.8)	5047 (32.2)	6 (35.3)	224 (30.1)	396 (23.1)	191 (24.0)	21 (26.2)	4213 (34.0)
Tercile 3	4 065 738 (37.8)	4695 (29.9)	9 (52.9)	247 (33.2)	1143 (66.8)	509 (63.9)	42 (52.5)	2799 (22.6)
ICE for racial segregation, No. (%)								
Tercile 1 (highest concentration non-Hispanic White residents)	843 580 (7.8)	1442 (9.2)	[d]	25 (3.4)	16 (0.9)	14 (1.8)	[d]	1375 (11.1)
Tercile 2	3 830 528 (35.6)	6772 (43.2)	[d]	289 (38.9)	168 (9.8)	153 (19.2)	16 (20.0)	6139 (49.6)
Tercile 3	6 076 558 (56.4)	7463 (47.6)	13 (76.5)	429 (57.7)	1528 (89.3)	630 (79.0)	62 (77.5)	4867 (39.3)

(continued)

Table 1. (continued)

Variable	All residents[a]	All patients[a]	Racialized group (US census categories)[b]					
			American Indian or Alaska Native	Asian or Pacific Islander	Black	Hispanic	"Other" racialized group	White non-Hispanic
ICE for racialized economic segregation, No. (%)								
Tercile 1 (highest concentration non-Hispanic White high-income households)	3 016 857 (28.0)	5504 (35.1)	[d]	249 (33.5)	117 (6.8)	88 (11.0)	17 (21.2)	5023 (40.6)
Tercile 2	3 119 345 (29.0)	4750 (30.3)	6 (35.3)	215 (28.9)	243 (14.2)	146 (18.3)	15 (18.8)	4131 (33.4)
Tercile 3	4 612 927 (42.9)	5423 (34.6)	9 (52.9)	279 (37.6)	1352 (79.0)	563 (70.6)	48 (60.0)	3227 (26.1)
ICE for home ownership, No. (%)								
Tercile 1 (highest concentration owner-occupied housing units)	1 365 091 (12.7)	2753 (17.6)	[d]	107 (14.4)	79 (4.6)	42 (5.3)	10 (12.5)	2509 (20.3)
Tercile 2	3 371 689 (31.3)	5827 (37.2)	[d]	222 (29.9)	387 (22.6)	164 (20.6)	18 (22.5)	5033 (40.7)
Tercile 3	6 012 348 (55.8)	7097 (45.3)	12 (70.6)	414 (55.7)	1246 (72.8)	591 (74.2)	52 (65.0)	4839 (39.1)
HOLC grade, No. (%)[i]								
A/Green	120 668 (1.1)	234 (1.5)	[d]	5 (0.7)	12 (0.7)	6 (0.8)	[d]	212 (1.7)
B/Blue	926 398 (8.6)	1517 (9.7)	[d]	63 (8.5)	114 (6.7)	47 (5.9)	4 (5.0)	1285 (10.4)
C/Yellow	4 214 152 (39.1)	5642 (36.0)	9 (52.9)	264 (35.5)	935 (54.6)	309 (38.8)	36 (45.0)	4126 (33.3)
D/Red	1 532 467 (14.2)	1716 (10.9)	5 (29.4)	99 (13.3)	368 (21.5)	183 (23.0)	15 (18.8)	1065 (8.6)
Mixed	1 041 296 (9.7)	1771 (11.3)	[d]	80 (10.8)	68 (4.0)	82 (10.3)	6 (7.5)	1533 (12.4)
No grade assigned	2 930 230 (27.2)	4809 (30.7)	[d]	233 (31.3)	215 (12.6)	170 (21.3)	17 (21.2)	4171 (33.7)

[a]Residents and patients resided—at time of diagnosis, for patients—in CTs in the following 28 Massachusetts municipalities with HOLC maps: Arlington, Belmont, Boston, Braintree, Brockton, Brookline, Cambridge, Chelsea, Chicopee, Dedham, Everett, Haverhill, Holyoke, Lexington, Malden, Medford, Melrose, Milton, Needham, Newton, Quincy, Revere, Saugus, Somerville, Waltham, Watertown, Winchester, Winthrop. ACS = American Community Survey; CT = census tract; ER = estrogen receptor; HOLC = Home Owners' Loan Corporation; ICE = Index of Concentration at the Extremes; PR = progesterone receptor; SD = standard deviation.

[b]99.5% of cancer patients have a single race reported, and for the remainder, race was reported as "unknown." Based on the availability of CT-level, census-defined, age-specific population data on racialized groups needed for estimating incidence rates, racialized group categories were constructed as follows: American Indian or Alaska Native, Asian or Pacific Islander, Black, Hispanic, Other, and White non-Hispanic.

[c]Complete descriptive data on individual characteristics, including small groups (eg, patients <5 and 5-14 years, identified as American Indian or Alaska Native, with grade IV tumors), are included for transparency, to enable us to report the original variables; avoid biasing the sample through selection by excluding them; and, regarding racialized group membership, to make visible groups that have historically and contemporaneously been rendered invisible in empirical analyses of cancer inequities.

[d]Indicates data suppression, as required by the authors' data use agreement with the Massachusetts Cancer Registry. Cells for which there are fewer than 5 patients from a population of <20 000 are suppressed.

[e]"Other" racialized group includes individuals identified in the Massachusetts Cancer Registry data as "some other known race" (information regarding a patient's racialized group could be abstracted from their medical records but could not be assigned to one of the other available codes) and individuals identified in the census data as "some other race alone" (individuals selected this category and none of the other available racial categories).

[f]Percent missing based on total; otherwise, distributions are based on observed cases only. Missingness between 0% and 0.2% (inclusive) for all variables with missingness not shown above.

[g]"—" indicates cells for which there are no applicable data (ie, cancer variables are not available or applicable for the general population of Massachusetts).

[h]Census tract ICE, poverty, and percent foreign-born measures are based on ACS 5-year annual estimates centered in the years 2008 (2006-2010), 2009 (2007-2011), 2010 (2008-2012), 2011 (2009-2013), 2012 (2010-2014), 2013 (2011-2015), 2014 (2012-2016), and 2015 (2013-2017). Census tract ICE, poverty, and percent foreign-born measures for the years 2005-2007 are based on linear interpolation using decennial census data for the year 2000 and the ACS 5-year estimate for 2008 (2006-2010) as anchors. All decennial census and ACS data are normalized to 2010 CT boundaries.

[i]Operational definition: A/Green = CTs whose land area is [(100% A) OR (≥50% A and <100% A)]; B/Blue = CTs whose land area is [(100% B) OR (≥50% B and <100% B)]; C/Yellow = CTs whose land area is [(100% C) OR (≥50% C and <100% C)]; D/Red = CTs whose land area is [(100% D) OR (≥50% D and <100% D)]; Mixed = no category with ≥50%; No grade assigned = ≥50% of land area is unknown.

