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## Temporal trends in the black/white breast cancer case ratio for estrogen receptor status: disparities are historically contingent, not innate

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### Abstract

**Objective**—For at least three decades, many investigators have reported on the US black/white breast cancer case ratio for estrogen receptor (ER) status as if it reflected an intrinsic biological difference. In light of racial/ethnic differences in declines in the incidence of ER+ breast cancer, as linked to changing use of hormone therapy, we empirically tested whether the black/white breast cancer estrogen receptor ratio has changed over time.

**Methods**—We examined temporal trends in the odds of being ER+ among white as compared to black women among all cases of invasive breast cancer occurring among women residing in the catchment area of the SEER 13 Registries Database between 1992 and 2005.

**Results**—During the study period, the odds of being ER+ among the white compared to black cases increased from 1992 to 2002 (a statistically significant joinpoint;  $p < 0.05$ ; peak odds ratio (2002) = 2.25 (95% confidence interval 2.13, 2.39)). Thereafter, the odds ratio leveled off (post-2002 slope not significantly different from zero;  $p = 0.326$ ). Among women aged 45–54, moreover, the post-2002 decline tended toward statistical significance ( $p = 0.0891$ ).

**Conclusions**—The results suggest the black/white breast cancer case estrogen receptor ratio is historically contingent, not innate.

### Keywords

Black; Breast cancer; Cancer disparities; Estrogen receptor; Social determinants of health; White

### Introduction

For at least three decades, many investigators have reported on the US black/white breast cancer case ratio for estrogen receptor (ER) status as if it reflected an intrinsic biological difference [1–5]. Suggesting it is timely to revisit this assumption, however, are two considerations. The first is new data on changes in the incidence of ER-positive (ER+) breast cancer as linked to declines in the use of hormone therapy [6,7], following the 2002 publication of the Women's Health Initiative (WHI) study, which found no benefit of hormone therapy for preventing cardiovascular disease while reconfirming elevated risk for breast cancer [8]. The second concerns well-known US racial/ethnic and socioeconomic disparities in use of hormone therapy, whereby use has been highest among white and more affluent women [9,10]. The net implication is that changes in hormone therapy use would be

likely result in changes in observed racial/ethnic differences in ER+ status among women with breast cancer.

Supporting the inference that the social patterning of ER status among breast cancer cases might change over time, we recently have reported that post-WHI declines in US breast cancer incidence rates were evident only among non-Hispanic white women living in affluent counties who had ER+ tumors [11]. Here, we present ancillary findings on the temporal trends, among the cases, for the odds of being ER+ among the non-Hispanic white as compared to black women diagnosed with breast cancer.

## Materials and methods

The study base consisted of all cases of primary invasive breast cancer among women residing in the catchment area of the public access SEER 13 Registries Database [12] from January 1, 1992 through December 31, 2005 and included 261,476 white non-Hispanic cases and 30,093 black non-Hispanic cases. Use of these de-identified public access county-level cancer registry data was approved as exempt by the Harvard School of Public Health Human Subjects Committee (HSC protocol #P14605-101).

Analytically, the first step was to calculate, for each year, the percent of observed ER+ tumors among the women, stratified by race/ethnicity and age, and compute the age-standardized percent, using the year 2000 standard million [13]. We additionally calculated the age-standardized 3-year average annual percent, for women of all ages and also stratified by age (<45, 45–54, and 55+ years old), for three time points: the start of the study period (1992–1994), the years immediately preceding and including publication of the WHI (2000–2002), and the post-WHI period (2003–2005). We then employed logistic regression models using a linear spline approach with a fixed joinpoint of 2002 [14], set at when the WHI was published, to model the temporal trend in the non-Hispanic white/black odds ratio for being ER+, using the yearly ER data and including age at diagnosis and cancer registry as covariates. We deliberately restricted these analyses to cases for whom ER data were available, so as to replicate the analytic approach used in prior studies on the black/white odds ratio for ER status [1–5]; in our discussion, we consider the implications of missing data for our results.

## Results

As shown in Fig. 1a, during the study period (1992–2005), the odds of being ER+ among the white compared to black cases increased from 1992 to 2002 (a statistically significant joinpoint;  $p < 0.05$ ), with the peak odds ratio in 2002 equal to 2.25 (95% CI 2.13, 2.39) (fitted estimate based on the joinpoint model). Thereafter, the white/black odds ratio leveled off (post-2002 slope not significantly different from zero;  $p = 0.326$ ). As shown by Fig. 1b, this trend was most pronounced among women aged 45–54 years old (post-2002 decline in the odds ratio tending toward statistical significance;  $p = 0.0819$ ). By contrast, among women age 55 and older and also under age 45, the post-2002 decline in the odds ratio was not statistically significant ( $p$  values of 0.4633 and 0.4177, respectively).

Driving these temporal change in the odds ratio were changes in the percent of ER+ tumors, which varied by time period, race/ethnicity, and age (Table 1). Among both the non-Hispanic white and non-Hispanic black women in all three age groups (<45, 45–54, and 55+ years old), the percent increased from 1992 to 1994 through 2000–2002 (except among non-Hispanic black women under age 45, for whom it remained stable). Thereafter, the percent of ER+ tumors either leveled off or decreased slightly in each of these groups of women.

