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# Disparities in DCIS

Georgia Syrnioti[1,2] · Josh Johnson[1] · Claire M. Eden[1] · Antonia Syrnioti[3] · Lisa A. Newman[1]

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## Abstract

**Purpose of Review** Although the impact of socioeconomic and racial/ethnic disparities in the pathogenesis and outcomes of invasive breast cancer has been well defined, data regarding DCIS are sparse. The purpose of this review is to address the influence of disparities in the pathogenesis and prognosis of DCIS and examine the factors that are associated with adverse outcomes in underserved and minority populations.

**Recent Findings** Racial/ethnic disparities in DCIS are evident in all aspects of cancer care continuum, from prevention to development of invasive cancer. Increased prevalence of preventable risk factors and disproportionate screening are evident in socioeconomically disadvantaged populations. Furthermore, unequal access to different treatment modalities as well as unfavorable hormonal receptor profiling in certain racial/ethnic groups may be associated with worse morbidity and higher incidence of subsequent breast cancer events.

**Summary** Failure to understand socioeconomic disparities can affect the quality of care of patients with DCIS and subsequently invasive breast cancer.

**Keywords** Ductal Carcinoma in Situ · DCIS Disparities · Cancer Burden · Socioeconomic Context · Cancer Care Inequity

## Introduction

The World Health Organization (WHO) defines ductal carcinoma in situ (DCIS) as “a neoplastic proliferation of epithelial cells confined to the mammary ductal-lobular system and characterized by subtle to marked cytologic atypia and an inherent but not necessarily obligate tendency to progression to invasive breast cancer” [1]. Although it is not an obligatory precursor of invasive breast cancer, studies have shown that it can lead to invasive disease in 20–50% of cases if left untreated [2, 3]. DCIS most commonly presents as an incidental finding on imaging in asymptomatic patients [4••]. With the introduction of screening mammography in the general population, the diagnosis of DCIS has increased by 500% from 1983 to 2003 [5–7] and currently comprises 20–25% of all breast cancer cases in the USA [8]. Treatment of DCIS is currently multidisciplinary and involves a combination of partial or total mastectomy with or without sentinel lymph node biopsy, postoperative radiation therapy, and administration of endocrine therapy in eligible patients [9]. In an effort to reduce the morbidity associated with the various treatment strategies and reduce the burden of overtreatment, a shift towards de-escalation of management is highly debated [10]. The understanding of the clinical and pathophysiological features of the disease will further define the risk factors for progression to invasive cancer which will subsequently individualize the treatment and management.

Racial and ethnic disparities in the epidemiology and prognosis of invasive breast cancer have been well described.

✉ Georgia Syrnioti
gsirnioti@gmail.com

Josh Johnson
jaj9048@med.cornell.edu

Claire M. Eden
cle9019@med.cornell.edu

Antonia Syrnioti
tonia.syrt@gmail.com

Lisa A. Newman
lan4002@med.cornell.edu

[1] Department of Breast Surgery, New York Presbyterian-Weill Cornell Medicine, 1300 York Ave, New York, NY 10065, USA

[2] Department of Surgery, One Brooklyn Health-Brookdale University Hospital and Medical Center, 1 Brooklyn Plaza, Brooklyn, New York, NY 11212, USA

[3] Department of Pathology, Aristotle University of Thessaloniki, Thessaloniki, Greece

However, the impact of race and ethnicity on the biological course of DCIS is still poorly understood. Most available population studies that examine race/ethnicity-related variations in DCIS outcomes focus on comparison between African American and non-Hispanic White populations, while few data are available regarding other ethnic groups, including West Indians, Asians, and Hispanics [11–13]. Data regarding the impact of socioeconomic status on DCIS outcomes is also scarce. This review aims to address the influence of racial and ethnic disparities in the pathogenesis and prognosis of DCIS as well as examine the social determinants of health that are associated with adverse outcomes in underserved and minority populations. An overview of the discriminatory care and disparities in the pathogenesis and management of DCIS can be viewed in Fig. 1.

