



Published in final edited form as:

Curr Breast Cancer Rep. 2020 September ; 12(3): 175–184. doi:10.1007/s12609-020-00370-3.

Breast Cancer Health Disparities in Hispanics/Latinas

Silvia J. Serrano-Gomez¹, Maria Carolina Sanabria-Salas², Laura Fejerman^{3,*}

¹Grupo de investigación en biología del cáncer, Instituto Nacional de Cancerología, Bogotá, Colombia

²Subdirección de Investigaciones - Instituto Nacional de Cancerología, Bogotá, Colombia.

³Department of Medicine, Division of General Internal Medicine, University of California San Francisco, CA.

Abstract

Purpose of the review: Breast cancer incidence and mortality rates are lower in some Hispanic/Latino subpopulations compared to Non-Hispanic White women. However, studies suggest that the risk of breast cancer-specific mortality is higher in US Hispanics/Latinas. In this review we summarized current knowledge on factors associated with breast cancer incidence and risk of mortality in women of Hispanic/Latino origin.

Recent findings: Associative studies have proposed a multiplicity of factors likely contributing to differences in breast cancer incidence and survival between population groups, including socioeconomic/sociodemographic factors, lifestyle choices as well as access to and quality of care. Reports of association between global genetic ancestry overall as well as subtype-specific breast cancer risk among Hispanic/Latinas suggest that incidence and subtype distribution could result from differential exposure to environmental and lifestyle related factors correlated with genetic ancestry as well as germline genetic variation.

Summary: Hispanic/Latino in the United States have been largely underrepresented in cancer research. It is important to implement inclusive programs that facilitate the access of this population to health services and that also include education programs for the community on the importance of screening. In addition, it is important to continue promoting the inclusion of Hispanics/Latinos in genomic studies that allow understanding the biological behavior of this disease in the context of all human genetic diversity.

Terms of use and reuse: academic research for non-commercial purposes, see here for full terms. <http://www.springer.com/gb/open-access/authors-rights/aam-terms-v1>

*Corresponding author: Laura Fejerman, PhD. Laura.fejerman@ucsf.edu. Phone number: 510 2217515. Address: 550 16th Street, San Francisco 94143 CA.

Publisher's Disclaimer: This Author Accepted Manuscript is a PDF file of an unedited peer-reviewed manuscript that has been accepted for publication but has not been copyedited or corrected. The official version of record that is published in the journal is kept up to date and so may therefore differ from this version.

Conflict of Interest

Silvia J. Serrano-Gomez, Maria Carolina Sanabria-Salas and Laura Fejerman declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

Keywords

Hispanic Americans; Breast Neoplasms; Risk factors; diagnosis; genetics

Introduction

Breast cancer is the most common cancer and the leading cause of cancer death in women worldwide [1]. Differences in incidence have been reported according to population groups. Age-adjusted breast cancer incidence rates in the US for the period 2012 – 2016 were 130.8 in non-Hispanic Whites (NHWs), 126.7 in non-Hispanic Blacks (NHBs), 94.7 in Native Americans/Alaskan Natives, 93.7 in Hispanics/Latinas and 93.2 in Asians/Pacific Islanders [2]. Age-adjusted mortality rates for the period between 2013 – 2017 were 28.4 in NHBs, 20.3 in NHWs, 14.6 in Native Americans/Alaskan Natives, 14.0 in Hispanics/Latinas and 11.5 in Asians/Pacific Islanders [2].

The approximately 30% lower breast cancer incidence in US Hispanics/Latinas compared to NHWs, can be partially explained by differences in detection practices, reproductive/hormonal factors [3], and other factors, including genetic predisposition [4–6].

Breast cancer mortality rates overall have been decreasing over time [2, 7]. However, for the period between 1990 – 2016, breast cancer mortality rates decreased 29% in Hispanics/Latinas compared to 39% in NHW women [8]. This difference is also reflected by the slower change in mortality rates between 2007 and 2016 with a 1.1% per year reduction in Hispanics/Latinas versus 1.8% in NHWs [8]. In addition, some studies have reported higher risk of breast cancer-specific mortality in Hispanics/Latinas compared to NHWs, after adjustment for some tumor characteristics and socioeconomic status [9–12].

The low incidence of breast cancer in US Hispanics/Latinas compared to NHWs and the worse outcomes reported for Hispanics/Latinas are the result of individual (including genetics), family, community and society level factors and their interactions [13]. In this review we will discuss some of the known or hypothesized factors that contribute to breast cancer disparities affecting Hispanic/Latina women.

Factors associated with breast cancer incidence among Hispanics/Latinas

Individuals identified as Hispanic or Latino are diverse including different cultures, environments, nativity and socioeconomic levels [14]. In addition, it constitutes a group genetically heterogeneous, product of the admixture between Europeans (mostly of migrants from the Iberian Peninsula and Southern Europe), Africans (who arrived in the Americas in the last five centuries as a result of the trans-Atlantic slave transportation), Indigenous Americans [14, 15] and to a lesser extent (due to relatively recent immigration) Asian populations.

The genetic ancestry of Hispanics/Latinos varies significantly between and within countries in Latin America and in US Hispanic/Latino subgroups [16, 17]. For example, on average, countries such as Mexico, Guatemala, Peru and Bolivia have relatively high Indigenous

American ancestry while Cuba, Venezuela and Northeast Brazil present higher African ancestry proportions and Argentina and Uruguay higher European ancestry [15, 17]. Caution has to be taken when discussing average ancestry proportion for countries given that large variation in average ancestry exists between regions within different countries [18–20]. In the United States, Latinos are mainly from Mexico (63.2%), Puerto Rico (9.5%), Cuba (3.9%), Salvador (3.8%), Dominican Republic (3.3%) and other Central and South American countries [21].

Genetic ancestry and genetics

Latina women with high Indigenous American (IA) ancestry in the US and in Latin America have an overall lower incidence of breast cancer than women of European descent. A study that used 48 population-based cancer registries in 13 countries showed that the highest incidence rates for breast cancer in Latin America are reported in countries such as Argentina, Brazil and Uruguay (Age-Standardized Rates (ASR): 71.9, 70.2 and 67.7, respectively) while the lowest incidence rates have been reported in Bolivia and El Salvador (ASR: 12.7 and 7.9, respectively) [22]. This is consistent with studies showing that Hispanics/Latinas with high IA ancestry have lower risk of breast cancer compared to Latina women with high European ancestry in multivariate analyses that included known risk factors as covariates [23, 24]. This first findings led to the discovery of a protective variant near the estrogen receptor 1 (*ESR1*) gene that is only present in women with IA ancestry such as Hispanics/Latinas and contributes to the lower risk of breast cancer in this population. The frequency of this variant correlates with the proportion of IA ancestry in different Latin American countries, for example, its frequency in Puerto Ricans was 5% while its frequency in Peruvians was 23% [4, 5, 25].

Other studies have assessed genetic variation in candidate genes and their relationship with breast cancer among Hispanics/Latinas [26–30], replicating previous associations reported in European studies. Future larger studies among Hispanics/Latinas might identify additional variants that could explain the lower risk of breast cancer among women with higher IA ancestry.

