Twenty-Five Year Trends in the Incidence of Ductal Carcinoma in Situ in US Women

Tawakalitu O Oseni, MD, FACS, Biqi Zhang, BS, Suzanne B Coopey, MD, FACS, Michele A Gadd, MD, FACS, Kevin S Hughes, MD, FACS, David C Chang, PhD, MPH, MBA

BACKGROUND: The rising incidence of ductal carcinoma in situ (DCIS) since the widespread enactment of mammography screening has been well documented. Patterns in DCIS incidence among women of various ages and across different racial and ethnic groups have not been well described.

STUDY DESIGN: The Surveillance, Epidemiology, and End Results public-use data set was queried for all women aged 40 years and older diagnosed with DCIS between 1990 and 2014. Annual age-adjusted incidence rates were compared among white, black, Hispanic, and Asian-Pacific Islander women. Additionally, using mammography screening data obtained from the CDC, patterns in mammography screening over time and as they relate to DCIS incidence rates by race and ethnicity were evaluated.

RESULTS: We identified 200,400 women aged 40 years or older with DCIS. Between 1998 and 2014, a period that saw flux in national breast screening guidelines, DCIS incidence rates increased in blacks, Hispanics, and Asian-Pacific Islanders, but remained relatively unchanged in whites (increase in number of DCIS diagnoses per 100,000 individuals in the population per year among blacks +0.66/p < 0.01, Hispanics +3.0/p < 0.01, Asian-Pacific Islanders +0.53/p < 0.01, and whites +0.07/p = 0.21). After accounting for age, year of diagnosis, and mammography screening rates, DCIS incidence was found to be similar between white and black women (0.8 fewer diagnoses per 100,000 individuals compared with whites; p = 0.36) but lower for Hispanic women (9.7 fewer diagnoses per 100,000 individuals compared with whites; p < 0.01).

CONCLUSIONS: The DCIS incidence rates are influenced substantially by breast cancer mammography screening patterns. However, differences exist by race and ethnicity and are not fully explained by screening mammography trends alone. Consideration should be given to including race and ethnicity in determining optimal breast screening guidelines. (J Am Coll Surg 2019;228:932–939. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

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From the Department of Surgery (Oseni, Zhang, Coopey, Gadd, Hughes, Chang) and Codman Center for Clinical Effectiveness in Surgery (Chang), Massachusetts General Hospital, Boston, MA.

Correspondence address: Tawakalitu O Oseni, MD, FACS, Department of Surgery, Massachusetts General Hospital, 55 Fruit St, Yawkey 7, Boston, MA 02114. email: toseni@mgh.harvard.edu

Since the mid-1980s, there has been widespread adoption of screening mammography among women in the US.[1] Concomitant with this trend has been the rising incidence of invasive breast cancers (IBCs).[2,3] Studies of IBC have revealed subgroup differences by race and ethnicity; relative to white women, black women are more likely to present with hormone receptor-negative IBC, later-stage disease, and at younger ages.[4,5] It is possible that trends in the incidence of ductal carcinoma in situ (DCIS) also differ by race and ethnicity. Current US Preventative Task Force screening guidelines do not reflect the impact of race and ethnicity on breast cancer incidence. Breast cancer screening recommendations can be improved by identifying subgroups of women who are at increased risk for disease.

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Abbreviations and Acronyms
API = Asian-Pacific Islander
DCIS = ductal carcinoma in situ
IBC = invasive breast cancer
SEER = Surveillance, Epidemiology, and End Results

To highlight the need to consider race and ethnicity when optimizing breast cancer screening for women, we sought to identify differences in national trends of DCIS incidence and the impact of breast cancer screening by race and ethnicity. We hypothesized that the relationship between mammography screening and DCIS incidence rates vary by racial and ethnic group.