## Disparities in Risk Factor Burden and Diagnosis of DCIS

Since both invasive breast cancer and DCIS share common pathways, data regarding the disparities of risk factor burden in breast cancer are extremely relevant to DCIS. The increased prevalence of preventable risk factors in addition to poor access to screening can increase the incidence of certain cancers, including breast cancer. The interplay between genetic factors and environmental exposure to various carcinogens from prenatal life to menopause can increase a woman's risk for development of breast cancer. According to the American Cancer Society, primary prevention of breast cancer involves avoiding tobacco smoking, limiting alcohol consumption, maintaining normal weight, following a healthy diet, increasing physical activity, and avoiding exposure to radiation and post-menopausal hormone use [14–16]. Undoubtedly, low-income and underserved populations are exposed to a multitude of potential environmental risk factors which could increase the risk for developing DCIS and subsequently breast cancer. Indeed, the prevalence of smoking is almost double in underserved communities [17] and is more frequent in individuals with low education level and the uninsured [18]. Similarly, obesity is more prevalent in residents of rural areas, while lack of access to recreational activities and relative prevalence of fast-food restaurants can promote physical inactivity and weight gain [19, 20]. A population-based case–control study that included 497 patients with DCIS showed that obesity at the time of DCIS diagnosis was associated with a 1.6-fold increase of risk for any second breast cancer and a 2.2-fold increased risk of a contralateral breast cancer [21], while a study performed by Almekinders et al. showed that

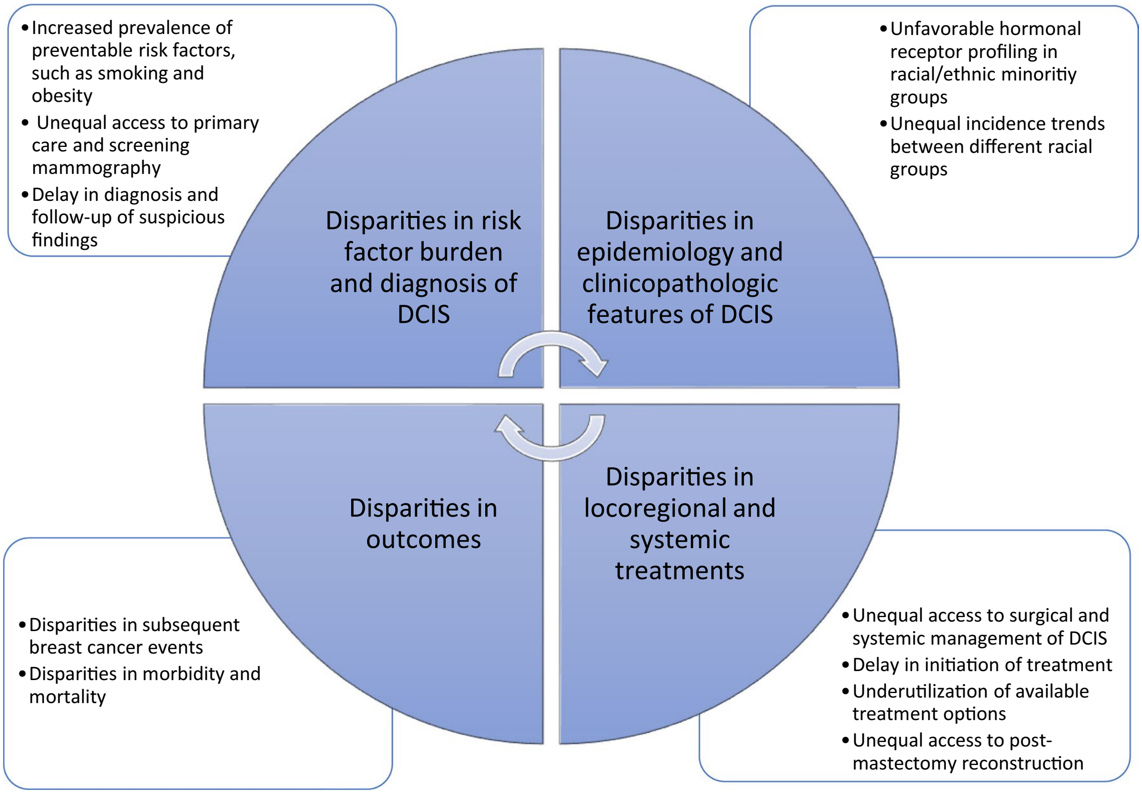

**Fig. 1** Discriminatory patterns and disparities in the pathogenesis and management of DCIS

increased breast adipocyte size in patients with DCIS is associated with higher risk for development of ipsilateral invasive breast cancer [22••]. Although these studies do not highlight the direct association between obesity and development of DCIS, they describe patterns that may be associated with increased risk for progression to invasive breast cancer.