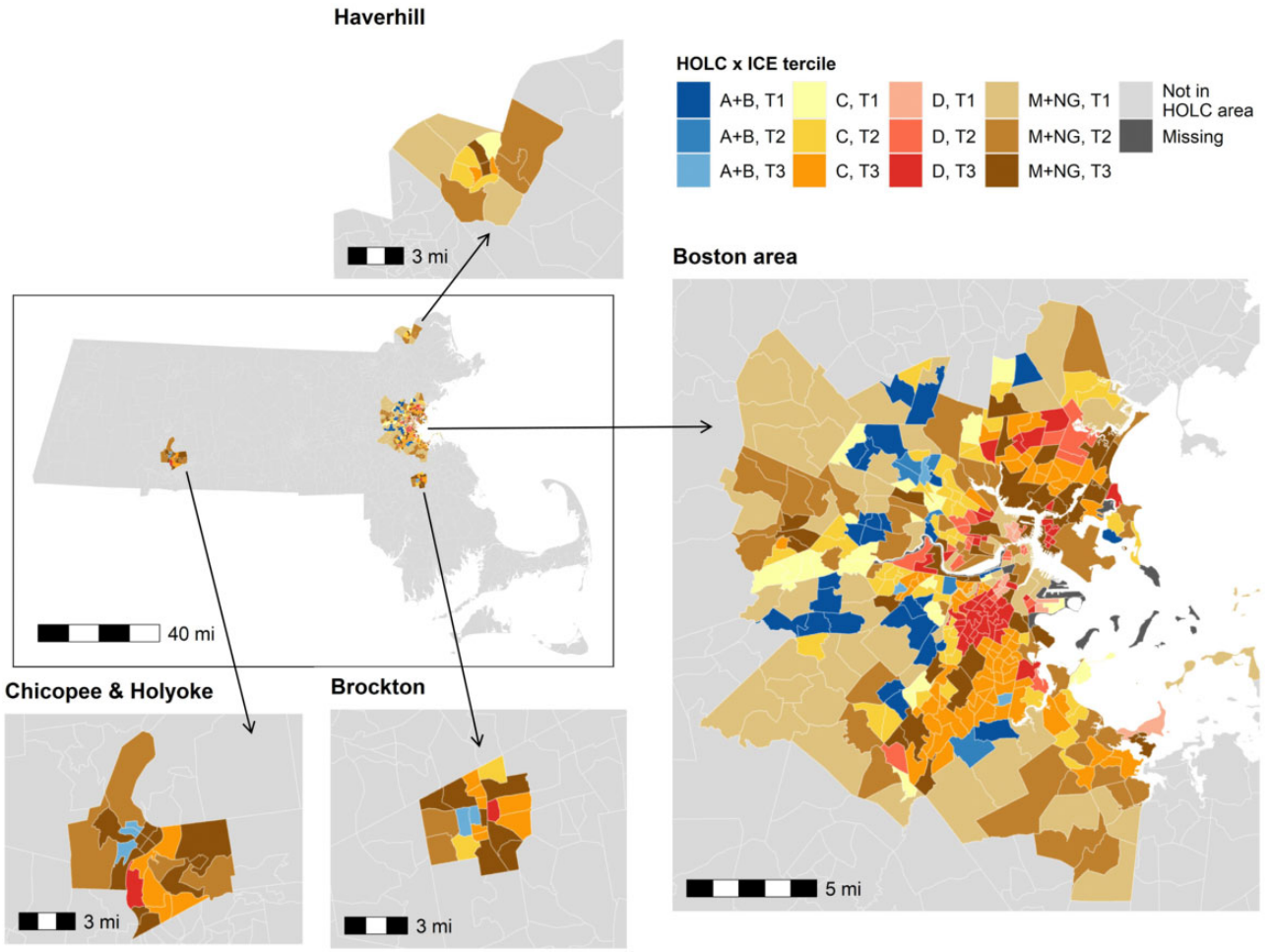

Figure 1. HOLC grade (1937-1938) by ICE for racialized economic segregation tercile (2005-2015) trajectories for Massachusetts CTs (n = 474), 2010 boundaries, in municipalities (n = 28) with 1930s HOLC maps. HOLC grade operational definition: A/Green = CTs whose land area is [(100% A) OR (≥50% A and <100% A)]; B/Blue = CTs whose land area is [(100% B) OR (≥50% B and <100% B)]; C/Yellow = CTs whose land area is [(100% C) OR (≥50% C and <100% C)]; D/Red = CTs whose land area is [(100% D) OR (≥50% D and <100% D)]; Mixed = no category with ≥50%; No grade assigned = ≥50% of land area is unknown. CT ICE measures were calculated for each year in the study period: 2005-2015. CT ICE measures are based on ACS 5-year annual estimates centered in the years 2008 (2006-2010), 2009 (2007-2011), 2010 (2008-2012), 2011 (2009-2013), 2012 (2010-2014), 2013 (2011-2015), 2014 (2012-2016), and 2015 (2013-2017). CT ICE measures for the years 2005-2007 are based on linear interpolation using decennial census data for the year 2000 and the ACS 5-year estimate for 2008 (2006-2010) as anchors. For these maps, CTs were assigned to the ICE tercile they most commonly (mode) were categorized as during the years in the study period. All decennial census and ACS data are normalized to 2010 CT boundaries. ACS = American Community Survey; CT = census tract; HOLC = Home Owners' Loan Corporation; ICE = Index of Concentration at the Extremes; M = mixed; NG = no grade; T1 = tercile 1 (highest concentration non-Hispanic White high-income households); T2 = tercile 2; T3 = tercile 3.

95% CI = 0.93 to 1.75), as well as in mixed and no grade CTs, in ways that varied by contemporary CT characteristics (mixed-T1, no grade-T2, no grade-T3 for ER-negative and mixed-T1, no grade-T2 for PR-negative BC). The lowest IRs were in CTs with T1 ICE and the lowest HOLC grade (D-T1 for ER-negative and PR-negative BC; eg, $IRR_{ER-;\ D\text{-}T1} = 0.84$, 95% CI = 0.56 to 1.25) and similarly low in D-T3 CTs for PR-negative BC.

Discussion

Results from our novel, exploratory study suggest that research on breast cancer inequities, including by hormone receptor status, would be strengthened by considering the impact of combined histories of redlining and contemporary residential CT characteristics. For all, ER-positive, and PR-positive BC, observed IR extremes (highest in CTs with the most contemporary privilege and mixed HOLC grade; lowest in CTs with most contemporary deprivation and no HOLC grade) suggest contemporary conditions may matter most, albeit modified by living in mixed HOLC areas or areas that were primarily industrial, commercial, or undeveloped and, thus, not assigned a HOLC grade in the 1930s (4). For ER-negative and PR-negative BC, evidence suggests that areas with the highest IRs (CTs with most contemporary deprivation and best HOLC grade) experienced a downward trajectory in their socioeconomic privilege, whereas areas with the lowest IRs (CTs with most contemporary privilege and worst HOLC grade) experienced an upward trajectory. We likewise found higher ER-negative and PR-negative BC incidence among those in the mixed and ungraded HOLC areas, in ways that varied by contemporary CT characteristics, again suggesting combined histories matter.

The strengths and limitations of our study must be considered. Although we accounted for age and racialized group, we lacked data on patients' household- or individual-level socioeconomic position or lifetime residential history. Thus, we cannot offer interpretations about the causal or mechanistic

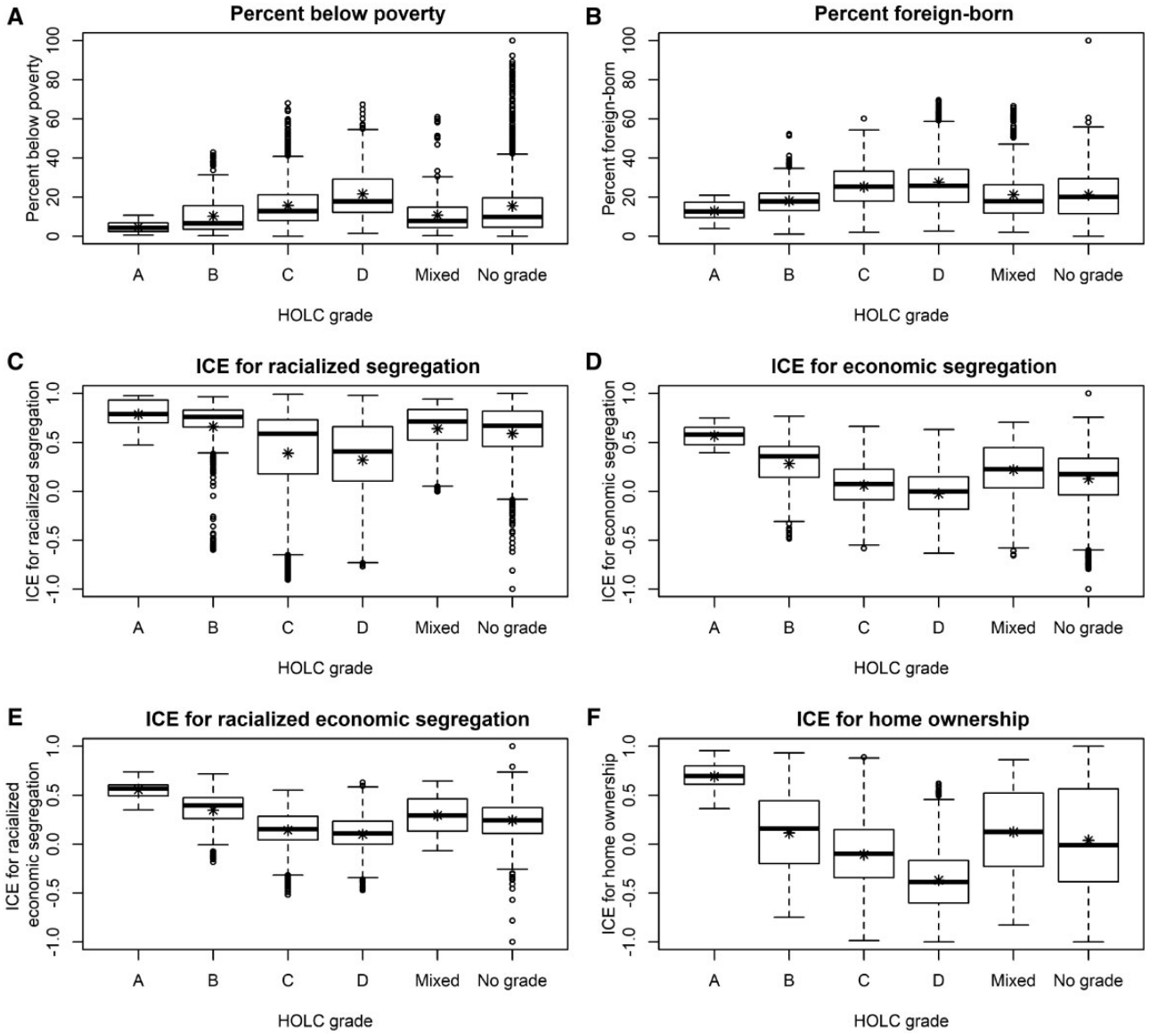

Figure 2. Boxplots of current CT characteristics (2005-2015; 2010 boundaries) by HOLC grade (1937-1938): 28 Massachusetts municipalities with HOLC maps (n = 474 CTs). Results for **(A)** percentage of persons living below the US federal poverty line, **(B)** percentage of persons foreign-born, **(C)** ICE for racialized segregation, **(D)** ICE for economic segregation, **(E)** ICE for racialized economic segregation, and **(F)** ICE for home ownership. Each boxplot within each panel visualizes—in order of the features arranged from the minimum to the maximum of the *y*-axis—the smallest value greater than the lower quartile minus 1.5 times the interquartile range, the lower quartile, the median value (**bold line**), the mean value (**asterisk**), the upper quartile, and the largest value less than the upper quartile plus 1.5 times the interquartile range for each variable. For each ICE variable, 1 = highest concentration of the most privileged group (100% of population); -1 = highest concentration of the most deprived group (100% of population). HOLC grade operational definition: A/Green = CTs whose land area is [(100% A) OR (≥50% A and <100% A)]; B/Blue = CTs whose land area is [(100% B) OR (≥50% B and <100% B)]; C/Yellow = CTs whose land area is [(100% C) OR (≥50% C and <100% C)]; D/Red = CTs whose land area is [(100% D) OR (≥50% D and <100% D)]; Mixed = no category with ≥50%; No grade assigned = ≥50% of land area is unknown. CT ICE, poverty, and foreign-born measures were calculated for each year in the study period: 2005-2015. CT measures are based on ACS 5-year annual estimates centered in the years 2008 (2006-2010), 2009 (2007-2011), 2010 (2008-2012), 2011 (2009-2013), 2012 (2010-2014), 2013 (2011-2015), 2014 (2012-2016), and 2015 (2013-2017). CT ICE measures for the years 2005-2007 are based on linear interpolation using decennial census data for the year 2000 and the ACS 5-year estimate for 2008 (2006-2010) as anchors. All decennial census and ACS data are normalized to 2010 CT boundaries. ACS = American Community Survey; CT = census tract; HOLC = Home Owners' Loan Corporation; ICE = Index of Concentration at the Extremes.

interaction of HOLC grade and ICE in relation to BC incidence (56,57). Combined histories of redlining and segregation shape selection processes into and out of neighborhoods (eg, in relation to socioeconomic position) as well as other complex, dynamic trajectories of people and areas (59,60) and, consequently, cumulative exposure to contexts relevant to breast cancer etiology. Furthermore, our estimates of additive interaction are not readily interpretable because HOLC grade and ICE tercile were variously protective across the BC types (61). Results should be interpreted as suggestive of effect heterogeneity and, more broadly, as a starting point for analyzing how HOLC grade and CT characteristics jointly shape present-day health inequities. Our definition of HOLC grades (ie, ≥50% land area) may dilute estimates for all, ER-positive, and PR-positive BC—compared with what would have been observed using a less stringent HOLC definition—if the excess risk associated with living in mixed-T1 CTs was attributed to A + B-T1 CTs and the reduced risk associated with no grade-T3 CTs was attributed