Hereditary breast cancer genetics—Many studies have been developed among NHWs from Europe and the US, focusing in *BRCA1* and *BRCA2* germline mutations [31]. However, similar studies among Hispanics/Latinas are scarce [32*-34*]. In unselected patients, the prevalence of *BRCA* mutations has been shown to be below 5% similar to the prevalence reported in NHWs [35]. A literature review that included 33 publications found that the prevalence of *BRCA1/2* mutations in Hispanic/Latina women with breast cancer ranged between 0.7% - 42% [34]. The vast majority of the studies included (36%) were based on data from Mexican or Mexican American patients among whom *BRCA1/2* mutations ranged between 4.3% - 23%. Studies from other Latin American countries showed a high prevalence of *BRCA1/2* mutation, with highest prevalence in Venezuela (17.2%) followed by Uruguay (17%), Colombia (1.2% - 15.6%) and lowest prevalence in countries such as Costa Rica (4.5%), Peru (4.9%) and Cuba (2.6%). These results must be analyzed with caution as the studies included were heterogeneous regarding case selection (whether

cases were selected or unselected for family history), clinical characteristics, cancer site and the type of testing [32, 34].

Differences in the prevalence of *BRCA1* vs. *BRCA2* mutations has also been reported. Most studies concluded that among Hispanics/Latinas, *BRCA1* mutations are more prevalent than *BRCA2* [34]. A multiethnic study that included 1,727 breast cancer cases from the Northern California Breast Cancer Family Registry [36] reported that Hispanics/Latinas had higher prevalence of *BRCA1* mutations (3.5%) than NHWs (2.2%). The most common pathogenic variant in *BRCA1* reported for Hispanics/Latinas is 185delAG (c.68_69delAG, rs80357914) [34, 36, 37]. On the other hand, studies in women from Costa Rica, Cuba, Puerto Rico and Uruguay have shown that the *BRCA2* gene is more frequently mutated in those populations [34]. Further studies should be conducted to confirm these observations, given that cancer risk, tumor pathology and clinical implications are different for *BRCA1* compared to *BRCA2* mutation carriers.

With the more generalized use of multigene panels, other homologous recombination repair genes (HR) have been found to be relevant in hereditary breast cancer, such as *CHEK2*, *PALB2*, *RAD50*, *RAD51D* and *BARD1*, as well as other genes such as *CDHI*, *MUTYH*, *TP53*, *MSH2* and *MSH6* [38]. A study that included 1054 *BRCA*-mutation-negative Hispanic/Latina women with hereditary breast cancer reported 49 patients with pathogenic variants (4.6%) [39]. The gene with the highest proportion of pathogenic variants was *CHEK2* (38.8%), followed by *PALB2* (36.7%), *ATM* (10.2%), *BRIPI* (4.1%), *TP53* (6.1%), *CDHI* (2%) and *NFI* (2%) [39*]. Additional studies in Hispanics/Latinas aiming to identify germline mutation carriers among affected individuals with high risk criteria are needed in order to estimate the real prevalence of relevant gene mutations and assess clinical implications and contributions to health disparities.

Breast cancer risk factors

According to the American Society of Cancer, in 2016, approximately one-third of Hispanics/Latinos in the US were foreign-born [21]. That proportion is expected to drop to less than one-quarter by 2060 [21]. It has been reported that for the period between 1988 – 2004 the incidence rates in NWH women were 34% higher than in US-born Hispanics/Latinas and 84% higher than in foreign-born Hispanics/Latinas [40]. Additionally, it has been suggested that migration age impacts the risk of breast cancer [41]. Long-term residents who migrated before the age of 20 have higher risk of developing breast cancer than those who migrated at a later age [41].

Differences in risk of breast cancer by nativity (US-born vs. foreign-born) are likely explained by changes in environmental and lifestyle factors [41]. For example, lower parity, later age at full-term pregnancy, no breast-feeding or short duration, use of estrogen/progestin-containing hormone therapy for menopausal symptoms and higher alcohol consumption could all contribute to the observed increase in breast cancer risk in US-born vs. foreign-born Hispanics/Latinas [40–42]. A study that analyzed data from The Neighborhoods and Breast Cancer study (NABC) found that US-born Hispanics/Latinas were more likely to report not having breastfed and to be obese, while foreign-born Hispanics/Latinas were more likely to report older age at menarche (14 years), have four

or more children, breastfeed for more than 12 months and have limited alcohol consumption [43]. Another study reported that foreign-born Hispanics/Latinas had higher fruit and vegetable consumption when compared with US-born Hispanics/Latinas. Moreover, recent immigrants (<14 years) had higher fruit and vegetable intake than those residing in the US for 15 years or more [44].

Mammographic breast density (MBD) has been associated with breast cancer risk [45]. A study that investigated the association between migration history and breast density in US-born and foreign-born Hispanics/Latinas predominately from Dominican Republic, Puerto Rico and Cuba [46] found a lower MBD in the foreign-born women with shorter residence in the US. These results suggest that lifestyle changes associated with migration from low- to high- breast cancer incidence regions could affect breast cancer risk in part through their effect on mammographic density [46].

Demographic factors—The residential environment may play a role in breast cancer incidence and mortality through the differential distribution of breast cancer risk factors, such as diet and physical activity, access to quality healthcare and medical treatment, and through psychosocial factors such as stress and social support [47].

Studies focused on neighborhood socioeconomic status (nSES) have reported that higher nSES is associated with higher breast cancer incidence in Hispanics/Latinas [40, 48]. An analysis conducted using data from the NABC study evaluated if the known association between breast cancer risk and the nSES may be influenced by individual factors such as education level. Results suggested that foreign-born Hispanics/Latinas with a vocational/technical degree or some college had higher odds of developing breast cancer compared to foreign-born Hispanics/Latinas with less than a high school degree, independent of nSES (OR: 1.62, 95% CI 1.13 – 2.32). The opposite association was observed for US-born Hispanics/Latinas where higher education was associated with reduced odds of breast cancer (vocational/technical degree or some college, OR: 0.63, 95% CI 0.42 – 0.96; College or higher degree, OR: 0.53, 95% CI 0.42 – 0.96) [43].

It has been suggested that Latinos living in areas with more immigrants may be more likely to maintain healthy behaviors. Women living in immigrant neighborhoods were reported to have higher vegetable and fruit intake irrespective of being immigrants themselves [44]. In addition, residing in a tract with higher proportion of immigrants was associated with lower consumption of fat and higher physical inactivity [49].

The complexity of the results focused on nSES, educational attainment, and the composition of neighborhoods in terms of number of recent immigrants and enclave [40, 50], points to the need for larger epidemiological studies with adequate and complete demographic (including ancestry proportions), lifestyle and neighborhood context/physical environment information that could be used to disentangle individual level factors, from socioeconomic and cultural factors and the physical environment.

Factors associated with breast cancer outcomes among Hispanics/Latinas

Multiple studies have shown that despite the lower incidence of breast cancer in Hispanics/Latinas compared to NHW women, Hispanics/Latinas have a higher risk of breast cancer-specific mortality [11, 12, 51, 52]. This outcome could result from disparities in access to quality care [53], longer times to follow up of abnormal results [54, 55], and the higher frequency of advanced stage at diagnosis in Hispanics/Latinas [8, 12]. Additionally, this disparity could also be explained, in part, by the higher risk in Hispanics/Latinas to develop HER2 positive and triple negative breast cancer (TNBC) subtypes compared to NHW women [56–60].

Screening

Screening mammography allows to detect earlier stage, less aggressive tumors [21]. Multiple studies have showed that women from minority groups are less likely to receive breast cancer screening [61, 62]. A meta-analysis that included 33 studies reported that Hispanics/Latinas were less likely to have received a mammography compared to NHW women (pooled OR: 0.63, 95% CI 0.39 – 0.99) [63]. Additionally, a study that included 21,427 women from different population groups from The National Comprehensive Cancer Network (NCCN) Breast Cancer Outcomes Database examined the association between time to diagnosis, race and stage of the disease, finding that among women with an abnormal screening mammography, Hispanics/Latinas and NHBs had longer times to breast cancer definitive diagnosis (HR: 0.86, 95% CI 0.78 – 0.95 and HR: 0.80, 95% CI 0.73 – 0.87) [64].