METHODS

Ductal carcinoma in situ incidence rates

To evaluate DCIS incidence patterns over time for differences by race and ethnicity, we conducted a retrospective cohort analysis of women aged 40 years and older diagnosed with DCIS between 1990 and 2014 in the Surveillance, Epidemiology and End Results (SEER) public-use data set. The SEER program was established by the National Cancer Institute in 1973 to collect cancer incidence and survival information from numerous registries throughout the US. Currently, SEER publishes cancer data including patient demographics, tumor characteristics, and treatment use covering approximately 28% of the US population.[6]

In this study, DCIS was defined as behavioral type carcinoma in situ (ICD for Oncology, 3rd edition, code 2). Patients with ICD for Oncology, 3rd edition codes of 8520/2 (lobular carcinoma in situ), 8522/2 (intraductal and lobular carcinoma in situ), and 8720/2 (melanoma in situ) were excluded.

The DCIS incidence rates were calculated using SEER county population estimates, which are modifications of population data collected by the US Census Bureau's Population Estimates Program and the National Center for Health Statistics, with support from the National Cancer Institute.[7] Because detailed race and ethnicity information is only available in the SEER population data set from 1992 onward, 1992 population data were used to calculated DCIS incidence rates for 1990 and 1991.

Race and ethnicity was grouped into mutually exclusive categories of non-Hispanic white (white), non-Hispanic black (black), Hispanic, and Asian-Pacific Islander (API). Age was operationalized as a categorical variable with 3 levels to match mammography screening data from the CDC: age 40 to 49 years, 50 to 64 years, and 65 years and older.

Mammography screening rates

To assess patterns in mammography screening over time and test the relationship between screening and DCIS incidence, we obtained screening data for US women aged 40 years and older from the CDC.[8] White, black, Hispanic, and API race and ethnicity, as defined in our study, were matched to CDC data for non-Hispanic/Latina whites, non-Hispanic/Latina blacks/African Americans, Hispanics, and Asians, respectively. Screening data for API women by age group is not available, so API women were not included in multivariate linear regression analyses where age was a covariate.

Statistical testing

Trends in DCIS incidence during the study period were described for the general population of women aged 40 years and older and then by racial and ethnic group. Multivariate linear regression was performed to analyze the association between DCIS incidence rate and year after adjusting for race and ethnicity and age group. A second regression was performed to assess the impact of mammography screening rates on DCIS incidence with calendar year, age group, and race and ethnicity as covariates.

The significance level was set at $\alpha = 0.05$. All statistical analyses were performed using STATA 13 (Stata Corp).

RESULTS

Trends in ductal carcinoma in situ incidence

We identified 200,400 women aged 40 years and older with DCIS in SEER and included in our analyses of DCIS incidence rates (Table 1).

On unadjusted analysis, the incidence rate of DCIS in the general population of women aged 40 years and older increased continually through the 1990s before plateauing after 1998 (Fig. 1A). Between 1990 and 1998, the incidence rate rose from 12.5 to 30.2 per 100,000 individuals, representing a nearly 2.5-fold increase in less than a decade. From 1998 to 2014, there was little change in DCIS incidence in the general population: 30.2 to 31.8 cases per 100,000 individuals, respectively. There were, however, differences in trends between 1998 to 2014 by race and ethnicity. Although the DCIS incidence rate remained relatively unchanged for white women during this period, it continued to increase for black, Hispanic, and API women (Fig. 1B). This trend persisted after adjusting for age at diagnosis.

Although DCIS incidence rose significantly for all women across the study period, the increase in incidence rate was higher for API and black women (average yearly increase in number of DCIS cases diagnosed per 100,000 APIs: +1.04; 95% CI +0.91 to +1.16, blacks: +1.01;

Table 1. US Women Aged 40 Years and Older Diagnosed with Ductal Carcinoma in Situ of the Breast by Racial and Ethnic Group, Surveillance, Epidemiology, and End Results Database, 1990 to 2014