## Discussion

Our study, based on US national cancer registry data, is the first to quantify and test for temporal trends in the odds ratio for comparisons of the observed ER status among black and white women with breast cancer. Results indicate that between 1992 and 2005, the odds for being ER+ among US non-Hispanic white as compared to black women diagnosed with breast cancer increased until 2002 and then leveled off, especially among women aged 45–54. These changes are temporally consistent with reported patterns of hormone therapy use preceding and then following publication of the WHI in 2002, whereby usage before the WHI was highest among newly menopausal and postmenopausal white and/or more affluent women, and with only women who used hormone therapy before the WHI being eligible to stop using hormone therapy after the WHI [9,10]. Additional research, from epidemiologic to basic science, has provided robust evidence that use of hormone therapy increases risk of ER+ breast cancer tumors [6,7,15].

A distinguishing feature of our study is our focus on temporal trends in the black/white difference in the observed ER status among women diagnosed with breast cancer. Most studies comparing the black/white odds among breast cancer cases for being ER+ typically have focused on cases diagnosed in a given year or in a small set of years, with results nonetheless often interpreted as if they constituted a time-invariant intrinsic racial/ethnic difference [1–5]. Yet, as demonstrated by other research on temporal changes in the magnitude of health inequities, both the size and direction of socioeconomic as well as racial/ethnic disparities in health can change over time [16,17]. Well-known examples include the class shift in smoking, and hence, smoking-related diseases, from professionals to the working class over the course of the twentieth century in wealthy countries [18,19], and also the US white/black reversal of breast cancer mortality rates, whereby in the mid-20th century, the age-adjusted breast cancer mortality rate was higher among white women, but by the mid-1980s was higher among black women [20,21].

We further note that we specifically restricted our study to analysis of only cases with observed ER status, so that our results could be compared to prior studies of the black/white odds ratio for ER status, which used data only on observed cases and did not take into account the impact of missing ER data [1–5]. In prior research, however, we have demonstrated that the black/white odds ratio for being ER– is biased upwards when analyses do not take into account the greater prevalence of missing data on ER status among women who live in less-affluent census tracts; we additionally have shown that the age-standardized statistically significant excess in risk of ER status unknown among black compared to white women was rendered statistically non-significant by controlling for socioeconomic position [22]. In our study of racial/ethnic and socioeconomic differentials in the decline of breast cancer incidence following publication of the WHI [11] (using the same case data as employed in this current study), we consequently included analysis of trends in the incidence of tumors with ER status unknown, as well as for tumors that were ER+ and ER–. Relevant to interpretation of our results for trends in the white/black odds ratio in ER+ tumors, we found that these incidence rates, for breast cancer with ER status unknown, were (1) among both the black and white women highest among women age 65 and older, followed by the women aged 50–69, but negligible among those under age 50, and also that (2) the socioeconomic gap, among women age 50 and older, was greater among the black as compared to white women [11]. The net implication is to suggest our present study's findings likely underestimate the magnitude of temporal changes in the white/black odds ratio for ER+ tumors.

In summary, our results provide novel evidence that the black/white breast cancer case estrogen receptor ratio is historically contingent, not innate. The larger implication is that

research on racial/ethnic disparities involving tumor biology—and health status more generally—should not automatically assume that observed differences are fixed and reflect intrinsic biology. Instead, also meriting consideration is the alternative hypothesis, supported by considerable evidence, that societal conditions shape the expression of observed biological characteristics and hence the existence of—and trends in—the magnitude of health inequities [16,17,23–25].

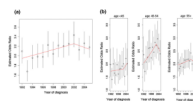
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**Fig. 1.** Odds ratio for breast cancer cases that are estrogen receptor positive (ER+), adjusted for age and cancer registry, comparing non-Hispanic white to non-Hispanic black women: a all ages; b stratified by age: <45, 45–54, ≥55: US SEER 13 Registries Database (1992–2005)

**Table 1**

Total number (*n*) and average annual age-standardized percent of primary invasive breast cancer cases that are estrogen receptor positive (ER+) among non-Hispanic white women (*n* = 261,476) and non-Hispanic black women (*n* = 30,093), overall and by age: US SEER 13 Registries Database (1992–2005)

Years	All ages		<45 years old		45–54 years old		55+ years old									
	White <i>n</i>	Black <i>n</i>	White <i>n</i>	Black <i>n</i>	White <i>n</i>	Black <i>n</i>	White <i>n</i>	Black <i>n</i>								
1992–1994	30,318	63	2,265	53	2,940	50	395	44	5,218	70	456	53	22,160	81	1,414	67
1995–1999	60,695	68	4,666	53	5,599	58	757	45	11,914	74	1,066	55	43,182	82	2,843	69
2000–2002	40,227	75	3,312	52	3,633	70	528	43	8,079	77	780	56	28,515	84	2,004	70
2003–2005	39,206	73	3,966	52	3,705	66	634	43	8,375	77	935	57	27,126	82	2,397	69

Age standardized to the Year 2000 standard million