Some of the barriers that Hispanics/Latinas experienced for mammography use include: 1) knowledge, for example, when and how often start screening; 2) psychocultural factors such as fear, motivation; and 3) economic-based barriers such as cost of mammography and health insurance [65]. This last aspect is important as Hispanics/Latinos are more likely to be uninsured compared to other population groups [53].

A multi-ethnic study that included 29,951 women analyzed breast cancer screening in foreign-born and US-born women from different population groups reporting that foreign-born women from Mexico, the Caribbean and South America were less likely to have ever had a mammogram compared to US-born women (85.8%, 87.3%, 89.4% vs. 94.1%, respectively). In a multivariable model including sociodemographic characteristics such as educational attainment, age, marital status and place of care, these differences were attenuated and no longer significant [66].

Treatment

Systemic treatment based on chemotherapy or endocrine therapy is recommended for women diagnosed with early-stage breast cancer. Treatment selection depends on menopausal status, stage, axillary lymph node status, histologic and nuclear grade of the primary tumor, hormone receptors and HER2 status [67].

It has been reported that minority population groups such as NHBs, Hispanics/Latinas and Native Americans are less likely to receive recommended treatment regimens [68]. A study that included 17 population-based cancer registries from SEER program reported that

women from Mexico and South or Central America had the highest likelihood of receiving inappropriate treatment (OR: 1.2, 95% CI: 1.0–1.5 and OR: 1.3, 95% CI: 1.0–1.7, respectively). Additionally, they reported that NHBs and Hispanics/Latinas had increased odds of receiving inappropriate primary surgical and radiation breast cancer treatment (OR: 1.5, 95% CI: 1.3–1.6 and OR: 1.2, 95% CI: 1.1–1.3, respectively) [11]. One study did not find differences in the receipt of guideline-concordant chemotherapy by race/ethnicity after adjustment for age and suggested that factors influencing the receipt of guideline-concordant chemotherapy are: being uninsured, residing in high-poverty areas and low educational attainment [69].

Endocrine therapy—Adjuvant endocrine therapy reduces recurrence and improves survival for invasive breast cancer [70]. Even though the rates of guideline-concordant prescribing of adjuvant endocrine therapy are high, the long-term persistence with this type of treatment is low [70] and is more common among racial/ethnic minority populations [71, 72]. Delays in treatment initiation, persistence and adherence to endocrine therapy may contribute to mortality disparities between population groups specifically among women with Estrogen Receptor (ER)-positive tumors and in the early period after diagnosis [71].

A longitudinal study that analyzed factors associated with endocrine therapy initiation and persistence in 743 women diagnosed with invasive breast cancer selected from two SEER population-based cancer registries reported that from this cohort, 10.8% of the patients never initiated therapy, 15.1% started therapy but discontinued prematurely and 74.2% continued use at the second time point. Moreover, they found that initiation of therapy was associated with Hispanic/Latino ethnicity (OR 2.80, 95% CI 1.08 – 7.23) [70]. On the other hand, in a study that included 981,729 women with breast cancer from the National Cancer Database, it was found that the receipt of adjuvant endocrine therapy was less likely in Hispanics/Latinas and Asian women [73]. These results are concordant with those from a study that utilized the SEER-Medicare-linked data with part D plan and reported that Hispanic-Mexican and NHB women had lower odds of tamoxifen initiation (OR: 0.70, 95% CI 0.54 – 0.91 and OR: 0.25, 95% CI 0.10 – 0.62, respectively) compared to NHW women overall; and lower odds of tamoxifen initiation in 0 – 9 months after the date of diagnosis (OR: 0.72, 95% CI 0.55 – 0.93 and OR: 0.28, 95% CI 0.12 – 0.70, respectively) compared to NHW women [74]. Similarly, a study that enrolled 13,753 women from the Kaiser Permanent Northerns California (KPNC) reported that Hispanics/Latinas and Chinese women were less likely to initiate adjuvant hormonal therapy compared to NHW women (OR: 0.82, 95% CI 0.71 – 0.96 and OR:0.78, 95% CI 0.63 – 0.98, respectively) [75].

It has been suggested that economic interventions aimed at lowering out-of-pocket cost could help reduce racial/ethnic disparities in adjuvant endocrine therapy use [73]. Results from a study that investigated persistence and adherence to endocrine treatment in a cohort of 25,511 breast cancer patients aged ≥ 65 years from different race/ethnicities that were enrolled in a Medicare Prescription Drug Plan at the time of their cancer operation showed that NHBs and Hispanics/Latinas were more persistent with their medication than NHW women (69% and 70%, respectively vs. 61%) [76]. In stratified analyses by subsidy and race/ethnicity, they observed that subsidized women in all three race/ethnicity groups had

higher treatment persistence compared to unsubsidized women, which suggests that the subsidy is associated with an improved persistence to breast cancer hormonal therapy [76].

Cytotoxic Chemotherapy—Clinical trials and cohort studies have indicated that survival in women with loco-regional resected breast cancers has improved due to the use of adjuvant chemotherapy [77]. Studies have analyzed the impact of early and late initiation of adjuvant chemotherapy on survival, some of which reported no impact in survival in patients with early initiation of adjuvant chemotherapy [78, 79] while others reported that delays are associated with increased mortality [80–82].

Few studies have analyzed racial disparities in delays of adjuvant chemotherapy. NHBs and Hispanics/Latinas were reported to have higher risk of 60-day delay (RR, 1.36; 95% CI, 1.30 – 1.41 and RR, 1.31; 95% CI, 1.23 – 1.39, respectively) and 90-day delay (RR, 1.56; 95% CI, 1.44 – 1.69 and RR, 1.41; 95% CI, 1.26 – 1.59, respectively) compared to NHW women [83] and more than three month delay in chemotherapy initiation compared to NHW women (18%, 20.8% and 17%, respectively) [82].

The increased risk of delay in adjuvant chemotherapy initiation in minorities such as NHBs and Hispanics/Latinas could be attributed to lack of access to care, geographic distance to the treatment facility, and availability of transportation [83]. Other difficulties such navigating the health system and language barriers may also contribute to the disparities in treatment initiation [83, 84]. The use of a patient navigator increased the percentage of Hispanics/Latinas initiating breast cancer treatment within 30 – 60 days after diagnosis [85].

Tumor characteristics

Stage at diagnosis—Several studies have reported that Hispanics/Latinas are less likely to be diagnosed with breast cancer at a localized stage, compared to NHWs (57% vs 65%) [11, 64, 71, 86, 87]. This could be due the lower mammography utilization and the delay in follow-up after an abnormal mammogram [8, 88]. For example, a study reported that Hispanics/Latinas were less likely to be diagnosed with stage I tumors compared to NHW women (39.8% and 51.5%, respectively), and more likely to have stage III/IV tumors (39.2% and 28.4%, respectively) [89]. Another study that analyzed data from 18 SEER registries (N=373,563) reported lower odds of stage I breast cancer in Hispanics/Latinas compared to NHWs, after adjusting for age, income and ER status (OR 0.71, 95% CI 0.70 – 0.73) [12]. A study that used the California Cancer Registry data reported that stage at diagnosis explained 11% of the survival disparities in Hispanics/Latinas relative to NHW women [90].