Variable	Total	White	Black	Hispanic	Asian-Pacific Islander
Total n	200,440	143,564	20,343	16,640	18,783
Year of diagnosis, n (%)					
1990–1994	11,293 (5.63)	8,988 (6.26)	870 (4.28)	550 (3.31)	839 (4.47)
1995–1999	19,786 (9.87)	14,975 (10.43)	1,710 (8.41)	1,188 (7.14)	1,803 (9.60)
2000–2004	48,794 (24.34)	36,785 (25.62)	4,477 (22.01)	3,413 (20.51)	3,895 (20.74)
2005–2009	57,307 (28.59)	40,799 (28.42)	5,915 (29.08)	4,967 (29.85)	5,346 (28.46)
2010–2014	63,260 (31.56)	42,017 (29.27)	7,371 (36.23)	6,522 (39.19)	6,900 (36.74)
Age at diagnosis					
40–49 y, n (%)	41,821 (20.86)	27,736 (19.32)	4,170 (20.50)	4,599 (27.64)	5,030 (26.78)
50–64 y, n (%)	82,431 (41.13)	57,814 (40.27)	8,806 (43.29)	7,166 (43.06)	8,134 (43.31)
≥ 65 y, n (%)	76,188 (38.01)	58,014 (40.41)	7,367 (36.21)	4,875 (29.30)	5,619 (29.92)
Median (IQR)	62 (52–72)	63 (53–74)	59 (51–70)	59 (49–68)	58 (49–68)
Tumor grade, n (%)					
Low	23,007 (11.48)	15,925 (11.09)	2,785 (13.69)	1,937 (11.64)	2,184 (11.63)
Intermediate	64,710 (32.28)	44,767 (31.18)	6,871 (33.78)	5,878 (35.32)	6,853 (36.49)
High	50,753 (25.32)	36,899 (25.70)	4,978 (24.47)	3,910 (23.50)	4,684 (24.94)
Unknown	61,970 (30.92)	45,973 (32.02)	5,709 (28.06)	4,915 (29.54)	5,062 (26.95)
Tumor size, n (%)					
<15 mm	97,637 (48.71)	70,878 (49.37)	9,032 (44.40)	7,776 (46.73)	9,422 (50.16)
16–40 mm	33,384 (16.66)	22,358 (15.57)	3,451 (16.96)	3,142 (18.88)	4,246 (22.61)
>40 mm	9,617 (4.80)	6,199 (4.32)	1,262 (6.20)	976 (5.87)	1,122 (5.97)
Unknown	59,802 (29.84)	44,129 (30.74)	6,598 (32.43)	4,746 (28.52)	3,993 (21.26)
Estrogen receptor status, n (%)					
Positive	99,458 (49.62)	68,555 (47.75)	11,353 (55.81)	8,962 (53.86)	9,992 (53.20)
Negative	18,610 (9.28)	13,459 (9.37)	1,705 (8.38)	1,542 (9.27)	1,812 (9.65)
Borderline	234 (0.12)	181 (0.13)	26 (0.13)	11 (0.07)	14 (0.07)
Unknown	82,138 (40.98)	61,369 (42.75)	7,259 (35.68)	6,125 (36.81)	6,965 (37.08)
Progesterone receptor status, n (%)					
Positive	81,927 (40.87)	56,138 (39.10)	9,568 (47.03)	7,382 (44.36)	8,324 (44.32)
Negative	29,011 (14.47)	21,058 (14.67)	2,782 (13.68)	2,405 (14.45)	2,626 (13.98)
Borderline	459 (0.23)	353 (0.25)	45 (0.22)	33 (0.20)	27 (0.14)
Unknown	89,043 (44.42)	66,015 (45.98)	7,948 (39.07)	6,820 (40.99)	7,806 (41.56)

IQR, interquartile range.

95% CI +0.87 to +1.16) than for white and Hispanic women (whites: +0.68; 95% CI +0.54 to +0.81, Hispanics: +0.69; 95% CI +0.58 to +0.80). As Table 2 shows, although DCIS incidence rates were significantly lower after 1998—the natural inflection point in DCIS incidence rate as depicted in Figure 2—for women of all races, rates between 1998 and 2014 were at a plateau for white women, but exhibited an increase for non-white women throughout the same period. Specifically, DCIS incidence rates after 1998 were highest in absolute value for API women followed by black then Hispanic women.