Table 2. Observed individual and residential CT characteristics among women diagnosed with primary invasive breast cancer, 2005-2015, in the 28 Massachusetts municipalities with 1930s HOLC maps (n = 474 CTs) vs in the Massachusetts municipalities without HOLC maps (n = 1004 CTs): Massachusetts Cancer Registry data (n = 60 173 patients)

Variable	All Massachusetts patients	HOLC status	
		HOLC[a]	No HOLC
Individual characteristics			
Total number of patients	60 173	15 689	43 012
Age at diagnosis			
Mean (SD)	62.3 (14.1)	61.9 (14.5)	62.4 (14.0)
Median (min, max)	62 (14, 111)	62 (21, 103)	62 (14, 111)
Racialized group, No. (%)			
American Indian or Alaska Native	55 (0.1)	17 (0.1)	36 (0.1)
Asian or Pacific Islander	1572 (2.6)	744 (4.7)	801 (1.9)
Black	2881 (4.8)	1712 (11.0)	1089 (2.5)
"Other" racialized group[b]	150 (0.3)	80 (0.5)	66 (0.2)
White, non-Hispanic	53 560 (89.4)	12 392 (79.4)	39 853 (93.0)
Missing[c]	231 (0.4)	84 (0.5)	141 (0.3)
Hispanic ethnicity, No. (%)			
Hispanic	2065 (3.4)	797 (5.1)	1226 (2.9)
Non-Hispanic	58 108 (96.6)	14 892 (94.9)	41 786 (97.1)
ER status, No. (%)			
Negative	9452 (16.1)	2465 (16.2)	6765 (16.2)
Positive	49 043 (83.8)	12 767 (83.8)	35 056 (83.7)
Borderline	62 (0.1)	9 (0.1)	52 (0.1)
Missing[c]	1616 (2.7)	448 (2.9)	1139 (2.6)
PR status, No. (%)			
Negative	15 604 (26.7)	3976 (26.2)	11 263 (27.0)
Positive	42 506 (72.8)	11 147 (73.4)	30 288 (72.5)
Borderline	287 (0.5)	56 (0.4)	227 (0.5)
Missing[c]	1776 (3.0)	510 (3.3)	1234 (2.9)
Stage, No. (%)			
Early	41 688 (70.6)	10 852 (70.5)	29 826 (70.6)
Late	17 390 (29.4)	4532 (29.5)	12 422 (29.4)
Missing[c]	1095 (1.8)	305 (1.9)	764 (1.8)
Histologic type, No. (%)			
Ductal or lobular	55 954 (93.0)	14 548 (92.7)	40 030 (93.1)
Other	4219 (7.0)	1141 (7.3)	2982 (6.9)
Grade, No. (%)			
Grade I	13 218 (24.3)	3202 (22.5)	9696 (25.0)
Grade II	24 769 (45.6)	6467 (45.4)	17 712 (45.6)
Grade III	16 285 (30.0)	4545 (31.9)	11 354 (29.2)
Grade IV	96 (0.2)	18 (0.1)	76 (0.2)
Missing[c]	5805 (9.6)	1457 (9.3)	4174 (9.7)

(continued)

Table 2. (continued)

Variable	All Massachusetts patients	HOLC status	
		HOLC[a]	No HOLC
Place of birth, No. (%)			
United States	30 328 (84.1)	6260 (72.6)	23 334 (87.8)
Other Northern America	343 (1.0)	90 (1.0)	249 (0.9)
Latin America and Caribbean	1571 (4.4)	814 (9.4)	730 (2.7)
Europe	2298 (6.4)	762 (8.8)	1488 (5.6)
Africa	290 (0.8)	148 (1.7)	133 (0.5)
Asia	1196 (3.3)	548 (6.4)	632 (2.4)
Oceania	17 (0.0)	[d]	15 (0.1)
Missing[c]	24 130 (40.1)	7065 (45.0)	16 431 (38.2)
Residential CT characteristics[e]			
No. patients per CT			
Mean (SD)	40.2 (20.8)	33.5 (19.8)	43.4 (20.5)
Median (min, max)	39 (1, 141)	30 (1, 103)	42 (1, 141)
Missing[c]	1472 (2.4)	0 (0.0)	0 (0.0)
Percent of residents foreign-born			
<10%	29 464 (50.2)	2451 (15.6)	27 013 (62.8)
10%-19%	16 320 (27.8)	4972 (31.7)	11 348 (26.4)
20%-29%	8059 (13.7)	4705 (30.0)	3354 (7.8)
≥30%	4846 (8.3)	3549 (22.6)	1297 (3.0)
Missing[c]	1485 (2.5)	12 (0.1)	3 (0.0)
Percent of residents below poverty, No. (%)			
<5%	22 524 (38.4)	4009 (25.6)	18 515 (43.0)
5%-9%	18 910 (32.2)	4397 (28.0)	14 513 (33.7)
10%-19%	11 119 (18.9)	4768 (30.4)	6351 (14.8)
≥20%	6133 (10.5)	2503 (16.0)	3630 (8.4)
Missing[c]	1487 (2.5)	12 (0.1)	3 (0.0)
ICE for economic segregation, No. (%)			
Tercile 1 (highest concentration high-income households)	24 203 (41.2)	5935 (37.9)	18 268 (42.5)
Tercile 2	20 713 (35.3)	5047 (32.2)	15 666 (36.4)
Tercile 3	13 770 (23.5)	4695 (29.9)	9075 (21.1)
Missing[c]	1487 (2.5)	12 (0.1)	3 (0.0)
ICE for racial segregation, No. (%)			
Tercile 1 (highest concentration non-Hispanic White residents)	22 875 (39.0)	1442 (9.2)	21 433 (49.8)
Tercile 2	22 118 (37.7)	6772 (43.2)	15 346 (35.7)
Tercile 3	13 696 (23.3)	7463 (47.6)	6233 (14.5)
Missing[c]	1484 (2.5)	12 (0.1)	0 (0.0)
ICE for racialized economic segregation, No. (%)			
Tercile 1 (highest concentration non-Hispanic White high-income households)	24 306 (41.4)	5504 (35.1)	18 802 (43.7)
Tercile 2	20 793 (35.4)	4750 (30.3)	16 043 (37.3)
Tercile 3	13 587 (23.2)	5423 (34.6)	8164 (19.0)
Missing[c]	1487 (2.5)	12 (0.1)	3 (0.0)

(continued)

Table 2. (continued)

Variable	All Massachusetts patients	HOLC status	
		HOLC[a]	No HOLC
ICE for home ownership, No. (%)			
Tercile 1 (highest concentration owner-occupied housing units)	24 184 (41.2)	2753 (17.6)	21 431 (49.8)
Tercile 2	22 006 (37.5)	5827 (37.2)	16 179 (37.6)
Tercile 3	12 496 (21.3)	7097 (45.3)	5399 (12.6)
Missing[c]	1487 (2.5)	12 (0.1)	3 (0.0)
HOLC grade, No. (%)[f]			
A/Green	234 (0.4)	234 (1.5)	0 (0.0)
B/Blue	1517 (2.6)	1517 (9.7)	0 (0.0)
C/Yellow	5642 (9.6)	5642 (36.0)	0 (0.0)
D/Red	1716 (2.9)	1716 (10.9)	0 (0.0)
Mixed	1771 (3.0)	1771 (11.3)	0 (0.0)
No grade assigned	4809 (8.2)	4809 (30.7)	0 (0.0)
Not in HOLC area	43 012 (73.3)	0 (0.0)	43 012 (100.0)
Missing[c]	1472 (2.4)	0 (0.0)	0 (0.0)

[a]Patients resided, at time of diagnosis, within CTs in the following 28 Massachusetts municipalities with HOLC maps: Arlington, Belmont, Boston, Braintree, Brockton, Brookline, Cambridge, Chelsea, Chicopee, Dedham, Everett, Haverhill, Holyoke, Lexington, Malden, Medford, Melrose, Milton, Needham, Newton, Quincy, Revere, Saugus, Somerville, Waltham, Watertown, Winchester, Winthrop. ACS = American Community Survey; CT = census tract; ER = estrogen receptor; HOLC = Home Owners' Loan Corporation; ICE = Index of Concentration at the Extremes; PR = progesterone receptor; SD = standard deviation.

[b]"Other" racialized group includes individuals identified in the Massachusetts Cancer Registry data as "some other known race" (information regarding a patient's racialized group could be abstracted from their medical records but could not be assigned to one of the other available codes) and individuals identified in the census data as "some other race alone" (individuals selected this category and none of the other available racial categories).

[c]Percent missing based on total; otherwise, distributions are based on observed cases only.

[d]Indicates data suppression, as required by the authors' data use agreement with the Massachusetts Cancer Registry. Cells for which there are fewer than 5 patients from a population of <20 000 are suppressed.

[e]Census tract ICE, poverty, and percent foreign-born measures are based on ACS 5-year annual estimates centered in the years 2008 (2006-2010), 2009 (2007-2011), 2010 (2008-2012), 2011 (2009-2013), 2012 (2010-2014), 2013 (2011-2015), 2014 (2012-2016), and 2015 (2013-2017). Census tract ICE, poverty, and percent foreign-born measures for the years 2005-2007 are based on linear interpolation using decennial census data for the year 2000 and the ACS 5-year estimate for 2008 (2006-2010) as anchors. All decennial census and ACS data are normalized to 2010 CT boundaries.

[f]Operational definition: A/Green = CTs whose land area is [(100%) A OR (≥50% A and <100% A)]; B/Blue = CTs whose land area is [(100% B) OR (≥50% B and <100% B)]; C/Yellow = CTs whose land area is [(100% C) OR (≥50% C and <100% C)]; D/Red = CTs whose land area is [(100% D) OR (≥50% D and <100% D)]; Mixed = no category with ≥50%; No grade assigned = ≥50% of land area is unknown.