Stage at diagnoses is influenced by a number of factors including socioeconomic status, health insurance, uptake of screening and access to health care [90]. A study that analyzed 989 patients (411 NHBs, 397 NHWs, 181 Hispanics/Latinas) from the Breast Cancer Care in Chicago Study reported an association between stage at diagnosis and NHBs and Latino race/ethnicity (OR: 1.560 and 1.941, respectively) [91]. After adjusting for neighborhood context, mode of detection, and facilities, the observed differences in stage at diagnosis by race/ethnicity were no longer statistically significant. These results suggest that the disparity in stage at diagnosis in minorities such as Hispanics/Latinas could be explained by

differences in mode of detection and facility accreditation/resources [91]. Strategies must be designed to reduce the lower uptake of screening in minority groups such as Hispanics/Latinas or NHBs [90, 92].

Intrinsic subtypes—Breast cancer is a heterogeneous disease encompassing different subtypes that can be roughly defined by the expression of hormone receptors (HR), ER and progesterone receptor (PR) and the human epidermal growth factor receptor 2 (HER2) [93–95]. Tumors that express HR belong to the luminal subtype and are characterized by the expression of the *estrogen receptor 1 (ESR1)* gene and other genes regulated by estrogen [93, 95]. On the other hand, there are tumors without expression of HR: the HER2-enriched subtype characterized by the overexpression of HER2 and genes located in the 17q22.24 locus such as *GRB7* [95]; and the triple negative breast cancer subtype that lack expression of hormone receptors and HER2 but express basement membrane cytokeratins [96, 97]. The prognosis of these subtypes is variable. HR negative tumors have the worse outcomes compared to HR positive tumors [98]. Specifically, the TNBC is the subtype with the most aggressive biology and usually relapse in the first three years after diagnosis [99].

Differences in the distribution of breast cancer intrinsic subtypes have been reported between population groups [2, 100]. It has been shown that Hispanics/Latinas have a higher risk of developing more aggressive tumors such as HER2 positive and TNBC compared to NHWs [57, 58, 60, 101].

Studies in the United States that have analyzed the distribution of intrinsic subtypes based on immunohistochemistry surrogates have reported prevalences of TNBC in Hispanics/Latinas ranging from 10% to 18% while in NHWs prevalences range between 8% - 15% [102]. These results are consistent with the findings of a study based on SEER data and including 57,483 patients [58] suggesting that NHBs and Hispanics/Latinas were more likely to be diagnosed with TNBC compared to NHWs (OR: 2.0, 95% CI 1.8 – 2.2 and OR: 1.3, 95% CI 1.2 – 1.5, respectively) and also with HR⁻/HER2⁺ breast cancer (NHBs OR: 1.4, 95% CI 1.2 – 1.6; Hispanics/Latinas OR: 1.4, 95% CI 1.2 – 1.6). Another study that investigated the distribution of breast cancer subtypes based on gene expression data (PAM50, [103]) found a high prevalence of HER2-enriched tumors in Hispanics/Latinas compared to NHW women (15.6% vs. 12.5%, respectively) and also a higher percentage of triple negative subtype in Hispanics/Latinas when compared to NHW (11.6% and 8.20%, respectively) [104].

The prevalence of TNBC reported in studies from Latin America ranged between 12% - 24% and for HER2-enriched subtype ranged between 7% - 24%. A study assessing the association between tumor subtype, based on ER/PR and HER2 status, and genetic ancestry in breast cancer patients from Lima, Peru, reported a 1.2 increase in the odds of HER2 positive disease per 10% increase in IA ancestry [105••]. Additionally, a study from Colombia reported a higher expression of *ERBB2* in Colombian patients above the median Indigenous American ancestry compared to those below the median [106]. Further exploration of these results may lead to the discovery of specific factors (e.g. genetic variants) that could help explain the observed higher prevalence of HER2⁺ tumors in Hispanics/Latinas from regions with relatively high proportions of IA ancestry.

Conclusions

Hispanic/Latina women from Latin American countries with relatively important proportion of Indigenous American ancestry have lower breast cancer incidence than NHW or African American/Black women. However, they are more likely than NHW women to be diagnosed with advanced disease. This can lead not only to increase risk of mortality, but also a lower quality of life as a breast cancer survivor. Despite some evidence that germline variation or other inherited factors could play a role in the observed higher incidence of aggressive tumor subtypes such as HER2 positive tumors, most of the disparity in stage at diagnosis and mortality is likely driven by differences in socioeconomic status and structural inequities that lead to lower awareness, lower screening, lower quality of care, delay between diagnosis and treatment and lower treatment persistence. These disparities should and can be eliminated. Resources and efforts should be pointed at 1) making dramatic changes in awareness and education by developing programs that reach out to communities and that are tailored to different Hispanic/Latino sub-populations, 2) facilitating access to high quality care by building programs within comprehensive cancer centers linking the community to appropriate breast health services at no cost to them, and 3) ensuring that screening is only the beginning of the navigation process and therefore individuals with positive results access the resources and support they need to successfully and timely receive the care they need, not only within the care centers but also when they go back home. Institutions that are already implementing these types of efforts should communicate and transfer their knowledge and experience to others as to make this the norm for “usual care” and eliminate breast cancer health disparities.

REFERENCES

Papers of particular interest, published recently, have been highlighted as:

- Of importance
 - Of major importance
1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394–424. doi: 10.3322/caac.21492. [PubMed: 30207593] • This is the most recent report form Globocan on cancer statistics worldwide
 2. DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, et al. Breast cancer statistics, 2019. *CA Cancer J Clin.* 2019;69(6):438–51. doi: 10.3322/caac.21583. [PubMed: 31577379]
 3. Chlebowski RT, Chen Z, Anderson GL, Rohan T, Aragaki A, Lane D, et al. Ethnicity and breast cancer: factors influencing differences in incidence and outcome. *J Natl Cancer Inst.* 2005;97(6):439–48. doi: 10.1093/jnci/dji064. [PubMed: 15770008]
 4. Fejerman L, Chen GK, Eng C, Huntsman S, Hu D, Williams A, et al. Admixture mapping identifies a locus on 6q25 associated with breast cancer risk in US Latinas. *Hum Mol Genet.* 2012;21(8):1907–17. doi: 10.1093/hmg/ddr617. [PubMed: 22228098]
 5. Fejerman L, Ahmadiyeh N, Hu D, Huntsman S, Beckman KB, Caswell JL, et al. Genome-wide association study of breast cancer in Latinas identifies novel protective variants on 6q25. *Nat Commun.* 2014;5:5260. doi: 10.1038/ncomms6260. [PubMed: 25327703] • This is the first GWAS of breast cancer in Latinos and reported an Indigenous American-specific protective variant located near the ESR1 gene