After adjusting for race and ethnicity, subgroup analysis by age group revealed that there were significant increases in DCIS incidence rates for women of each age group, highest for age 65 years and older (+1.09 diagnoses per 100,000 individuals every year) followed by 50 to 64 years (+0.85 diagnoses per 100,000 individuals every year) then 40 to 49 years (+0.63 diagnoses per 100,000 individuals every year) (Table 3). These increases in DCIS incidence rates during the study period were driven primarily by trends before 1998; after 1998, incidence rates slowed significantly in each age group.

Effects of mammography screening on ductal carcinoma in situ incidence

On multivariate linear regression and after adjusting for age group, race and ethnicity, and calendar year, DCIS incidence rate was found to be independently associated

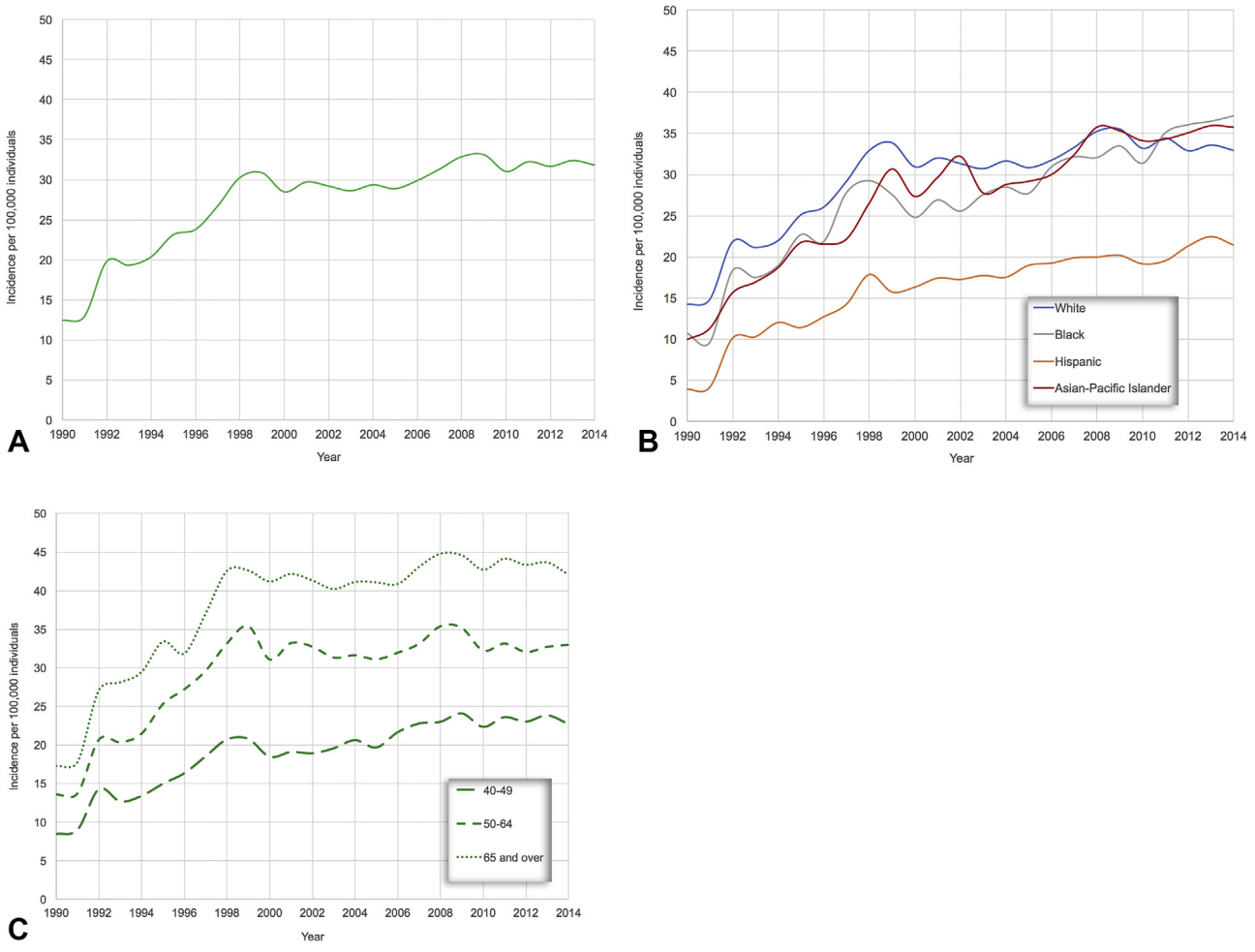

Figure 1. Incidence rates of ductal carcinoma in situ of the breast in US women aged 40 years and older between 1990 and 2014. (A) All women, (B) by racial and ethnic group, and (C) by age group.