Table 3. Incidence rates (age-standardized, per 100 000 person-years) and 95% confidence intervals of primary invasive breast cancer, 2005-2015, among women in the 28 Massachusetts municipalities with 1930s HOLC grades (n = 474 CTs), total and according to tumor hormone receptor status: imputed Massachusetts Cancer Registry data (n = 15 689 patients) and decennial Census and American Community Survey data (n = 10 765 212 residents)

	All breast cancer[b]	Hormone receptor status			
		ER-negative	ER-positive	PR-negative	PR-positive
Variable[a]	IR[c] (95% CI)[d]	IR (95% CI)	IR (95% CI)	IR (95% CI)	IR (95% CI)
Catchment area-wide rate	133.56 (131.45 to 135.70)	22.01 (21.14 to 22.90)	111.56 (109.63 to 113.51)	35.21 (34.12 to 36.32)	98.35 (96.53 to 100.20)
Age at diagnosis, y[e]					
<5	0.00 (0.00 to 0.68)	0.00 (0.00 to 0.68)	0.00 (0.00 to 0.68)	0.00 (0.00 to 0.68)	0.00 (0.00 to 0.68)
5-14	0.00 (0.00 to 0.37)	0.00 (0.00 to 0.37)	0.00 (0.00 to 0.37)	0.00 (0.00 to 0.37)	0.00 (0.00 to 0.37)
15-24	1.37 (0.87 to 2.06)	0.26 (0.07 to 0.64)	1.11 (0.67 to 1.75)	0.50 (0.22 to 0.97)	0.87 (0.48 to 1.44)
25-34	17.69 (15.87 to 19.67)	5.31 (4.33 to 6.44)	12.39 (10.87 to 14.05)	6.73 (5.63 to 7.99)	10.96 (9.54 to 12.54)
35-44	103.28 (98.07 to 108.70)	22.03 (19.66 to 24.61)	81.25 (76.63 to 86.07)	28.68 (25.97 to 31.60)	74.60 (70.18 to 79.23)
45-54	238.37 (230.34 to 246.60)	43.28 (39.90 to 46.87)	195.09 (187.83 to 202.55)	62.36 (58.29 to 66.64)	176.01 (169.12 to 183.10)
55-64	321.36 (311.17 to 331.79)	54.62 (50.47 to 59.03)	266.73 (257.46 to 276.25)	94.07 (88.59 to 99.79)	227.29 (218.74 to 236.09)
65-74	438.24 (423.56 to 453.29)	61.70 (56.28 to 67.51)	376.53 (362.94 to 390.50)	105.71 (98.57 to 113.23)	332.53 (319.76 to 345.67)
75-84	447.28 (429.58 to 465.53)	51.24 (45.37 to 57.66)	396.04 (379.39 to 413.23)	101.98 (93.62 to 110.88)	345.30 (329.77 to 361.38)
≥85	322.70 (302.82 to 343.55)	44.77 (37.57 to 52.96)	277.93 (259.51 to 297.32)	89.97 (79.62 to 101.29)	232.74 (215.90 to 250.54)
Racialized group[f]					
American Indian or Alaska Native	82.57 (46.17 to 134.89)	—[g]	75.97 (40.85 to 127.22)	—	72.22 (37.75 to 123.21)
Asian or Pacific Islander	83.15 (77.15 to 89.48)	14.64 (12.21 to 17.42)	68.50 (63.04 to 74.30)	24.72 (21.49 to 28.29)	58.43 (53.37 to 63.82)
Black	119.06 (113.45 to 124.87)	32.28 (29.40 to 35.37)	86.77 (81.97 to 91.78)	44.27 (40.89 to 47.85)	74.79 (70.33 to 79.45)
Hispanic	83.71 (77.63 to 90.11)	15.82 (13.31 to 18.65)	67.88 (62.38 to 73.72)	23.76 (20.64 to 27.19)	59.95 (54.74 to 65.49)
"Other" racialized group[h]	20.31 (15.75 to 25.71)	2.54 (1.04 to 4.95)	17.78 (13.53 to 22.85)	5.36 (3.18 to 8.34)	14.96 (11.05 to 19.71)
White, non-Hispanic	146.56 (143.91 to 149.25)	21.90 (20.85 to 22.98)	124.67 (122.23 to 127.14)	35.81 (34.49 to 37.17)	110.75 (108.44 to 113.10)
Percent of residents foreign-born					
<10%	138.57 (133.02 to 144.29)	23.69 (21.38 to 26.18)	114.88 (109.84 to 120.09)	37.91 (35.01 to 40.98)	100.66 (95.92 to 105.57)
10%-19%	144.24 (140.18 to 148.38)	22.79 (21.17 to 24.50)	121.45 (117.73 to 125.25)	36.06 (34.03 to 38.18)	108.18 (104.65 to 111.79)
20%-29%	133.77 (129.91 to 137.71)	20.66 (19.14 to 22.27)	113.11 (109.56 to 116.75)	34.50 (32.55 to 36.53)	99.27 (95.94 to 102.69)
≥30%	118.75 (114.84 to 122.75)	21.87 (20.20 to 23.64)	96.88 (93.35 to 100.50)	33.57 (31.50 to 35.75)	85.17 (81.86 to 88.59)
Percent of residents below poverty					
<5%	150.31 (145.58 to 155.15)	21.95 (20.12 to 23.90)	128.36 (124.00 to 132.83)	36.75 (34.40 to 39.21)	113.56 (109.44 to 117.80)
5%-9%	140.26 (136.06 to 144.54)	21.92 (20.25 to 23.69)	118.34 (114.49 to 122.28)	34.94 (32.84 to 37.15)	105.31 (101.67 to 109.05)
10%-19%	130.76 (127.03 to 134.58)	22.14 (20.60 to 23.77)	108.62 (105.22 to 112.10)	35.11 (33.16 to 37.14)	95.65 (92.45 to 98.94)
≥20%	110.04 (105.72 to 114.48)	22.38 (20.43 to 24.46)	87.66 (83.79 to 91.65)	34.28 (31.87 to 36.82)	75.76 (72.15 to 79.49)
ICE for economic segregation					
Tercile 1 (highest concentration high-income households)	149.73 (145.86 to 153.66)	22.18 (20.68 to 23.75)	127.55 (123.99 to 131.18)	36.67 (34.76 to 38.65)	113.06 (109.69 to 116.49)
Tercile 2	133.37 (129.67 to 137.16)	21.68 (20.19 to 23.26)	111.69 (108.30 to 115.15)	34.99 (33.09 to 36.97)	98.38 (95.19 to 101.65)
Tercile 3	118.16 (114.77 to 121.63)	22.32 (20.84 to 23.88)	95.85 (92.79 to 98.98)	34.11 (32.29 to 36.02)	84.05 (81.18 to 86.99)
ICE for racial segregation					
Tercile 1 (highest concentration non-Hispanic White residents)	137.36 (130.24 to 144.76)	20.39 (17.66 to 23.41)	116.97 (110.39 to 123.83)	33.13 (29.68 to 36.86)	104.23 (97.99 to 110.75)
Tercile 2	148.58 (144.98 to 152.25)	22.13 (20.72 to 23.61)	126.45 (123.14 to 129.83)	36.81 (35.01 to 38.69)	111.77 (108.64 to 114.96)
Tercile 3	122.07 (119.29 to 124.90)	22.28 (21.09 to 23.53)	99.79 (97.27 to 102.36)	34.48 (33.00 to 36.01)	87.60 (85.23 to 90.01)

(continued)

Table 3. (continued)

	All breast cancer[b]	Hormone receptor status			
		ER-negative	ER-positive	PR-negative	PR-positive
Variable[a]	IR[c] (95% CI)[d]	IR (95% CI)	IR (95% CI)	IR (95% CI)	IR (95% CI)
ICE for racialized economic segregation					
Tercile 1 (highest concentration non-Hispanic White high-income households)	149.55 (145.54 to 153.64)	21.15 (19.63 to 22.76)	128.40 (124.69 to 132.19)	35.88 (33.92 to 37.93)	113.67 (110.16 to 117.25)
Tercile 2	136.67 (132.75 to 140.68)	22.24 (20.64 to 23.92)	114.44 (110.84 to 118.11)	35.51 (33.48 to 37.64)	101.16 (97.76 to 104.64)
Tercile 3	118.94 (115.76 to 122.18)	22.68 (21.28 to 24.14)	96.26 (93.40 to 99.19)	34.61 (32.90 to 36.39)	84.33 (81.64 to 87.07)
ICE for home ownership					
Tercile 1 (highest concentration owner-occupied housing units)	152.11 (146.30 to 158.09)	23.98 (21.61 to 26.53)	128.13 (122.83 to 133.60)	38.86 (35.89 to 42.00)	113.25 (108.23 to 118.44)
Tercile 2	139.41 (135.79 to 143.11)	22.16 (20.70 to 23.69)	117.26 (113.94 to 120.64)	35.95 (34.10 to 37.87)	103.46 (100.33 to 106.67)
Tercile 3	124.04 (121.14 to 127.00)	21.55 (20.34 to 22.82)	102.49 (99.85 to 105.18)	33.78 (32.25 to 35.36)	90.26 (87.77 to 92.80)
HOLC grade[i]					
A + B	141.39 (134.72 to 148.30)	21.83 (19.18 to 24.73)	119.57 (113.44 to 125.93)	36.34 (32.96 to 39.96)	105.05 (99.30 to 111.05)
C	127.11 (123.78 to 130.51)	22.55 (21.14 to 24.03)	104.56 (101.53 to 107.65)	34.93 (33.19 to 36.74)	92.18 (89.33 to 95.09)
D	118.48 (112.89 to 124.27)	19.21 (16.97 to 21.65)	99.27 (94.15 to 104.61)	30.27 (27.45 to 33.29)	88.21 (83.36 to 93.26)
Mixed	147.23 (140.34 to 154.36)	22.82 (20.11 to 25.79)	124.40 (118.09 to 130.97)	37.28 (33.81 to 41.00)	109.95 (103.98 to 116.15)
No grade assigned	141.18 (137.12 to 145.32)	22.47 (20.82 to 24.21)	118.71 (114.98 to 122.51)	36.75 (34.66 to 38.92)	104.43 (100.93 to 108.02)

[a]Analyses were singly stratified by each variable. CI = confidence interval; CT = census tract; ER = estrogen receptor; ICE = Index of Concentration at the Extremes; IR = incidence rate; HOLC = Home Owners' Loan Corporation; PR = progesterone receptor.

[b]Patients resided, at time of diagnosis, within CTs in the following 28 MA municipalities with HOLC maps: Arlington, Belmont, Boston, Braintree, Brockton, Brookline, Cambridge, Chelsea, Chicopee, Dedham, Everett, Haverhill, Holyoke, Lexington, Malden, Medford, Melrose, Milton, Needham, Newton, Quincy, Revere, Saugus, Somerville, Waltham, Watertown, Winchester, Winthrop.

[c]Adjusted to the US year 2000 standard million.

[d]95% confidence intervals for age-standardized rates use the Dobson method. 95% confidence intervals for the age-specific rates use the exact method.

[e]Age-adjustment is not applied to age-specific rates.

[f]Based on the availability of CT-level, census-defined, age-specific population data on racialized groups needed for estimating incidence rates, racialized group categories were constructed as follows: American Indian or Alaska Native; Asian or Pacific Islander; Black; Hispanic; Other; White non-Hispanic. These categories are, thus, not fully mutually exclusive, because, for example, "Black" includes "Black, Hispanic" and "Black, not Hispanic" and "Hispanic" includes persons of all "races". We generate valid incidence rates for each named group (ie, the numerators and denominators match).