6. Hoffman J, Fejerman L, Hu D, Hunstman S, Li M, John E, et al. Identification of Novel Common Breast Cancer Risk Variants in Latinas at the 6q25 Locus. *bioRxiv*. 2018.
7. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin*. 2019;69(1):7–34. doi: 10.3322/caac.21551. [PubMed: 30620402]
8. Miller KD, Goding Sauer A, Ortiz AP, Fedewa SA, Pinheiro PS, Tortolero-Luna G, et al. Cancer Statistics for Hispanics/Latinos, 2018. *CA Cancer J Clin*. 2018;68(6):425–45. doi: 10.3322/caac.21494. [PubMed: 30285281]
9. DeSantis CE, Ma J, Goding Sauer A, Newman LA, Jemal A. Breast cancer statistics, 2017, racial disparity in mortality by state. *CA Cancer J Clin*. 2017;67(6):439–48. doi: 10.3322/caac.21412. [PubMed: 28972651]
10. Yedjou CG, Tchounwou PB, Payton M, Miele L, Fonseca DD, Lowe L, et al. Assessing the Racial and Ethnic Disparities in Breast Cancer Mortality in the United States. *Int J Environ Res Public Health*. 2017;14(5). doi: 10.3390/ijerph14050486.
11. Ooi SL, Martinez ME, Li CI. Disparities in breast cancer characteristics and outcomes by race/ethnicity. *Breast Cancer Res Treat*. 2011;127(3):729–38. doi: 10.1007/s10549-010-1191-6. [PubMed: 21076864]
12. Iqbal J, Ginsburg O, Rochon PA, Sun P, Narod SA. Differences in breast cancer stage at diagnosis and cancer-specific survival by race and ethnicity in the United States. *JAMA*. 2015;313(2):165–73. doi: 10.1001/jama.2014.17322. [PubMed: 25585328]
13. Alvidrez J, Castille D, Laude-Sharp M, Rosario A, Tabor D. The National Institute on Minority Health and Health Disparities Research Framework. *Am J Public Health*. 2019;109(S1):S16–S20. doi: 10.2105/AJPH.2018.304883. [PubMed: 30699025] * Multidimensional/multilevel framework proposed by NIMHD to think about health disparities
14. Conomos MP, Laurie CA, Stilp AM, Gogarten SM, McHugh CP, Nelson SC, et al. Genetic Diversity and Association Studies in US Hispanic/Latino Populations: Applications in the Hispanic Community Health Study/Study of Latinos. *Am J Hum Genet*. 2016;98(1):165–84. doi: 10.1016/j.ajhg.2015.12.001. [PubMed: 26748518]
15. G S-S, F K, E T-S. Admixture, Genetics and Complex Diseases in Latin Americans and US Hispanics. *Current Genetic Medicine Reports*. 2018.
16. Bryc K, Velez C, Karafet T, Moreno-Estrada A, Reynolds A, Auton A, et al. Colloquium paper: genome-wide patterns of population structure and admixture among Hispanic/Latino populations. *Proc Natl Acad Sci U S A*. 2010;107 Suppl 2:8954–61. doi: 10.1073/pnas.0914618107. [PubMed: 20445096]
17. Ruiz-Linares A, Adhikari K, Acuna-Alonzo V, Quinto-Sanchez M, Jaramillo C, Arias W, et al. Admixture in latin america: geographic structure, phenotypic diversity and self-perception of ancestry based on 7,342 individuals. *PLoS Genet*. 2014;10(9):e1004572. doi: 10.1371/journal.pgen.1004572. [PubMed: 25254375]
18. Avena S, Via M, Ziv E, Pérez-Stable EJ, Gignoux CR, Dejean C, et al. Heterogeneity in genetic admixture across different regions of Argentina. *PLoS One*. 2012;7(4):e34695. doi: 10.1371/journal.pone.0034695. [PubMed: 22506044]
19. Moreno-Estrada A, Gignoux CR, Fernández-López JC, Zakharia F, Sikora M, Contreras AV, et al. Human genetics. The genetics of Mexico recapitulates Native American substructure and affects biomedical traits. *Science*. 2014;344(6189):1280–5. doi: 10.1126/science.1251688. [PubMed: 24926019]
20. Homburger JR, Moreno-Estrada A, Gignoux CR, Nelson D, Sanchez E, Ortiz-Tello P, et al. Genomic Insights into the Ancestry and Demographic History of South America. *PLoS Genet*. 2015;11(12):e1005602. doi: 10.1371/journal.pgen.1005602. [PubMed: 26636962]
21. Society AAC. *Cancer Facts & Figures for Hispanics/Latinos 2018–2020*. 2018.
22. Di Sibio A, Abriata G, Forman D, Sierra MS. Female breast cancer in Central and South America. *Cancer Epidemiol*. 2016;44 Suppl 1:S110–S20. doi: 10.1016/j.canep.2016.08.010. [PubMed: 27678313]
23. Fejerman L, John EM, Huntsman S, Beckman K, Choudhry S, Perez-Stable E, et al. Genetic ancestry and risk of breast cancer among U.S. Latinas. *Cancer Res*. 2008;68(23):9723–8. doi: 10.1158/0008-5472.CAN-08-2039. [PubMed: 19047150]

24. Fejerman L, Romieu I, John EM, Lazcano-Ponce E, Huntsman S, Beckman KB, et al. European ancestry is positively associated with breast cancer risk in Mexican women. *Cancer Epidemiol Biomarkers Prev.* 2010;19(4):1074–82. doi: 10.1158/1055-9965.EPI-09-1193. [PubMed: 20332279]
25. Hoffman J, Fejerman L, Hu D, Huntsman S, Li M, John EM, et al. Identification of novel common breast cancer risk variants at the 6q25 locus among Latinas. *Breast Cancer Res.* 2019;21(1):3. doi: 10.1186/s13058-018-1085-9. [PubMed: 30642363]
26. Slattery ML, John EM, Torres-Mejia G, Lundgreen A, Herrick JS, Baumgartner KB, et al. Genetic variation in genes involved in hormones, inflammation and energetic factors and breast cancer risk in an admixed population. *Carcinogenesis.* 2012;33(8):1512–21. doi: 10.1093/carcin/bgs163. [PubMed: 22562547]
27. Fejerman L, Stern MC, Ziv E, John EM, Torres-Mejia G, Hines LM, et al. Genetic ancestry modifies the association between genetic risk variants and breast cancer risk among Hispanic and non-Hispanic white women. *Carcinogenesis.* 2013;34(8):1787–93. doi: 10.1093/carcin/bgt110. [PubMed: 23563089]
28. Slattery ML, Hines LH, Lundgreen A, Baumgartner KB, Wolff RK, Stern MC, et al. Diet and lifestyle factors interact with MAPK genes to influence survival: the Breast Cancer Health Disparities Study. *Cancer Causes Control.* 2014;25(9):1211–25. doi: 10.1007/s10552-014-0426-y. [PubMed: 24993294]
29. Slattery ML, John EM, Torres-Mejia G, Lundgreen A, Lewinger JP, Stern MC, et al. Angiogenesis genes, dietary oxidative balance and breast cancer risk and progression: the Breast Cancer Health Disparities Study. *Int J Cancer.* 2014;134(3):629–44. doi: 10.1002/ijc.28377. [PubMed: 23832257]
30. Slattery ML, John EM, Stern MC, Herrick J, Lundgreen A, Giuliano AR, et al. Associations with growth factor genes (FGF1, FGF2, PDGFB, FGFR2, NRG2, EGF, ERBB2) with breast cancer risk and survival: the Breast Cancer Health Disparities Study. *Breast Cancer Res Treat.* 2013;140(3):587–601. doi: 10.1007/s10549-013-2644-5. [PubMed: 23912956]
31. Armstrong N, Ryder S, Forbes C, Ross J, Quek RG. A systematic review of the international prevalence of. *Clin Epidemiol.* 2019;11:543–61. doi: 10.2147/CLEP.S206949. [PubMed: 31372057]
32. Lynce F, Graves KD, Jandorf L, Ricker C, Castro E, Moreno L, et al. Genomic Disparities in Breast Cancer Among Latinas. *Cancer Control.* 2016;23(4):359–72. [PubMed: 27842325] * Comprehensive review on Genomic Disparities in Breast Cancer Among Latinas
33. Cruz-Correa M, Pérez-Mayoral J, Dutil J, Echenique M, Mosquera R, Rivera-Román K, et al. Hereditary cancer syndromes in Latino populations: genetic characterization and surveillance guidelines. *Hered Cancer Clin Pract.* 2017;15:3. doi: 10.1186/s13053-017-0063-z. [PubMed: 28127413]
34. Dutil J, Golubeva VA, Pacheco-Torres AL, Diaz-Zabala HJ, Matta JL, Monteiro AN. The spectrum of BRCA1 and BRCA2 alleles in Latin America and the Caribbean: a clinical perspective. *Breast Cancer Res Treat.* 2015;154(3):441–53. doi: 10.1007/s10549-015-3629-3. [PubMed: 26564481] * Comprehensive description of previous studies reporting on the spectrum of BRCA alleles in Latin America and the Caribbean
35. Zavala VA, Serrano-Gomez SJ, Dutil J, Fejerman L. Genetic Epidemiology of Breast Cancer in Latin America. *Genes (Basel).* 2019;10(2). doi: 10.3390/genes10020153.
36. John EM, Miron A, Gong G, Phipps AI, Felberg A, Li FP, et al. Prevalence of pathogenic BRCA1 mutation carriers in 5 US racial/ethnic groups. *JAMA.* 2007;298(24):2869–76. doi: 10.1001/jama.298.24.2869. [PubMed: 18159056]
37. Weitzel JN, Clague J, Martir-Negron A, Ogaz R, Herzog J, Ricker C, et al. Prevalence and type of BRCA mutations in Hispanics undergoing genetic cancer risk assessment in the southwestern United States: a report from the Clinical Cancer Genetics Community Research Network. *J Clin Oncol.* 2013;31(2):210–6. doi: 10.1200/JCO.2011.41.0027. [PubMed: 23233716]
38. Oliver J, Quezada Urban R, Franco Cortés CA, Díaz Velásquez CE, Montealegre Paez AL, Pacheco-Orozco RA, et al. Latin American Study of Hereditary Breast and Ovarian Cancer. *Front Oncol.* 2019;9:1429. doi: 10.3389/fonc.2019.01429. [PubMed: 31921681]
39. Weitzel JN, Neuhausen SL, Adamson A, Tao S, Ricker C, Maoz A, et al. Pathogenic and likely pathogenic variants in PALB2, CHEK2, and other known breast cancer susceptibility genes among