with mammography screening rate (Table 4). With each additional percent of women receiving a mammogram, an average of 0.2 additional DCIS diagnoses were made per 100,000 individuals in the population every year throughout our study period. Additionally, DCIS incidence rate differed substantially by race and ethnicity; after adjusting for mammography screening, Hispanic ethnicity was associated with a significantly lower DCIS incidence rate (−9.7 diagnoses per 100,000 individuals) relative to white race. There appeared to be no significant difference in DCIS incidence rate between white and black women (relative to white, black women: −0.8

Table 2. Association Between Calendar Year and Ductal Carcinoma in Situ Incidence Rate, Stratified by Race and Ethnicity after Adjusting for Age Group

	Before 1998*		After 1998*	
Racial/ethnic group	**Coefficient†**	**95% CI**	**Coefficient†**	**95% CI**
White	+2.16 diagnoses/100,000	+1.74 to +2.58‡	+0.07 diagnoses/100,000	−0.04 to +0.17
Black	+2.67 diagnoses/100,000	+2.01 to +3.33‡	+0.66 diagnoses/100,000	+0.52 to +0.80‡
Hispanic	+1.83 diagnoses/100,000	+1.21 to +2.44‡	+0.30 diagnoses/100,000	+0.23 to +0.37‡
Asian-Pacific Islander	+2.00 diagnoses/100,000	+1.53 to +2.47‡	+0.52 diagnoses/100,000	+0.37 to +0.68‡

*The year 1998 was chosen as a cutoff point because ductal carcinoma in situ incidence rates evaluated over time revealed this to be a natural inflection in trends.
†The coefficient represents the average yearly increase in the number of ductal carcinoma in situ cases diagnosed per 100,000 individuals in the population.
‡Significant.

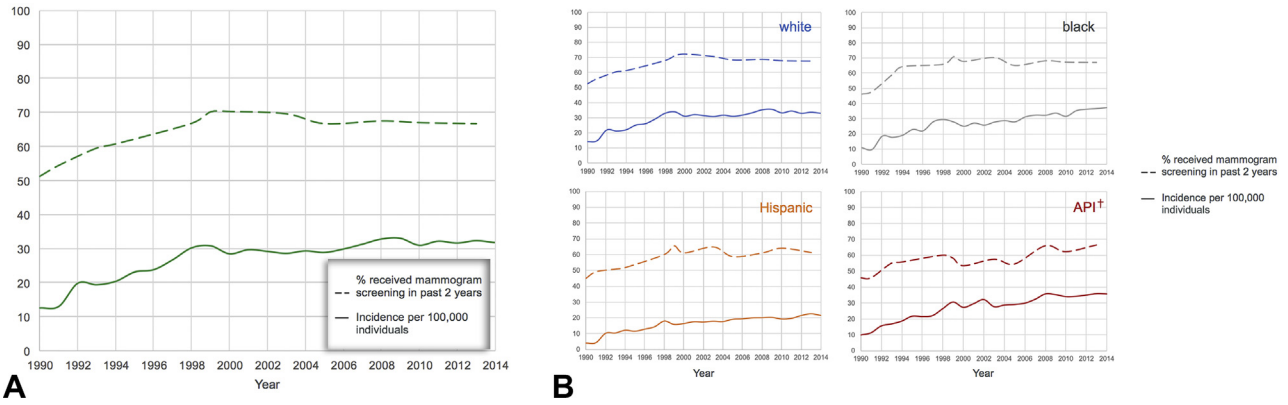

Figure 2. Mammography screening and ductal carcinoma in situ incidence rates in US women aged 40 years and older between 1990 and 2014. (A) All women (B) by racial and ethnic group. API, Asian-Pacific Islander. †Mammography screening data for APIs is not available. Screening data for Asian women only are depicted, exclusive of Pacific Islanders.

diagnoses/100,000; 95% CI −2.7 to +1.0). In addition, with respect to age group, age 50 years and older was associated with higher DCIS incidence rates relative to age 40 to 49 years. There was also a significant increase in DCIS incidence rates between 1990 and 1998, but not after 1998, depicted in Figure 3.