[g]"—" indicates cells for which no directly age-standardized rate should be published because fewer than 10 (1 to 2 for ER-negative and 2 to 4 for PR-negative, depending on the imputation) patients were observed in this stratum (54).

[h]"Other" racialized group includes individuals identified in the Massachusetts Cancer Registry data as "some other known race" (information regarding a patient's racialized group could be abstracted from their medical records but could not be assigned to one of the other available codes) and individuals identified in the census data as "some other race alone" (individuals selected this category and none of the other available racial categories).

[i]Operational definition: A/Green = CTs whose land area is [(100% A) OR (≥50% A and <100% A)]; B/Blue = CTs whose land area is [(100% B) OR (≥50% B and <100% B)]; C/Yellow = CTs whose land area is [(100% C) OR (≥50% C and <100% C)]; D/Red = CTs whose land area is [(100% D) OR (≥50% D and <100% D)]; Mixed = no category with ≥50%; No grade assigned = ≥50% of land area is unknown.

Table 4. Incidence rate ratios and 95% confidence intervals for all, ER-negative and -positive and PR-negative and -positive primary invasive breast cancer, 2005-2015, among women in the 28 Massachusetts municipalities with 1930s HOLC grades (n = 474 CTs): imputed Massachusetts Cancer Registry data (n = 15 689 patients) and decennial Census and American Community Survey data (n = 10 765 212 residents)

	All breast cancer[a]		ER-negative		ER-positive		PR-negative		PR-positive	
	Imputed		Imputed		Imputed		Imputed		Imputed	
	Model 1: Racialized group	Model 2:[c] Model 1 + ICE interaction	Model 1:[b] Racialized group	Model 2:[c] Model 1 + ICE interaction	Model 1:[b] Racialized group	Model 2:[c] Model 1 + ICE interaction	Model 1:[b] Racialized group	Model 2:[c] Model 1 + ICE interaction	Model 1:[b] Racialized group	Model 2:[c] Model 1 + ICE interaction
Variable	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)
Racialized group[d]										
American Indian or Alaska Native	0.29 (0.18 to 0.46)	0.30 (0.18 to 0.48)	0.05 (0.01 to 0.33)	0.05 (0.01 to 0.34)	0.29 (0.18 to 0.48)	0.30 (0.18 to 0.49)	0.08 (0.02 to 0.33)	0.08 (0.02 to 0.34)	0.28 (0.17 to 0.47)	0.29 (0.17 to 0.49)
Asian or Pacific Islander	0.60 (0.56 to 0.65)	0.60 (0.56 to 0.65)	0.69 (0.58 to 0.82)	0.69 (0.58 to 0.82)	0.58 (0.54 to 0.63)	0.59 (0.55 to 0.64)	0.73 (0.63 to 0.83)	0.73 (0.63 to 0.84)	0.56 (0.51 to 0.61)	0.56 (0.52 to 0.62)
Black	0.86 (0.81 to 0.90)	0.87 (0.82 to 0.92)	1.52 (1.36 to 1.69)	1.51 (1.34 to 1.70)	0.73 (0.69 to 0.78)	0.75 (0.70 to 0.80)	1.28 (1.17 to 1.41)	1.28 (1.16 to 1.42)	0.71 (0.66 to 0.76)	0.72 (0.68 to 0.78)
Hispanic	0.60 (0.56 to 0.64)	0.61 (0.57 to 0.66)	0.73 (0.62 to 0.86)	0.73 (0.61 to 0.86)	0.57 (0.53 to 0.62)	0.59 (0.54 to 0.64)	0.70 (0.61 to 0.80)	0.71 (0.61 to 0.81)	0.56 (0.52 to 0.61)	0.58 (0.53 to 0.63)
"Other" racialized group[e]	0.14 (0.11 to 0.17)	0.14 (0.11 to 0.17)	0.10 (0.05 to 0.19)	0.10 (0.05 to 0.19)	0.14 (0.11 to 0.18)	0.15 (0.12 to 0.19)	0.14 (0.09 to 0.22)	0.14 (0.09 to 0.22)	0.13 (0.10 to 0.17)	0.14 (0.10 to 0.18)
White non-Hispanic	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
HOLC grade main effect[f]										
A + B (best)	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent	Referent
C	0.97 (0.92 to 1.03)	0.97 (0.89 to 1.06)	1.01 (0.87 to 1.16)	1.09 (0.87 to 1.37)	0.96 (0.90 to 1.03)	0.94 (0.86 to 1.04)	0.97 (0.86 to 1.08)	1.01 (0.84 to 1.20)	0.97 (0.90 to 1.03)	0.95 (0.86 to 1.05)
D	0.94 (0.88 to 1.01)	0.95 (0.82 to 1.09)	0.87 (0.73 to 1.04)	0.84 (0.56 to 1.25)	0.96 (0.88 to 1.04)	0.94 (0.80 to 1.10)	0.85 (0.74 to 0.98)	0.88 (0.65 to 1.18)	0.97 (0.89 to 1.06)	0.97 (0.82 to 1.14)
Mixed	1.05 (0.98 to 1.12)	1.12 (1.03 to 1.22)	1.07 (0.90 to 1.27)	1.26 (1.01 to 1.58)	1.05 (0.97 to 1.13)	1.10 (1.01 to 1.21)	1.03 (0.90 to 1.18)	1.16 (0.98 to 1.38)	1.06 (0.98 to 1.14)	1.11 (1.01 to 1.23)
No grade	1.01 (0.95 to 1.07)	1.04 (0.97 to 1.13)	1.04 (0.90 to 1.21)	1.06 (0.87 to 1.31)	1.01 (0.94 to 1.07)	1.04 (0.96 to 1.13)	1.01 (0.90 to 1.14)	1.06 (0.91 to 1.24)	1.01 (0.94 to 1.08)	1.05 (0.96 to 1.15)
ICE for racialized economic segregation main effect										
T1 (highest concentration non-Hispanic White high-income households)	—[g]	Referent	—	Referent	—	Referent	—	Referent	—	Referent
T2	—	0.98 (0.85 to 1.12)	—	1.33 (0.95 to 1.86)	—	0.91 (0.78 to 1.06)	—	1.12 (0.85 to 1.48)	—	0.92 (0.78 to 1.09)
T3	—	1.07 (0.93 to 1.22)	—	1.27 (0.93 to 1.75)	—	0.98 (0.82 to 1.17)	—	1.23 (0.96 to 1.57)	—	1.00 (0.85 to 1.18)
HOLC[e] x ICE for racialized economic segregation interaction terms[h]										
C: Tercile 2	—	1.04 (0.89 to 1.22)	—	0.78 (0.53 to 1.16)	—	1.09 (0.91 to 1.30)	—	0.92 (0.67 to 1.26)	—	1.09 (0.90 to 1.31)
D: Tercile 2	—	1.04 (0.84 to 1.28)	—	0.92 (0.54 to 1.58)	—	1.09 (0.87 to 1.36)	—	0.95 (0.62 to 1.45)	—	1.08 (0.85 to 1.37)
M: Tercile 2	—	0.89 (0.74 to 1.08)	—	0.64 (0.40 to 1.01)	—	0.96 (0.79 to 1.18)	—	0.76 (0.52 to 1.10)	—	0.95 (0.76 to 1.18)
NG: Tercile 2	—	1.04 (0.89 to 1.21)	—	0.87 (0.60 to 1.27)	—	1.06 (0.89 to 1.25)	—	0.98 (0.72 to 1.32)	—	1.05 (0.88 to 1.26)
C: Tercile 3	—	0.92 (0.79 to 1.08)	—	0.78 (0.55 to 1.13)	—	0.98 (0.82 to 1.16)	—	0.82 (0.62 to 1.09)	—	0.97 (0.81 to 1.16)
D: Tercile 3	—	0.91 (0.74 to 1.10)	—	0.88 (0.53 to 1.45)	—	0.97 (0.77 to 1.22)	—	0.82 (0.56 to 1.22)	—	0.96 (0.76 to 1.21)
M: Tercile 3	—	0.81 (0.68 to 0.96)	—	0.67 (0.44 to 1.03)	—	0.85 (0.70 to 1.03)	—	0.73 (0.53 to 1.01)	—	0.84 (0.68 to 1.04)
NG: Tercile 3	—	0.83 (0.72 to 0.97)	—	0.87 (0.61 to 1.26)	—	0.84 (0.70 to 0.99)	—	0.78 (0.59 to 1.03)	—	0.86 (0.71 to 1.03)

[a]Patients resided, at time of diagnosis, within CTs in the following 28 Massachusetts municipalities with HOLC maps: Arlington, Belmont, Boston, Braintree, Brockton, Brookline, Cambridge, Chelsea, Chicopee, Dedham, Everett, Haverhill, Holyoke, Lexington, Malden, Medford, Melrose, Milton, Needham, Newton, Quincy, Revere, Saugus, Somerville, Waltham, Watertown, Winchester, Winthrop. CI = confidence interval; CT = census tract; ER = estrogen receptor; HOLC = Home Owners' Loan Corporation; ICE = Index of Concentration at the Extremes; IRR = incidence rate ratio; M = mixed; NG = no grade; PR = progesterone receptor; T1 = tercile 1 (highest concentration non-Hispanic White high-income households); T2 = tercile 2; T3 = tercile 3.

[b]Model 1: includes, separately, HOLC grade or ICE for racialized economic segregation terciles, controlling for racialized group.

[c]Model 2: controls for all variables in model 1 and additionally includes an interaction term between HOLC grade and ICE for racialized economic segregation.

[d]Based on the availability of CT-level, census-defined, age-specific population data on racialized groups needed for estimating incidence rates, racialized group categories were constructed as follows: American Indian or Alaska Native; Asian or Pacific Islander; Black; Hispanic; Other; White non-Hispanic. These categories are, thus, not fully mutually exclusive, because, for example, "Black" includes "Black, Hispanic" and "Black, not Hispanic," and "Hispanic" includes persons of all "races." We generate valid incidence rate ratios for each comparison of named groups (ie, for each named group, the numerators and denominators match and are mutually exclusive from that of the referent group).

[e]"Other" racialized group includes individuals identified in the Massachusetts Cancer Registry data as "some other known race" (information regarding a patient's racialized group could be abstracted from their medical records but could not be assigned to one of the other available codes) and individuals identified in the census data as "some other race alone" (individuals selected this category and none of the other available racial categories).