1054 BRCA-negative Hispanics with breast cancer. *Cancer*. 2019;125(16):2829–36. doi: 10.1002/cncr.32083. [PubMed: 31206626] * Description of rare high penetrance mutations among BRCA-negative Hispanics with breast cancer.

40. Keegan TH, John EM, Fish KM, Alfaro-Velcamp T, Clarke CA, Gomez SL. Breast cancer incidence patterns among California Hispanic women: differences by nativity and residence in an enclave. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2010;19(5):1208–18. doi: 10.1158/1055-9965.EPI-10-0021.
41. John EM, Phipps AI, Davis A, Koo J. Migration history, acculturation, and breast cancer risk in Hispanic women. *Cancer Epidemiol Biomarkers Prev*. 2005;14(12):2905–13. doi: 10.1158/1055-9965.EPI-05-0483. [PubMed: 16365008]
42. Pinheiro PS, Sherman RL, Trapido EJ, Fleming LE, Huang Y, Gomez-Marín O, et al. Cancer incidence in first generation U.S. Hispanics: Cubans, Mexicans, Puerto Ricans, and new Latinos. *Cancer Epidemiol Biomarkers Prev*. 2009;18(8):2162–9. doi: 10.1158/1055-9965.EPI-09-0329. [PubMed: 19661072] • Showed how cancer rates varies among Hispanic subpopulations by country of origin and immigration status
43. Conroy SM, Shariff-Marco S, Koo J, Yang J, Keegan TH, Sangaramoorthy M, et al. Racial/Ethnic Differences in the Impact of Neighborhood Social and Built Environment on Breast Cancer Risk: The Neighborhoods and Breast Cancer Study. *Cancer Epidemiol Biomarkers Prev*. 2017;26(4):541–52. doi: 10.1158/1055-9965.EPI-16-0935. [PubMed: 28196846]
44. Dubowitz T, Subramanian SV, Acevedo-Garcia D, Osypuk TL, Peterson KE. Individual and neighborhood differences in diet among low-income foreign and U.S.-born women. *Womens Health Issues*. 2008;18(3):181–90. doi: 10.1016/j.whi.2007.11.001. [PubMed: 18222706]
45. McCormack VA, dos Santos Silva I. Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2006;15(6):1159–69. doi: 10.1158/1055-9965.EPI-06-0034. [PubMed: 16775176]
46. Tehranifar P, Rodriguez CB, April-Sanders AK, Desperito E, Schmitt KM. Migration History, Language Acculturation, and Mammographic Breast Density. *Cancer Epidemiol Biomarkers Prev*. 2018;27(5):566–74. doi: 10.1158/1055-9965.EPI-17-0885. [PubMed: 29475965]
47. 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. [PubMed: 25885593]
48. Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer Causes Control*. 2001;12(8):703–11. doi: 10.1023/a:1011240019516. [PubMed: 11562110]
49. Osypuk TL, Diez Roux AV, Hadley C, Kandula NR. Are immigrant enclaves healthy places to live? The Multi-ethnic Study of Atherosclerosis. *Soc Sci Med*. 2009;69(1):110–20. doi: 10.1016/j.socscimed.2009.04.010. [PubMed: 19427731]
50. Pruitt SL, Tiro JA, Xuan L, Lee SJ. Hispanic and Immigrant Paradoxes in U.S. Breast Cancer Mortality: Impact of Neighborhood Poverty and Hispanic Density. *Int J Environ Res Public Health*. 2016;13(12). doi: 10.3390/ijerph13121238.
51. Pinheiro PS, Williams M, Miller EA, Easterday S, Moonie S, Trapido EJ. Cancer survival among Latinos and the Hispanic Paradox. *Cancer Causes Control*. 2011;22(4):553–61. doi: 10.1007/s10552-011-9727-6. [PubMed: 21279543]
52. Li CI, Malone KE, Daling JR. Differences in breast cancer stage, treatment, and survival by race and ethnicity. *Arch Intern Med*. 2003;163(1):49–56. doi: 10.1001/archinte.163.1.49. [PubMed: 12523916]
53. Rodriguez-Alcalá ME, Qin H, Jeanetta S. The Role of Acculturation and Social Capital in Access to Health Care: A Meta-study on Hispanics in the US. *J Community Health*. 2019;44(6):1224–52. doi: 10.1007/s10900-019-00692-z. [PubMed: 31273620]
54. Press R, Carrasquillo O, Sciacca RR, Giardina EG. Racial/ethnic disparities in time to follow-up after an abnormal mammogram. *J Womens Health (Larchmt)*. 2008;17(6):923–30. doi: 10.1089/jwh.2007.0402. [PubMed: 18554094]