DISCUSSION

Ductal carcinoma in situ is a disease made prominent by the improved medical technology of the 20th century. We have evaluated the incidence rates of DCIS in the US population between 1990 and 2014. Previous studies have reported DCIS incidence rates based on SEER data for varying periods ending in 2010.[9,10] This report focuses on trends in DCIS incidence rates specifically among the 4 major racial and ethnic groups in the US and highlights the impact of mammography screening on DCIS incidence by racial and ethnic group. Overall, the rise in DCIS incidence rates between 1990 and 2014 was greatest in API women, followed by non-Hispanic black, Hispanic, and then non-Hispanic white women.

Mammography screening has altered the patterns of breast cancer seen in the US. The identification of early-stage breast cancer has become more common, and that of locally advanced breast cancer has become less so. Our study has demonstrated a clear relationship between mammography screening and DCIS incidence. Consistent with earlier studies, our study has also documented a rise in DCIS incidence rates during the past 2 decades.[2,3] The DCIS incidence patterns have not, however, mirrored those of IBC.[11,12] The national incidence rates of IBC rose rapidly with the adoption of mammography screening in the 1980s to 1990s, but slowed thereafter. This slower increase seen in the late 1990s has been attributed to rising rates of obesity and the use of hormone replacement therapy.[11] The same patterns over time have not been reflected in DCIS, the incidence rate of which rose rapidly between 1990 and 1998 and subsequently plateaued for white women, while continuing to increase in non-white women. The observation that IBC rates did not decline appreciably during these periods suggests possible overdiagnosis of DCIS that would not have progressed to IBC. This rests on the assertion that DCIS is a precursor to IBC, which has been supported by numerous studies documenting the coincidence of DCIS in excised IBC specimens, as well as longitudinal studies demonstrating recurrent invasive ductal carcinoma at sites of previously treated

Table 3. Association Between Calendar Year and Ductal Carcinoma in Situ Incidence Rate, Stratified by Age Group after Adjusting for Race and Ethnicity

	Before 1998*		After 1998*	
Age group	Coefficient†	95% CI	Coefficient†	95% CI
40–49 y	+1.26 diagnoses/100,000	+1.00 to +1.52‡	+0.42 diagnoses/100,000	+0.34 to +0.50‡
50–64 y	+2.34 diagnoses/100,000	+1.96 to +2.73‡	+0.29 diagnoses/100,000	+0.17 to +0.40‡
≥ 65 y	+2.90 diagnoses/100,000	+2.37 to +3.42‡	+0.46 diagnoses/100,000	+0.31 to +0.60‡

*The year 1998 was chosen as a cutoff point because ductal carcinoma in situ incidence rates evaluated over time revealed this to be a natural inflection in trends.
†The coefficient represents the average yearly increase in the number of ductal carcinoma in situ cases diagnosed per 100,000 individuals in the population.
‡Statistically significant.

Table 4. Multivariate Linear Regression of Ductal Carcinoma in Situ Incidence Rate with Mammography Screening, Age Group, Race and Ethnicity, and Calendar Year* as Covariates

Covariate	Coefficient†	p Value	95% CI
Screening (% population with mammogram in last 2 y)	+0.2 diagnoses/100,000	0.02‡	+0.1 to +0.4
Age group			
40–49 y	Reference		
50–64 y	+7.5 diagnoses/100,000	<0.01‡	+5.0 to +10.0
≥ 65 y	+19.2 diagnoses/100,000	<0.01‡	+17.5 to +21.0
Race and ethnicity§			
White	Reference		
Black	−0.8 diagnoses/100,000	0.36	−2.7 to +1.0
Hispanic	−9.7 diagnoses/100,000	<0.01‡	−12.0 to −7.5

*Calendar year data are not shown here (see Figure 3).
†The coefficient represents the average yearly increase in the number of DCIS cases diagnosed per 100,000 individuals in the population.
‡Statistically significant.
§Age-specific mammography screening data for Asian-Pacific Islander women are not made available by our data source, the CDC.