Detection of DCIS is largely based on screening mammography since most patients are asymptomatic [4••]. A study performed by Ganguly et al. revealed that African American patients had significantly lower rates of completion of screening mammography compared to other ethnic groups [23••]. Results from a large systematic review and meta-analysis conducted by Ahmed et al. showed that Hispanic and African American populations had lower rates of screening mammography utilization, while no difference was noted between Asians/Pacific Islanders and non-Hispanic Whites [24]. Racial disparities are also evident in the interval from diagnosis to definite management. A small retrospective study performed by Pocock et al. revealed that African American women were 64% more likely to have delayed surgery compared to non-Hispanic Whites [25]. Surveillance mammography is also necessary after the initial diagnosis and management of DCIS, thereby influencing early detection of DCIS recurrence or ipsilateral invasive breast cancer. A study performed by Byng et al. showed that African American and Hispanic patients had a lower probability of undergoing surveillance screening after surgical management of DCIS. On the other hand, patients with private insurance had higher rates of surveillance screening compared to patients with government insurance [26]. Similar results were reported by Brawarsky et al. who showed decreased rates of surveillance mammography in non-Hispanic Blacks, Hispanics, and patients with low socioeconomic status [27]. These studies highlight the underutilization of screening mammography by racial minorities and underserved populations which could potentially lead to increased rate of DCIS recurrence and invasive breast cancer in these patients.

Although the systematic assessment of the interventions that could potentially increase the utilization of mammographic screening in minority and underserved populations is difficult, several studies have highlighted the significance of patient- and system-targeted interventions [28]. A study performed by Skinner et al. revealed that individually tailored recommendations regarding screening mammography were more likely to be followed compared to standardized recommendations, especially in low-income and African American groups [29]. Studies have shown that addressing the geographic barriers by means of mobile mammography as well as the imaging cost can improve the screening rates of underserved and rural populations [30–32]. A systematic review and meta-analysis performed by Gardner et al. revealed that the implementation of multiple strategies which combine access-enhancing with system/provider-directed interventions has proven to be the most effective when comparing intervention and control groups [33]. Similar findings have been published by Legler et al. who showed that the combination of strategies increased mammographic screening by 27% [34]. These findings highlight the heterogeneity and diversity of minority and underserved populations and the need for multidisciplinary approaches in order to overcome their barriers to equal healthcare delivery.

## Disparities in Epidemiology and Clinicopathologic Features of DCIS

The utilization of screening mammography has increased the diagnosis and subsequently the incidence of DCIS. More specifically, the incidence of DCIS in the USA significantly increased from 1.87 per 100,000 in 1973–1975 to 32.5 per 100,000 women in 2004 [35]. A study performed by Innos et al. that included all women aged 40 years and above that were diagnosed with DCIS in California between 1988 and 1999 showed that the incidence of DCIS was increased among all ethnic groups, but the Asian-Pacific Islander patients exhibited the largest increase [36]. A retrospective study by Ryser et al. that included patients from the Surveillance, Epidemiology, and End Results (SEER) database between 2000 and 2014 revealed that the incidence of DCIS increased by 1.6% in non-Hispanic Blacks despite unchanged mammogram utilization. The authors suggested the possibility of other etiologic factors to be responsible for this increase [37]. The rise in the incidence of DCIS in the USA warrants additional research which could discover significant associations between race/ethnicity and the pathogenesis of DCIS.

In regards to invasive breast cancer, the prognostic value of estrogen and progesterone receptor status has been well established. Studies regarding invasive breast cancer have shown that estrogen receptor (ER)-negative and triple-negative tumors are encountered at a higher frequency in African American patients [38] [39]. The phenotypic variations of hormonal receptor profiling in DCIS have not been concisely described. A study performed by Bailes et al. that compared the demographic and histopathological characteristics of 1902 patients with DCIS and their association with race/ethnicity revealed that African Americans aged above 70 years and Hispanics aged below 50 years had higher probability of having ER-positive DCIS compared to other ethnic groups [40]. On the other hand, a retrospective study performed by Nelson et al. including 532 patients diagnosed with DCIS between 1974 and 2009 showed that African American patients had lower DCIS grade of differentiation, lower percentage of necrosis, and higher frequency of ER-positive disease compared to non-Hispanic Whites

[41]. Data regarding the prognostic value of PR positivity and association with racial/ethnic disparities is conflicting. A large study performed by Liu et al. including 163,892 women with newly diagnosed DCIS from the SEER database between 1990 and 2015 showed that non-Hispanic Blacks and Asian patients had a higher incidence of developing subsequent ER-/PR-invasive breast cancer compared to non-Hispanic Whites [42]. Larger studies need to be performed in order to define the disparities regarding hormonal receptor variability in the prognosis of patients with DCIS.