55. Goldman LE, Walker R, Hubbard R, Kerlikowske K, Consortium BCS. Timeliness of abnormal screening and diagnostic mammography follow-up at facilities serving vulnerable women. *Med Care*. 2013;51(4):307–14. doi: 10.1097/MLR.0b013e318280f04c. [PubMed: 23358386]
56. Banegas MP, Tao L, Altekruze S, Anderson WF, John EM, Clarke CA, et al. Heterogeneity of breast cancer subtypes and survival among Hispanic women with invasive breast cancer in California. *Breast Cancer Res Treat*. 2014;144(3):625–34. doi: 10.1007/s10549-014-2882-1. [PubMed: 24658879]
57. Hines LM, Risendal B, Byers T, Mengshol S, Lowery J, Singh M. Ethnic disparities in breast tumor phenotypic subtypes in Hispanic and non-Hispanic white women. *J Womens Health (Larchmt)*. 2011;20(10):1543–50. doi: 10.1089/jwh.2010.2558. [PubMed: 21721934]
58. Howlader N, Altekruze SF, Li CI, Chen VW, Clarke CA, Ries LA, et al. US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. *J Natl Cancer Inst*. 2014;106(5). doi: 10.1093/jnci/dju055.
59. Parise CA, Bauer KR, Caggiano V. Variation in breast cancer subtypes with age and race/ethnicity. *Crit Rev Oncol Hematol*. 2010;76(1):44–52. doi: 10.1016/j.critrevonc.2009.09.002. [PubMed: 19800812]
60. Serrano-Gomez SJ, Fejerman L, Zabaleta J. Breast Cancer in Latinas: A Focus on Intrinsic Subtypes Distribution. *Cancer Epidemiol Biomarkers Prev*. 2018;27(1):3–10. doi: 10.1158/1055-9965.EPI-17-0420. [PubMed: 29054978]
61. Wells KJ, Roetzheim RG. Health disparities in receipt of screening mammography in Latinas: a critical review of recent literature. *Cancer Control*. 2007;14(4):369–79. doi: 10.1177/107327480701400407. [PubMed: 17914337]
62. Society AC. *Breast Cancer Facts & Figures 2017–2018*. 2017.
63. Purc-Stephenson RJ, Gorey KM. Lower adherence to screening mammography guidelines among ethnic minority women in America: a meta-analytic review. *Prev Med*. 2008;46(6):479–88. doi: 10.1016/j.jpmed.2008.01.001. [PubMed: 18295872]
64. Warner ET, Tamimi RM, Hughes ME, Ottesen RA, Wong YN, Edge SB, et al. Time to diagnosis and breast cancer stage by race/ethnicity. *Breast Cancer Res Treat*. 2012;136(3):813–21. doi: 10.1007/s10549-012-2304-1. [PubMed: 23099438]
65. Molina Y, Plascak JJ, Patrick DL, Bishop S, Coronado GD, Beresford SA. Neighborhood Predictors of Mammography Barriers Among US-Based Latinas. *J Racial Ethn Health Disparities*. 2017;4(2):233–42. doi: 10.1007/s40615-016-0222-3. [PubMed: 27059049]
66. Clarke TC, Endeshaw M, Duran D, Saraiya M. Breast Cancer Screening Among Women by Nativity, Birthplace, and Length of Time in the United States. *Natl Health Stat Report*. 2019(129):1–15.
67. Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. *J Natl Cancer Inst*. 2002;94(5):334–57. doi: 10.1093/jnci/94.5.334. [PubMed: 11880473]
68. Chen L, Li CI. Racial disparities in breast cancer diagnosis and treatment by hormone receptor and HER2 status. *Cancer Epidemiol Biomarkers Prev*. 2015;24(11):1666–72. doi: 10.1158/1055-9965.EPI-15-0293. [PubMed: 26464428]
69. Wu XC, Lund MJ, Kimmick GG, Richardson LC, Sabatino SA, Chen VW, et al. Influence of race, insurance, socioeconomic status, and hospital type on receipt of guideline-concordant adjuvant systemic therapy for locoregional breast cancers. *J Clin Oncol*. 2012;30(2):142–50. doi: 10.1200/JCO.2011.36.8399. [PubMed: 22147735]
70. Friese CR, Pini TM, Li Y, Abrahamse PH, Graff JJ, Hamilton AS, et al. Adjuvant endocrine therapy initiation and persistence in a diverse sample of patients with breast cancer. *Breast Cancer Res Treat*. 2013;138(3):931–9. doi: 10.1007/s10549-013-2499-9. [PubMed: 23542957]
71. Warner ET, Tamimi RM, Hughes ME, Ottesen RA, Wong YN, Edge SB, et al. Racial and Ethnic Differences in Breast Cancer Survival: Mediating Effect of Tumor Characteristics and Sociodemographic and Treatment Factors. *J Clin Oncol*. 2015;33(20):2254–61. doi: 10.1200/JCO.2014.57.1349. [PubMed: 25964252]
72. Neugut AI, Subar M, Wilde ET, Stratton S, Brouse CH, Hillyer GC, et al. Association between prescription co-payment amount and compliance with adjuvant hormonal therapy in women with

- early-stage breast cancer. *J Clin Oncol*. 2011;29(18):2534–42. doi: 10.1200/JCO.2010.33.3179. [PubMed: 21606426]
73. Daly B, Olopade OI, Hou N, Yao K, Winchester DJ, Huo D. Evaluation of the Quality of Adjuvant Endocrine Therapy Delivery for Breast Cancer Care in the United States. *JAMA Oncol*. 2017;3(7):928–35. doi: 10.1001/jamaoncol.2016.6380. [PubMed: 28152150]
74. Farias AJ, Du XL. Ethnic differences in initiation and timing of adjuvant endocrine therapy among older women with hormone receptor-positive breast cancer enrolled in Medicare Part D. *Med Oncol*. 2016;33(2):19. doi: 10.1007/s12032-016-0732-1. [PubMed: 26786154]
75. Livaudais JC, Hershman DL, Habel L, Kushi L, Gomez SL, Li CI, et al. Racial/ethnic differences in initiation of adjuvant hormonal therapy among women with hormone receptor-positive breast cancer. *Breast Cancer Res Treat*. 2012;131(2):607–17. doi: 10.1007/s10549-011-1762-1. [PubMed: 21922245]
76. Biggers A, Shi Y, Charlson J, Smith EC, Smallwood AJ, Nattinger AB, et al. Medicare D Subsidies and Racial Disparities in Persistence and Adherence With Hormonal Therapy. *J Clin Oncol*. 2016;34(36):4398–404. doi: 10.1200/JCO.2016.67.3350. [PubMed: 27998232]
77. (EBCTCG) EBCTCG. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;365(9472):1687–717. doi: 10.1016/S0140-6736(05)66544-0. [PubMed: 15894097]
78. Jara Sánchez C, Ruiz A, Martín M, Antón A, Munárriz B, Plazaola A, et al. Influence of timing of initiation of adjuvant chemotherapy over survival in breast cancer: a negative outcome study by the Spanish Breast Cancer Research Group (GEICAM). *Breast Cancer Res Treat*. 2007;101(2):215–23. doi: 10.1007/s10549-006-9282-0. [PubMed: 16823507]
79. Buzdar AU, Smith TL, Powell KC, Blumenschein GR, Gehan EA. Effect of timing of initiation of adjuvant chemotherapy on disease-free survival in breast cancer. *Breast Cancer Res Treat*. 1982;2(2):163–9. doi: 10.1007/bf01806452. [PubMed: 6897369]
80. Hershman DL, Wang X, McBride R, Jacobson JS, Grann VR, Neugut AI. Delay of adjuvant chemotherapy initiation following breast cancer surgery among elderly women. *Breast Cancer Res Treat*. 2006;99(3):313–21. doi: 10.1007/s10549-006-9206-z. [PubMed: 16583264]
81. Colleoni M, Bonetti M, Coates AS, Castiglione-Gertsch M, Gelber RD, Price K, et al. Early start of adjuvant chemotherapy may improve treatment outcome for premenopausal breast cancer patients with tumors not expressing estrogen receptors. The International Breast Cancer Study Group. *J Clin Oncol*. 2000;18(3):584–90. doi: 10.1200/JCO.2000.18.3.584.
82. Nurgalieva ZZ, Franzini L, Morgan RO, Vernon SW, Liu CC, Du XL. Impact of timing of adjuvant chemotherapy initiation and completion after surgery on racial disparities in survival among women with breast cancer. *Med Oncol*. 2013;30(1):419. doi: 10.1007/s12032-012-0419-1. [PubMed: 23292872]
83. Fedewa SA, Ward EM, Stewart AK, Edge SB. Delays in adjuvant chemotherapy treatment among patients with breast cancer are more likely in African American and Hispanic populations: a national cohort study 2004–2006. *J Clin Oncol*. 2010;28(27):4135–41. doi: 10.1200/JCO.2009.27.2427. [PubMed: 20697082]
84. Katz SJ, Wallner LP, Abrahamse PH, Janz NK, Martinez KA, Shumway DA, et al. Treatment experiences of Latinas after diagnosis of breast cancer. *Cancer*. 2017;123(16):3022–30. doi: 10.1002/cncr.30702. [PubMed: 28398629]
85. Ramirez A, Perez-Stable E, Penedo F, Talavera G, Carrillo JE, Fernández M, et al. Reducing time-to-treatment in underserved Latinas with breast cancer: the Six Cities Study. *Cancer*. 2014;120(5):752–60. doi: 10.1002/cncr.28450. [PubMed: 24222098]
86. Power EJ, Chin ML, Haq MM. Breast Cancer Incidence and Risk Reduction in the Hispanic Population. *Cureus*. 2018;10(2):e2235. doi: 10.7759/cureus.2235. [PubMed: 29713580]
87. Akinyemiju T, Moore JX, Ojesina AI, Waterbor JW, Altekruze SF. Racial disparities in individual breast cancer outcomes by hormone-receptor subtype, area-level socio-economic status and healthcare resources. *Breast Cancer Res Treat*. 2016;157(3):575–86. doi: 10.1007/s10549-016-3840-x. [PubMed: 27255533]