DCIS.[13-15] As such, risk-stratifying patients by likelihood of progression to invasive disease remains a top priority in DCIS management. Several randomized clinical trials including the LORIS, LORD (NCT02492607), and COMET (NCT02926911) trials have been initiated to determine whether certain subtypes of DCIS can be managed conservatively.[16] Given our study results demonstrating rising DCIS incidence rates, especially among minority populations, these trial results will have important implications for ensuring access to appropriate treatment for all women.

The reason that DCIS incidence rates plateaued among white women but have continued to increase among non-white women between 1998 and 2014 is likely multifactorial. Anecdotally, there has been greater baseline awareness of breast cancer screening among white women. This has likely had an impact on the saturation of mammography screening use in the white population. Past studies have also demonstrated that newer technologies are more slowly adopted by institutions serving a greater proportion of minority patients; a similar trend in breast screening technology might account for delayed saturation in breast screening among minority women.[17,18] In addition, the efficacy of screening can vary by race and ethnicity. Digital mammography, which has replaced film mammography, has been shown to be more diagnostically accurate in younger women and in women with denser breasts.[19] The recent addition of tomosynthesis to digital mammography, which was FDA-approved in 2011 and has quickly become the standard of care for breast cancer screening, has also increased cancer detection rates.[20] The impact of these newer technologies on DCIS incidence patterns remains to be seen, particularly as they saturate minority populations. Institutional analyses might be better able to distinguish trends in the use of digital mammography vs tomosynthesis and shed light on the relationship between DCIS incidence and these new screening technologies.

There were noticeable subgroup differences in DCIS incidence rates by race and ethnicity for women in our study. Although rates increased in all subgroups, a greater increase was seen among non-whites, similar to what has been reported previously.[21,22] A retrospective analysis of breast cancer rates by DeSantis and colleagues[11] showed similar trends in non-white women, although API women in their cohort had the lowest cancer incidence overall. Their study was, however, a combined analysis of in situ and invasive ductal carcinoma; patterns for DCIS alone can reasonably differ.

In this study, we revealed that after accounting for differences due to age and race and ethnicity, there exists a clear relationship between mammography screening and DCIS incidence rates. Our analysis of CDC data revealed that

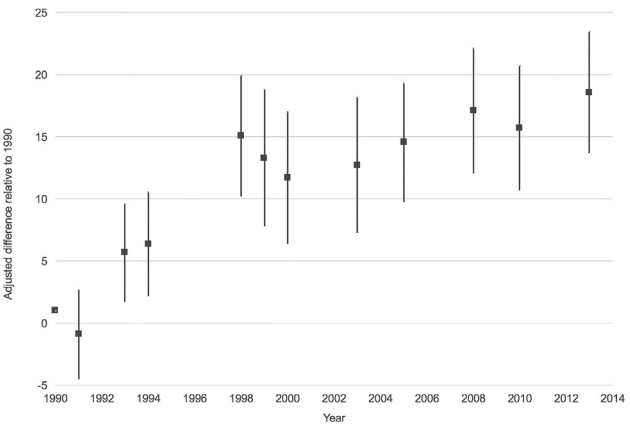

Figure 3. Ductal carcinoma in situ incidence rate over time relative to year 1990 after adjusting for mammography screening rate, age group (40 to 49 years, 50 and 64 years, and 65 years and older), and race and ethnicity (non-Hispanic white, non-Hispanic black, Hispanic).