[f]Operational definition: A/Green = CTs whose land area is [(100% A) OR (≥50% A and <100% A)]; B/Blue = CTs whose land area is [(100% B) OR (≥50% B and <100% B)]; C/Yellow = CTs whose land area is [(100% C) OR (≥50% C and <100% C)]; D/Red = CTs whose land area is [(100% D) OR (≥50% D and <100% D)]; Mixed = no category with ≥50%; no grade assigned = ≥50% of land area is unknown.

[g]"—" indicates cells for which there are no applicable results because the indicated covariate was not included in the indicated model.

[h]The referent groups for this interaction analysis are best HOLC grade (A + B) and most privileged ICE tercile (T1).

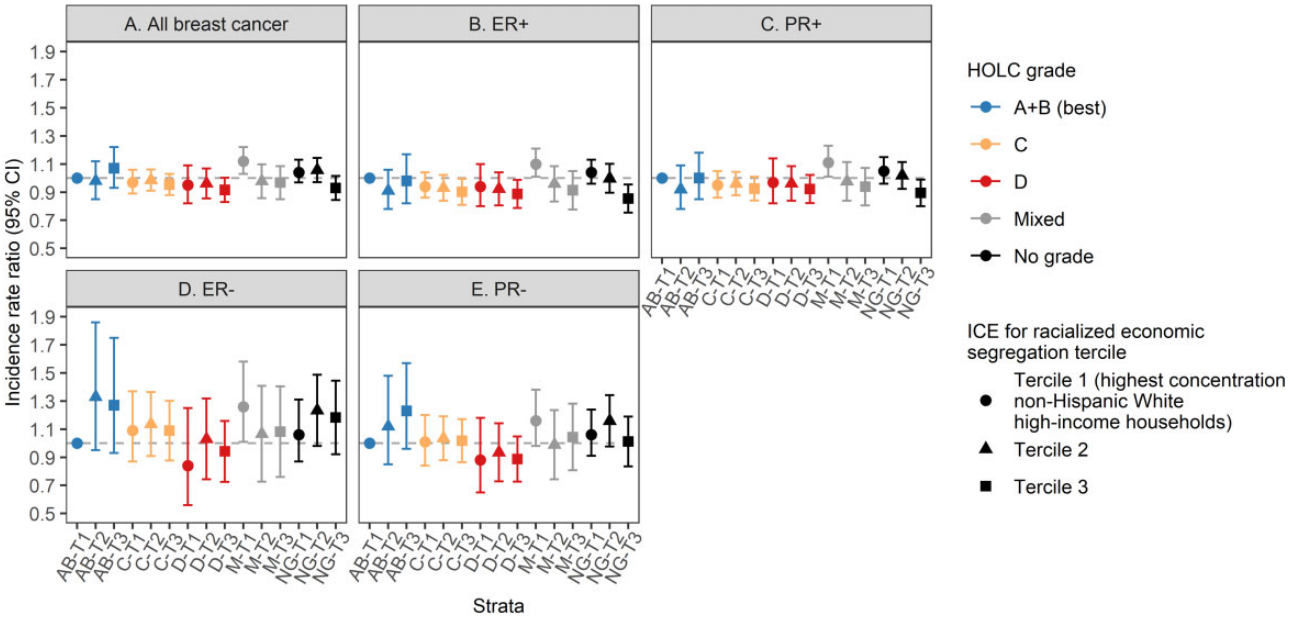

Figure 3. Incidence rate ratios and 95% confidence intervals, 2005-2015, of primary invasive breast cancer, overall and by tumor hormone receptor status, for combinations of historical HOLC grade and contemporary ICE for racialized economic segregation tercile: imputed Massachusetts Cancer Registry (n = 15 689 patients) and decennial Census and ACS data (n = 10 765 212 residents). Results for **(A)** all breast cancer combined, **(B)** ER-positive breast cancer, **(C)** PR-positive breast cancer, **(D)** ER-negative breast cancer, and **(E)** PR-negative breast cancer. HOLC grade operational definition: A/Green = CTs whose land area is [(100% A) OR (≥50% A and <100% A)]; B/Blue = CTs whose land area is [(100% B) OR (≥50% B and <100% B)]; C/Yellow = CTs whose land area is [(100% C) OR (≥50% C and <100% C)]; D/Red = CTs whose land area is [(100% D) OR (≥50% D and <100% D)]; Mixed = no category with ≥50%; No grade assigned = ≥50% of land area is unknown. CT ICE measures were calculated for each year in the study period: 2005-2015. CT measures are based on ACS 5-year annual estimates centered in the years 2008 (2006-2010), 2009 (2007-2011), 2010 (2008-2012), 2011 (2009-2013), 2012 (2010-2014), 2013 (2011-2015), 2014 (2012-2016), and 2015 (2013-2017). CT ICE measures for the years 2005-2007 are based on linear interpolation using decennial census data for the year 2000 and the ACS 5-year estimate for 2008 (2006-2010) as anchors. All decennial census and ACS data are normalized to 2010 CT boundaries. ACS = American Community Survey; CI = confidence interval; CT = census tract; ER- = estrogen receptor–negative breast cancer; ER+ = estrogen receptor–positive breast cancer; HOLC = Home Owners' Loan Corporation; ICE = Index of Concentration at the Extremes; M = mixed; NG = no grade; PR- = progesterone receptor–negative breast cancer; PR+ = progesterone receptor–positive breast cancer; T1 = tercile 1 (highest concentration non-Hispanic White high-income households); T2 = tercile 2; T3 = tercile 3.

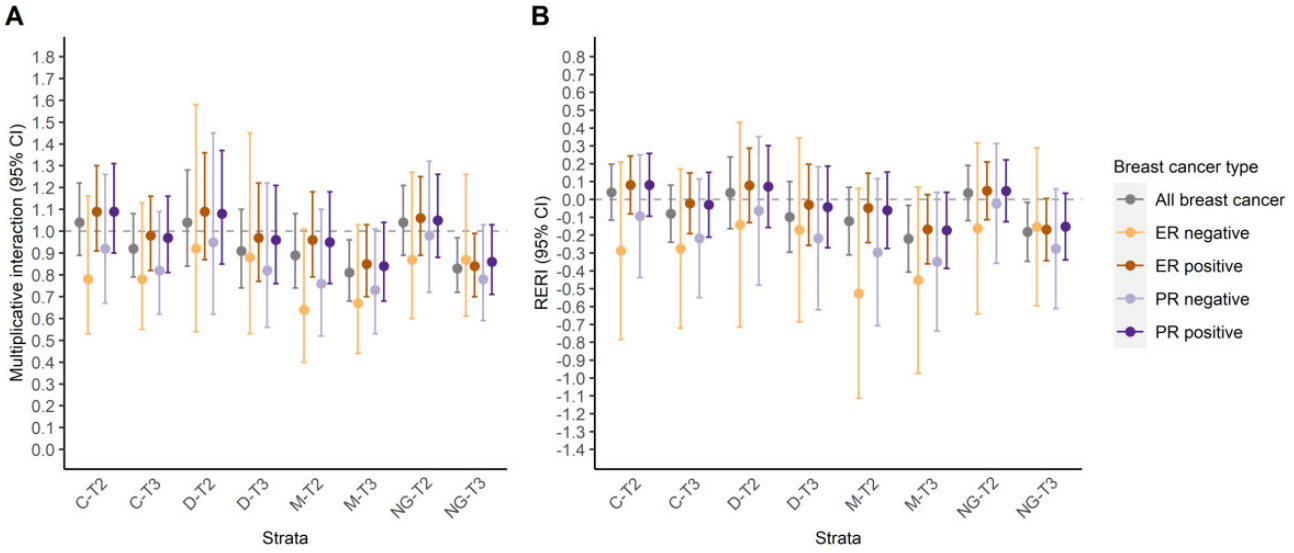

Figure 4. Measures of multiplicative and additive interaction and 95% confidence intervals, 2005-2015, for interactions between historical HOLC grade and contemporary ICE for racialized economic segregation tercile in relation to incidence rates of primary invasive breast cancer, overall and by tumor hormone receptor status: imputed Massachusetts Cancer Registry (n = 15 689 patients) and decennial Census and American Community Survey data (n = 10 765 212 residents). Results regarding **(A)** multiplicative interaction and **(B)** additive interaction. HOLC grade operational definition: A/Green = CTs whose land area is [(100% A) OR (≥50% A and <100% A)]; B/Blue = CTs whose land area is [(100% B) OR (≥50% B and <100% B)]; C/Yellow = CTs whose land area is [(100% C) OR (≥50% C and <100% C)]; D/Red = CTs whose land area is [(100% D) OR (≥50% D and <100% D)]; Mixed = no category with ≥50%; No grade assigned = ≥50% of land area is unknown. CT ICE measures were calculated for each year in the study period: 2005-2015. CT measures are based on ACS 5-year annual estimates centered in the years 2008 (2006-2010), 2009 (2007-2011), 2010 (2008-2012), 2011 (2009-2013), 2012 (2010-2014), 2013 (2011-2015), 2014 (2012-2016), and 2015 (2013-2017). CT ICE measures for the years 2005-2007 are based on linear interpolation using decennial census data for the year 2000 and the ACS 5-year estimate for 2008 (2006-2010) as anchors. All decennial census and ACS data are normalized to 2010 CT boundaries. ACS = American Community Survey; CI = confidence interval; CT = census tract; ER = estrogen receptor; HOLC = Home Owners' Loan Corporation; ICE = Index of Concentration at the Extremes; M = mixed; NG = no grade; PR = progesterone receptor RERI = relative excess risk due to interaction; T1 = tercile 1 (highest concentration non-Hispanic White high-income households); T2 = tercile 2; T3 = tercile 3.

to the C- and D-T3 CTs. Despite the strength of our multicity analysis of HOLC maps, results cannot be generalized to the rest of Massachusetts as these cities were geographically clustered around Massachusetts' largest city. Small numbers precluded conducting analyses simultaneously stratified by racialized group and hormone receptor status. Our study also did not account for spatial correlation among CTs or the available margins of error for ACS estimates. This is a focus of our ongoing work (62).

Two lines of evidence lend credibility to our findings that the combination of HOLC and current CT characteristics may shape risk. First, research on subtype-specific BC incidence has reported that for all BC, ER-positive, and PR-positive BC, the highest IRs are most commonly linked to individual and contemporary area-based measures of racialized and/or economic affluence (30,31,41,44,63-65). Moreover, for ER-negative and PR-negative BC, IRs are highest among women with low educational attainment or income and US-born Black women (44,64-66), but few have analyzed IR gradients by area-level characteristics (30,31). Second, new studies provide suggestive evidence regarding associations between historical redlining and increased health risk, across a range of outcomes, including birth outcomes, firearm injury, and our group's study on cancer stage at diagnosis (8-15). Still others show associations of historical redlining with adverse contextual exposures (eg, urban heat islands, alcohol retailers) that may shape health, including potentially BC risk (67-72).