## Disparities in Locoregional and Systemic Treatments

The management of DCIS is based on locoregional disease control by means of partial or total mastectomy with and without sentinel lymph node biopsy and administration of postoperative radiation therapy and systemic treatment with administration of endocrine therapy in hormonal receptor-positive patients. Low socioeconomic status and lack of insurance have been linked with adverse outcomes in patients with invasive breast cancer [43, 44]; however, data regarding DCIS are lacking. Zhang et al. performed a large retrospective study examining 9195 women with DCIS diagnosed between 1996 and 2011 and its association with neighborhood characteristics. The study revealed that socioeconomically disadvantaged patients had a lower probability of any surgical treatment or postoperative radiation therapy, while they also exhibited delays in the initiation of radiation therapy and a higher probability of developing ipsilateral tumors. Furthermore, residents of rural regions have a lower probability of undergoing postoperative radiation therapy after breast conserving surgery compared to residents of urban centers [45]. A study performed by Madubata et al. showed that African American patients had a higher probability of postoperative radiation therapy delay more than 8 weeks from surgery, although no difference was noted in mastectomy and endocrine therapy compared to non-Hispanic Whites [46]. Patients with low income were also shown to have decreased utilization of radiation therapy [47]. Regarding post-mastectomy reconstruction in patients with DCIS, a retrospective study performed by Kruper et al. showed that Hispanic and Asian patients had significantly lower rates of reconstruction compared to non-Hispanic Whites. Similarly, reconstruction rates were higher in patients with private insurance compared to Medicaid [48]. Language barriers also constitute a significant key factor that is associated with suboptimal management of patients with DCIS. In a study performed by Kaplan et al., English-speaking Hispanic patients had a higher probability of undergoing postoperative radiation therapy compared to their Spanish-speaking counterparts [49]. Spanish-speaking Hispanic women have also been reported to have lower satisfaction in regards to decision-making in the management of DCIS [50].

## Disparities in Outcomes

Regardless of the surgical treatment modality or the use of adjuvant radiation and/or endocrine therapy, patients with DCIS have excellent outcomes. According to a large study utilizing data from the SEER database, women with DCIS have 3.3% 20-year breast cancer mortality regardless of the type of treatment [51]. Of all local recurrences after DCIS in patients that were treated with breast conserving surgery, equal risk for invasive and non-invasive carcinoma has been noted [52]. Thus, the studies that evaluate race/ethnicity and its relations with outcomes mainly focus on the risk for locoregional, invasive, and distant recurrence.

According to a large SEER database analysis of 108,196 women with DCIS, African American patients had experienced worse breast cancer-related mortality compared to non-Hispanic Whites (7% for African Americans vs 3% for non-Hispanic Whites, $p$ value $<0.001$). The risk remained elevated after adjusting for income, treatment, and tumor characteristics [51]. The risk of advanced (stage III and IV) invasive breast cancer has also been reported to be 130% higher in Hispanic women compared to non-Hispanic Whites [53]. Data regarding other racial/ethnic groups are scarce. In a study published by Joslyn et al., postmenopausal Asian women had a significantly lower mortality rate following diagnosis of DCIS compared to non-Hispanic Whites [54]. A retrospective study that included disaggregated data from the Hawaiian Tumor Registry revealed that the risk for ipsilateral and contralateral second breast cancer was significantly higher in Native Hawaiian and Filipino patients with DCIS, while Japanese patients had a higher risk for developing ipsilateral invasive breast cancer compared to non-Hispanic Whites [55]. These studies highlight that racial and ethnic disparities are significant prognosticators that may influence the approach and clinical decision-making in patients with DCIS.

The impact of socioeconomic background and prognosis of DCIS is poorly understood. A retrospective study performed by Zhang et al. showed that more socioeconomically deprived women had a higher probability of developing ipsilateral breast tumors. The risk continued to be elevated after adjusting for histopathological tumor characteristics, treatment modality, and insurance. The same study showed that the risk for developing ipsilateral or contralateral breast tumors was not statistically different between women that resided in rural and urban areas (45). Multi-institutional and prospective studies will help define the effect of social determinants of health on the survival outcomes of patients with DCIS.

## Closing the Gap

Failure to understand socioeconomic disparities can affect the quality of care of patients with DCIS and subsequently invasive breast cancer. Racial/ethnic disparities in DCIS are evident from prenatal life to menopause and affect all aspects of cancer care continuum, from prevention to development of invasive cancer and death. Since screening mammography is the main method of DCIS diagnosis, discrepancies associated with poor access and adherence are particularly relevant. Delayed initiation of treatment in certain minority populations has also been well documented. A multidisciplinary approach that addresses the individual's access to care along with consideration of financial costs and patients' satisfaction is significant in promoting equality in the management of DCIS.

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**Data Availability** Data is available for use in the public domain as permitted by Journal practices.

## Declarations

**Competing interests** The authors declare no competing interests.

**Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

**Conflict of Interest** The authors declare no competing interests.

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- • Of importance
- •• Of major importance

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