although there has been increased use of screening mammography since the 1970s, mammography screening plateaued by 1998 in all groups except API women. Although mammography screening has been available since the mid-1970s, the adoption of mammography screening appears to have varied substantially along racial and ethnic lines.[23-25] Studies informed by national data show that since the advent of mammography screening, white women have exhibited the highest use rates, and Hispanic and API women the lowest. A possible contributor to these differences in use might be non-uniform adoption of new screening guidelines by government-assisted vs private healthcare institutions. Institutions receiving federal support for patient care, such as the Veterans Affairs health system, which sees a higher proportion of minority patients, were likely faster to implement the latest US Preventive Services Task Force breast screening recommendations as governmental guidelines than private providers.[26] Variability in the penetrance of screening by race and ethnicity is made more unpredictable by regional analyses; despite earlier studies revealing later adoption of screening among black relative to white women, more recent analyses show the inverse in certain US states.[11] Given differences in screening saturation by race and ethnicity, and especially with multiple and conflicting national screening guidelines,[27-30] it is important to explicitly consider race and ethnicity in future screening guidelines.

Sustained increases in DCIS incidence rate after 1998 seen among non-Hispanic white and Hispanic women even after accounting for trends in mammography screening suggest that there are other contributing factors not yet explored here. Changes in reproductive behaviors and sociobiological patterns can affect DCIS patterns.[31,32] Late childbearing and nulliparity remain risks for breast cancer. Studies of cultural trends among Hispanic women show that they have their first child at younger ages and look more favorably on breastfeeding, both of which are protective against breast cancer.[33-36] Acculturation to the general population by delaying childbearing and having fewer children can contribute to rising DCIS incidence rates seen in recent years.

Our conclusions must be taken in the context of our study limitations. We were unable to account for racial and ethnic differences in family history, genetic mutation, or receptor status, which can influence disease expression. In addition, socioeconomic factors and access to care that directly impact the availability of screening were not examined here. More granular subdivision of race and ethnicity, particularly for API women, in national data collection efforts is sorely needed, because the natural history of IBC has shown significant variation among those from the Asian continent. Similar differences can be seen in DCIS trends. These API subgroup differences are important to better elucidate, particularly as they relate to screening, acknowledging that our study found different results for API women than earlier studies. In turn, screening can become more effective if race and ethnicity are factored into assessing a woman's breast cancer risk, as is done with family history.

CONCLUSIONS

The rise of DCIS in the general US population has been directly associated with the wider adoption of mammography screening in the 1990s. However, trends in mammography screening do not fully explain patterns of DCIS incidence rates for women of different racial and ethnic groups, particularly for women of Hispanic ethnicity. Optimal mammography screening guidelines should be developed with explicit consideration of race and ethnicity.

Author Contributions

Study conception and design: Oseni, Zhang, Chang
Acquisition of data: Zhang, Chang
Analysis and interpretation of data: Oseni, Zhang, Coopey, Gadd, Hughes, Chang
Drafting of manuscript: Oseni, Zhang, Chang
Critical revision: Oseni, Zhang, Coopey, Gadd, Hughes, Chang

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Invited Commentary

Jennifer LaFemina, MD, FACS
Worcester, MA

Ductal carcinoma in situ (DCIS) is considered to be a noninvasive, nonobligate precursor lesion that demonstrates a wide variability in its ability to progress to invasive disease. Studies report that 13% to 50% of DCIS cases will progress to invasive ductal carcinoma.[1-4] Despite its frequency and extensively studied nature, DCIS remains a process surrounded by controversy and unknowns, the most striking of which is the lack of identifiable, reliable markers that predict disease progression. Oseni and colleagues certainly use their current work to highlight yet another unknown as it relates to the correlation of race and ethnicity with the incidence of this disease in the US.

Not as controversial, certainly, is the global trend in DCIS incidence, particularly as it relates to mammographic screening patterns. Previous reports have demonstrated that with widespread adoption of screening mammography through the 1990s, there was a parallel rise in DCIS diagnoses.[5,6] This study reiterates these previous reports and the positive impact of mammographic screening on DCIS incidence. The data further confirm a steady plateau in diagnoses through 2014, substantiating trends suggested by previous information and reporting on earlier time frames.