Our findings support calls for research investigating the continued health implications of historical redlining and, by extension, other historical, explicitly unjust policies, singly and jointly with measures of present-day legacies of these policies (18). Our novel results add impetus for analyses in other contexts and, ideally, that combine multiple cities to provide sufficient sample sizes to do meaningful analyses by BC hormone receptor status and stratified by racialized group. Evidence from such research is highly relevant to ongoing policy debates regarding fair housing, economic development, and health equity (eg, disparate impact remedies under the Fair Housing Act, Low-Income Housing Tax Credits) (3,4,73) and civic discourse about historical redlining and societal accountability for its harmful impacts (eg, public exhibits, news articles, videos) (74-77). Analysis of the intertwined histories of redlining, neighborhood characteristics, and health indicates how theoretically and methodologically rigorous epidemiologic research on structural racism can produce needed evidence for understanding, rectifying, and preventing health inequities.

Funding

This work was supported by the American Cancer Society Clinical Research Professor Award to NK.

Notes

The role of the funder: The funder had no role in the design of the study; the collection, analysis, and interpretation of the data; the writing of the manuscript; and the decision to submit the manuscript for publication.

Disclosures: None of the authors have any conflicts of interest to disclose.

Author contributions: EW: project administration; visualization; formal analysis; writing—original draft; writing—review & editing; conceptualization; methodology; investigation; validation; data curation. PDW: data curation; project administration; writing—review & editing; conceptualization; visualization. CT: software; validation; writing—review & editing; data curation; conceptualization; formal analysis. JTC: conceptualization; data curation; software; methodology; investigation; validation; writing—review & editing; formal analysis; visualization; supervision. NK: conceptualization; funding acquisition; supervision; investigation; methodology; writing—review & editing.

Acknowledgements: The authors acknowledge Mariana Arcaya, PhD, and Eric Robsky Huntley, PhD, for their contributions to our recent published manuscript that developed the measure of historical redlining used here and examined its association with cancer stage at diagnosis in Massachusetts, which informed and enriched this current work. The authors also acknowledge the Massachusetts Cancer Registry staff for their support in procuring the cancer registry data.

Data Availability

The cancer data underlying this article cannot be shared publicly per the policies of the Massachusetts Cancer Registry (MCR) to protect the privacy of individuals whose information is collected in this registry, as stipulated in the requirements of the authors' Data Use Agreement with the MCR. All other data are publicly available at the referenced websites and using the referenced R packages.

References

1. Vaccarella S, Lortet-Tieulent J, Saracci R, Conway DI, Straif K, Wild CP, eds. *Reducing Social Inequalities in Cancer: Evidence and Priorities for Research*. Lyons, France: International Agency on Cancer Research (IARC); 2019. http://publications.iarc.fr/580. Accessed May 04, 2021.
2. Landrine H, Corral I, Lee JGL, Efird JT, Hall MB, Bess JJ. Residential segregation and racial cancer disparities: a systematic review. *J Racial Ethn Health Disparities*. 2017;4(6):1195–1205. doi:10.1007/s40615-016-0326-9.
3. Rothstein R. *The Color of Law: A Forgotten History of How Our Government Segregated America* 1st ed. New York, NY: Liveright Publishing Corporation; 2017.
4. Nelson RK, Winling L, Marciano R, et al. Mapping inequality: redlining in New Deal America, 1935-1940. In: RK Nelson, EL Ayers, eds. *American Panorama: An Atlas of United States History*. Richmond, VA: Digital Scholarship Laboratory, University of Richmond; 2019. https://dsl.richmond.edu/panorama/redlining/#loc=4/36.71/-96.93&opacity=0.8. Accessed October 13, 2020.
5. Aaronson D, Hartley DA, Mazumder B. *The Effects of the 1930s HOLC "Redlining" Maps*. Rochester, NY: Social Science Research Network; 2020. https://papers.ssrn.com/abstract=3038733. Accessed October 18, 2020.
6. Aaronson D, Faber J, Hartley D, Mazumder B, Sharkey P. The long-run effects of the 1930s HOLC "redlining" maps on place-based measures of economic opportunity and socioeconomic success. *Reg Sci Urban Econ*. 2021;86. doi:10.1016/j.regsciurbeco.2020.103622.
7. Faber JW. We built this: consequences of New Deal era intervention in America's racial geography. *Am Sociol Rev*. 2020;85(5):739–775. doi:10.1177/0003122420948464.
8. Benns M, Ruther M, Nash N, Bozeman M, Harbrecht B, Miller K. The impact of historical racism on modern gun violence: redlining in the city of Louisville, KY. *Injury*. 2020;51(10):2192–2198. doi:10.1016/j.injury.2020.06.042.
9. Huggins JC. A cartographic perspective on the correlation between redlining and public health in Austin, Texas-1951. *Cityscape*. 2017;19(2):267–280.
10. Jacoby SF, Dong B, Beard JH, Wiebe DJ, Morrison CN. The enduring impact of historical and structural racism on urban violence in Philadelphia. *Soc Sci Med*. 2018;199:87–95. doi:10.1016/j.socscimed.2017.05.038.
11. Krieger N, Van Wye G, Huynh M, et al. Structural racism, historical redlining, and risk of preterm birth in New York City, 2013-2017. *Am J Public Health*. 2020;110(7):1046–1053. doi:10.2105/AJPH.2020.305656
12. Krieger N, Wright E, Chen JT, Waterman PD, Huntley ER, Arcaya M. Cancer stage at diagnosis, historical redlining, and current neighborhood characteristics: breast, cervical, lung, and colorectal cancers, Massachusetts, 2001-2015. *Am J Epidemiol*. 2020;189(10):1065–1075. doi:10.1093/aje/kwaa045.
13. McClure E, Feinstein L, Cordoba E, et al. The legacy of redlining in the effect of foreclosures on Detroit residents' self-rated health. *Health Place*. 2019;55:9–19. doi:10.1016/j.healthplace.2018.10.004.