88. Siegel RL, Fedewa SA, Miller KD, Goding-Sauer A, Pinheiro PS, Martinez-Tyson D, et al. Cancer statistics for Hispanics/Latinos, 2015. *CA Cancer J Clin.* 2015;65(6):457–80. doi: 10.3322/caac.21314. [PubMed: 26375877]
89. Martínez ME, Gomez SL, Tao L, Cress R, Rodriguez D, Unkart J, et al. Contribution of clinical and socioeconomic factors to differences in breast cancer subtype and mortality between Hispanic and non-Hispanic white women. *Breast Cancer Res Treat.* 2017;166(1):185–93. doi: 10.1007/s10549-017-4389-z. [PubMed: 28698973]
90. Ellis L, Canchola AJ, Spiegel D, Ladabaum U, Haile R, Gomez SL. Racial and Ethnic Disparities in Cancer Survival: The Contribution of Tumor, Sociodemographic, Institutional, and Neighborhood Characteristics. *J Clin Oncol.* 2018;36(1):25–33. doi: 10.1200/JCO.2017.74.2049. [PubMed: 29035642]
91. Warnecke RB, Campbell RT, Vijayasiri G, Barrett RE, Rauscher GH. Multilevel Examination of Health Disparity: The Role of Policy Implementation in Neighborhood Context, in Patient Resources, and in Healthcare Facilities on Later Stage of Breast Cancer Diagnosis. *Cancer Epidemiol Biomarkers Prev.* 2019;28(1):59–66. doi: 10.1158/1055-9965.EPI-17-0945. [PubMed: 30352817]
92. Guan A, Lichtensztajn D, Oh D, Jain J, Tao L, Hiatt RA, et al. Breast Cancer in San Francisco: Disentangling Disparities at the Neighborhood Level. *Cancer Epidemiol Biomarkers Prev.* 2019;28(12):1968–76. doi: 10.1158/1055-9965.EPI-19-0799. [PubMed: 31548180]
93. Perou CM, Sorlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. *Nature.* 2000;406(6797):747–52. doi: 10.1038/35021093. [PubMed: 10963602]
94. Hu Z, Fan C, Oh DS, Marron JS, He X, Qaqish BF, et al. The molecular portraits of breast tumors are conserved across microarray platforms. *BMC Genomics.* 2006;7:96. doi: 10.1186/1471-2164-7-96. [PubMed: 16643655]
95. Network CGA. Comprehensive molecular portraits of human breast tumours. *Nature.* 2012;490(7418):61–70. doi: 10.1038/nature11412. [PubMed: 23000897]
96. Cheang MC, Voduc D, Bajdik C, Leung S, McKinney S, Chia SK, et al. Basal-like breast cancer defined by five biomarkers has superior prognostic value than triple-negative phenotype. *Clin Cancer Res.* 2008;14(5):1368–76. doi: 10.1158/1078-0432.CCR-07-1658. [PubMed: 18316557]
97. Nielsen TO, Hsu FD, Jensen K, Cheang M, Karaca G, Hu Z, et al. Basal-Like Subtype of Invasive Breast Carcinoma: Immunohistochemical and Clinical Characterization of the. *clin Cancer Res.* 2004;10.
98. Sorlie T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proc Natl Acad Sci U S A.* 2001;98(19):10869–74. doi: 10.1073/pnas.191367098. [PubMed: 11553815]
99. Lehmann BD, Bauer JA, Chen X, Sanders ME, Chakravarthy AB, Shyr Y, et al. Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. *J Clin Invest.* 2011;121(7):2750–67. doi: 10.1172/JCI45014. [PubMed: 21633166]
100. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, et al. Race, Breast Cancer Subtypes, and Survival in the Carolina Breast Cancer Study. *Journal of the American Medical Association.* 2006;295(21).
101. Parise CA, Caggiano V. Disparities in race/ethnicity and socioeconomic status: risk of mortality of breast cancer patients in the California Cancer Registry, 2000–2010. *BMC Cancer.* 2013;13:449. doi: 10.1186/1471-2407-13-449. [PubMed: 24083624]
102. Fejerman L, Serrano-Gómez SJ, Tamayo L. Breast Cancer Risk and Mortality in Women of Latin American Origin. In: Trapido AGREJ, editor. *Advancing the Science of Cancer in Latinos* Springer Open; 2020.
103. Parker JS, Mullins M, Cheang MC, Leung S, Voduc D, Vickery T, et al. Supervised risk predictor of breast cancer based on intrinsic subtypes. *J Clin Oncol.* 2009;27(8):1160–7. doi: 10.1200/JCO.2008.18.1370. [PubMed: 19204204]
104. Sweeney C, Bernard PS, Factor RE, Kwan ML, Habel LA, Quesenberry CP Jr, et al. Intrinsic subtypes from PAM50 gene expression assay in a population-based breast cancer cohort:

differences by age, race, and tumor characteristics. *Cancer Epidemiol Biomarkers Prev.* 2014;23(5):714–24. doi: 10.1158/1055-9965.EPI-13-1023. [PubMed: 24521995]

105. Marker KM, Zavala VA, Vidaurre T, Lott PC, Vásquez JN, Casavilca-Zambrano S, et al. Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer Is Associated with Indigenous American Ancestry in Latin American Women. *Cancer Research.* 2020. doi: 10.1158/0008-5472.can-19-3659. • This study reported for the first time an association between Indigenous American ancestry and an increased risk for HER2 positive tumors in Latina women
106. Serrano-Gómez SJ, Sanabria-Salas MC, Garay J, Baddoo MC, Hernández-Suarez G, Mejía JC, et al. Ancestry as a potential modifier of gene expression in breast tumors from Colombian women. *PLoS One.* 2017;12(8):e0183179. doi: 10.1371/journal.pone.0183179. [PubMed: 28832682]