14. Nardone A, Casey JA, Morello-Frosch R, Mujahid M, Balmes JR, Thakur N. Associations between historical residential redlining and current age-adjusted rates of emergency department visits due to asthma across eight cities in California: an ecological study. *Lancet Planet Health*. 2020;4(1):e24–e31. doi:10.1016/S2542-5196(19)30241-4.
15. Nardone AL, Casey JA, Rudolph KE, Karasek D, Mujahid M, Morello-Frosch R. Associations between historical redlining and birth outcomes from 2006 through 2015 in California. *PLoS One*. 2020;15(8):e0237241. doi: 10.1371/journal.pone.0237241
16. Krieger N, Discrimination and health inequities. In: LF Berkman, I Kawachi, M Glymour, eds. *Social Epidemiology* 2nd ed. New York, NY: Oxford University Press; 2014:63–125.
17. Williams DR, Lawrence JA, Davis BA. Racism and health: evidence and needed research. *Annu Rev Public Health*. 2019;40:105–125. doi: 10.1146/annurev-publhealth-040218-043750.
18. Krieger N. Measures of racism, sexism, heterosexism, and gender binarism for health equity research: from structural injustice to embodied harm—an ecosocial analysis. *Annu Rev Public Health*. 2020;41:37–62. doi: 10.1146/annurev-publhealth-040119-094017.
19. Waks AG, Winer EP. Breast cancer treatment: a review. *JAMA*. 2019;321(3): 288–300. doi:10.1001/jama.2018.19323.
20. Krieger N. History, biology, and health inequities: emergent embodied phenotypes and the illustrative case of the breast cancer estrogen receptor. *Am J Public Health*. 2013;103(1):22–27. doi:10.2105/AJPH.2012.300967
21. Krieger N, Jahn JL, Waterman PD, Chen JT. Breast cancer estrogen receptor status according to biological generation: US Black and White women born 1915-1979. *Am J Epidemiol*. 2018;187(5):960–970. doi:10.1093/aje/kwx312
22. Krieger N, Jahn JL, Waterman PD. Jim Crow and estrogen-receptor-negative breast cancer: US-born black and white non-Hispanic women, 1992-2012. *Cancer Causes Control*. 2017;28(1):49–59. doi:10.1007/s10552-016-0834-2
23. Krieger N, Theoretical frameworks and cancer inequities. In: S Vaccarella, J Lortet-Tieulent, R Saracci, DI Conway, K Straif, CP Wild, eds. *Reducing Social Inequalities in Cancer: Evidence and Priorities for Research*. Lyons, France: International Agency on Cancer Research (IARC), 2019:111-120. http://publications.iarc.fr/580. Accessed May 04, 2021.
24. Krieger N, *Epidemiology and the People's Health: Theory and Context*. New York, NY: Oxford University Press; 2011.
25. Potischman N, Troisi R, Vatten L. A life course approach to cancer epidemiology. In: D Kuh, Y Ben-Shlomo, eds. *A Life Course Approach to Chronic Disease Epidemiology* 2nd ed. New York, NY: Oxford University Press; 2004:260–280. http://oxford.universitypressscholarship.com/view/10.1093/acprof:oso/9780198578154.001.0001/acprof-9780198578154. Accessed October 18, 2020.
26. Saini G, Ogden A, McCullough LE, Torres M, Rida P, Aneja R. Disadvantaged neighborhoods and racial disparity in breast cancer outcomes: the biological link. *Cancer Causes Control*. 2019;30(7):677–686. doi: 10.1007/s10552-019-01180-4
27. Carpenter DO, Bushkin-Bedient S. Exposure to chemicals and radiation during childhood and risk for cancer later in life. *J Adolesc Health*. 2013;52(suppl 5):S21–29. doi:10.1016/j.jadohealth.2013.01.027
28. Krieger N, Singh N, Waterman P. Metrics for monitoring cancer inequities: residential segregation, the Index of Concentration at the Extremes (ICE), and breast cancer estrogen receptor status (USA, 1992-2012). *Cancer Causes Control*. 2016;27(9):1139–1151. doi:10.1007/s10552-016-0793-7.
29. Linnenbringer E, Geronimus AT, Davis KL, Bound J, Ellis L, Gomez SL. Associations between breast cancer subtype and neighborhood socioeconomic and racial composition among Black and White women. *Breast Cancer Res Treat*. 2020;180(2):437–447. doi:10.1007/s10549-020-05545-1.
30. Palmer JR, Boggs DA, Wise LA, Adams-Campbell LL, Rosenberg L. Individual and neighborhood socioeconomic status in relation to breast cancer incidence in African-American women. *Am J Epidemiol*. 2012;176(12):1141–1146. doi:10.1093/aje/kws211
31. Akinyemiju TF, Pisu M, Waterbor JW, Altekruse SF. Socioeconomic status and incidence of breast cancer by hormone receptor subtype. *Springerplus*. 2015;4: 508–508. doi:10.1186/s40064-015-1282-2.
32. Fritz AG, Percy C, Jack A, et al. eds. *International Classification of Diseases for Oncology (ICD-O)* 3rd ed., first revision. Geneva: World Health Organization; 2013.
33. Massachusetts Department of Public Health Office of Data Management and Outcomes Assessment. Massachusetts Cancer Registry. https://www.mass.gov/massachusetts-cancer-registry. Accessed April 11, 2021.
34. Bureau of the Census, US Department of Commerce. Summary file 3 dataset. Census 2000. https://www.census.gov/data/datasets/2000/dec/summary-file-3.html. Published August 06, 2002. Accessed March 16, 2020.
35. Walker K, Herman M, Tidycensus: load US census boundary and attribute data as "tidyverse" and 'Sf'-Ready Data Frames; 2021. https://CRAN.R-project.org/package=tidycensus. Accessed September 14, 2020.
36. United Nations Statistics Division. Standard country or area codes for statistical use (M49): geographical regions. UNSD methodology. https://unstats.un.org/unsd/methodology/m49/. Accessed October 13, 2020.
37. ESRI. *ArcGIS, Release* 10.4.1; 2020. Redlands, CA: ESRI.
38. SAS Institute, Inc. *SAS, Version* 9.4. Cary, NC: SAS Institute, Inc.; 2019. https://www.sas.com/en_us/software/sas9.html. Accessed November 16, 2019.
39. Massey D, The prodigal paradigm returns: ecology comes back to sociology. In: A Booth, AC Crouter, eds. *Does It Take a Village?: Community Effects on Children, Adolescents, and Families*. Mahwah, NJ: Lawrence Erlbaum Associates; 2001:41–48.
40. Krieger N, Waterman PD, Spasojevic J, Li W, Maduro G, Van Wye G. Public health monitoring of privilege and deprivation with the Index of Concentration at the Extremes. *Am J Public Health*. 2016;106(2):256–263. doi: 10.2105/AJPH.2015.302955.
41. Krieger N, Feldman JM, Kim R, Waterman PD. Cancer incidence and multilevel measures of residential economic and racial segregation for cancer registries. *JNCI Cancer Spectr*. 2018;2(1):pky009. doi:10.1093/jncics/pky009.
42. Collaborative Stage Work Group of the American Joint Committee on Cancer. *Collaborative Stage Data Collection System User Documentation and Coding Instructions, Version 02.05*; 2014. Chicago, IL: American Joint Committee on Cancer. https://www.facs.org/quality-programs/cancer/ajcc/cs-schema. Accessed September 19, 2020.
43. Hammond MEH, Hayes DF, Dowsett M, et al. American Society of Clinical Oncology/College of American Pathologists Guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. *J Clin Oncol*. 2010;28(16):2784–2795. doi:10.1200/J Clin Oncol.2009.25.6529
44. Howlader N, Altekruse SF, Li CI, et al. US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. *J Natl Cancer Inst*. 2014; 106(5):dju055. doi:10.1093/jnci/dju055.
45. Szymiczek A, Lone A, Akbari MR. Molecular intrinsic versus clinical subtyping in breast cancer: a comprehensive review. *Clin Genet*. 2021;99(5):613–637. doi:10.1111/cge.13900
46. Perou CM, Sørlie T, Eisen MB, et al. Molecular portraits of human breast tumours. *Nature*. 2000;406:747–752. doi: 10.1038/35021093
47. Loibl S, Poortmans P, Morrow M, Denkert C, Curigliano G. Breast cancer. *Lancet*. 2021;397(10286):1750–1769. doi:10.1016/S0140-6736(20)32381-3
48. R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2021. https://www.R-project.org/. Accessed April 1, 2021.
49. van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *J Stat Softw*. 2011;45(3):1–67. doi:10.18637/jss.v045.i03.
50. Krieger N, Chen JT, Waterman PD, Soobader M-J, Subramanian SV, Carson R. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter?: the Public Health Disparities Geocoding Project. *Am J Epidemiol*. 2002;156(5):471–482. doi:10.1093/aje/kwf068.
51. Krieger N, Chen JT, Waterman PD, Rehkopf DH, Subramanian SV. Painting a truer picture of US socioeconomic and racial/ethnic health inequalities: the Public Health Disparities Geocoding Project. *Am J Public Health*. 2005;95(2): 312–323. doi:10.2105/AJPH.2003.032482.
52. Bureau of the Census, US Department of Commerce. Statistical brief: poverty areas; 1995. https://www.census.gov/library/publications/1995/demo/sb95-13.html. Accessed June 8, 2019.
53. Surveillance, Epidemiology, and End Results Program (SEER). National Cancer Institute. Standard populations (millions) for age-adjustment. Standard population data. https://seer.cancer.gov/stdpopulations/index.html. Accessed April 11, 2021.
54. Morris JK, Tan J, Fryers P, Bestwick J. Evaluation of stability of directly standardized rates for sparse data using simulation methods. *Popul Health Metr*. 2018;16(1):19. doi:10.1186/s12963-018-0177-1
55. Dobson AJ, Kuulasmaa K, Eberle E, Scherer J. Confidence intervals for weighted sums of poisson parameters. *Stat Med*. 1991;10(3):457–462. doi: 10.1002/sim.4780100317.
56. VanderWeele TJ, Knol MJ. A tutorial on interaction. *Epidemiol Methods*. 2014; 3(1):33–72. doi:10.1515/em-2013-0005.
57. VanderWeele T, *Explanation in Causal Inference: Methods for Mediation and Interaction*. New York, NY: Oxford University Press, 2015.
58. Rubin DB, *Multiple Imputation for Nonresponse in Surveys*. New York, NY: Wiley; 1987. http://hdl.handle.net/2027/mdp.39015049377727. Accessed April 6, 2021.
59. Barrett RE, Cho YI, Weaver KE, et al. Neighborhood change and distant metastasis at diagnosis of breast cancer. *Ann Epidemiol*. 2008;18(1):43–47. doi: 10.1016/j.annepidem.2007.07.001.
60. Gibbons J, Barton MS. The association of minority self-rated health with Black versus White gentrification. *J Urban Health*. 2016;93(6):909–922. doi: 10.1007/s11524-016-0087-0.
61. Knol MJ, VanderWeele TJ. Recommendations for presenting analyses of effect modification and interaction. *Int J Epidemiol*. 2012;41(2):514–520. doi: 10.1093/ije/dyr218.
62. Krieger N, Nethery RC, Chen JT, et al. Impact of differential privacy and census tract data source (decennial census versus American Community Survey) for monitoring health inequities. *Am J Public Health*. 2021;111(2): 265–268. doi:10.2105/AJPH.2020.305989.
63. Akinyemiju TF, Genkinger JM, Farhat M, Wilson A, Gary-Webb TL, Tehranifar P. Residential environment and breast cancer incidence and mortality: a systematic review and meta-analysis. *BMC Cancer*. 2015;15:191.doi: 10.1186/s12885-015-1098-z.

64. Newman LA. Breast cancer disparities: socioeconomic factors versus biology. *Ann Surg Oncol*. 2017;24(10):2869–2875. doi:10.1245/s10434-017-5977-1.
65. Williams DR, Mohammed SA, Shields AE. Understanding and effectively addressing breast cancer in African American women: unpacking the social context. *Cancer*. 2016;122(14):2138–2149. doi:10.1002/cncr.29935.
66. Dietze EC, Sistrunk C, Miranda-Carboni G, O'Regan R, Seewaldt VL. Triple-negative breast cancer in African-American women: disparities versus biology. *Nat Rev Cancer*. 2015;15(4):248–254. doi:10.1038/nrc3896.
67. Trangenstein PJ, Gray C, Rossheim ME, Sadler R, Jernigan DH. Alcohol outlet clusters and population disparities. *J Urban Health*. 2020;97(1):123–136. doi:10.1007/s11524-019-00372-2
68. Lee JP, Ponicki W, Mair C, Gruenewald P, Ghanem L. What explains the concentration of off-premise alcohol outlets in Black neighborhoods? *SSM Popul Health*. 2020;12:100669. doi:10.1016/j.ssmph.2020.100669
69. Schwartz E, Onnen N, Craigmile PF, Roberts ME. The legacy of redlining: associations between historical neighborhood mapping and contemporary tobacco retailer density in Ohio. *Health Place*. 2021;68:102529. doi:10.1016/j.healthplace.2021.102529.
70. Hoffman JS, Shandas V, Pendleton N. The effects of historical housing policies on resident exposure to intra-urban heat: a study of 108 US urban areas. *Climate*. 2020;8(12):1–15. doi:10.3390/cli8010012
71. Namin S, Xu W, Zhou Y, Beyer K. The legacy of the Home Owners' Loan Corporation and the political ecology of urban trees and air pollution in the United States. *Soc Sci Med*. 2020;246:112758. doi:10.1016/j.socscimed.2019.112758.
72. Nardone A, Rudolph KE, Morello-Frosch R, Casey JA. Redlines and greenspace: the relationship between historical redlining and 2010 greenspace across the United States. *Environ Health Perspect*. 2021;129(1):17006. doi:10.1289/EHP7495.
73. Metzger MW, Webber HS. *Facing Segregation: Housing Policy Solutions for a Stronger Society*. New York, NY: Oxford University Press; 2018.
74. Shiman LJ, Freeman K, Bedell J, Bassett MTM. Making injustice visible: how a health department can demonstrate the connection between structural racism and the health of whole neighborhoods. *J Public Health Manag Pract*. 2021;27(5):442–448. doi:10.1097/PHH.0000000000001259.
75. Plumer B, Popovich N, Palmer B. How decades of racist housing policy left neighborhoods sweltering. *The New York Times*. https://www.nytimes.com/interactive/2020/08/24/climate/racism-redlining-cities-global-warming.html. Published August 24, 2020. Published August 24, 2020. Accessed August 27, 2020.
76. Badger E. How redlining's racist effects lasted for decades. *The New York Times*. https://www.nytimes.com/2017/08/24/upshot/how-redlinings-racist-effects-lasted-for-decades.html. Published August 24, 2017. Accessed April 17, 2021.
77. Designing the WE. Undesign the redline. http://www.designingthewe.com/undesign-the-redline. Accessed April 17, 2021.