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### Title

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### Permalink

<https://escholarship.org/uc/item/2pk25833>

### Journal

Cancer Epidemiology Biomarkers & Prevention, 27(1)

### ISSN

1055-9965

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### Publication Date

2018

### DOI

10.1158/1055-9965.epi-17-0420

Peer reviewed



# HHS Public Access

Author manuscript

*Cancer Epidemiol Biomarkers Prev.* Author manuscript; available in PMC 2019 January 01.

Published in final edited form as:

*Cancer Epidemiol Biomarkers Prev.* 2018 January ; 27(1): 3–10. doi:10.1158/1055-9965.EPI-17-0420.

## Breast cancer in Latinas: a focus on intrinsic subtypes distribution

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### Abstract

Breast cancer is the most frequent cancer in women worldwide. It is classified into intrinsic subtypes characterized by different molecular profiles and prognosis. The prevalence of the different intrinsic subtypes varies between population groups. Immunohistochemistry surrogates based on the expression of the estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) have been widely used to study the distribution of intrinsic subtypes in Non-Hispanic Whites and African Americans, but data is limited for Hispanic/Latina women. Similarly, most studies analyzing gene expression profiles only include women of European descent. The present review focuses on studies that describe the distribution of breast cancer subtypes in Hispanic/Latina women and highlights the need for more research in this population.

### Introduction

Breast cancer is the most common cancer in women worldwide (1–3). In the United States, it accounts for 29% of all cancer cases diagnosed and 15% of all cancer related-deaths reported annually (1,3,4).

There are notable differences in breast cancer incidence and mortality between populations in the United States (U.S.). Data from the Surveillance, Epidemiology and End Results Program (SEER) showed that the age-adjusted incidence for non-Hispanic White (NHW) women was 128.0, 125.2 for African-Americans (AA), 92.4 for Hispanic/Latinas, 97.3 for Asian/Pacific Islanders (API) and 81.2 for Native Americans/Alaskan Natives (5). Despite the relatively low incidence of breast cancer in Hispanic/Latinas, their risk of mortality is higher than in NHWs (HR=1.4 CI 95% 1.3–1.5), even after adjustment for tumor characteristics and treatment (HR=1.1 CI 95% 1.0–1.2) (1,6–8).

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The reason for the differences in the mortality rates between population groups is still not fully understood. Some researchers propose that differences in socioeconomic and cultural factors limit health care and treatment access, contributing to increased mortality rates in Hispanic/Latinas and AA women (9). However, other studies reported that the observed differences remained significant after adjustment for access to health care, treatment and other socio-demographic factors (10–13). A better understanding of the similarities and differences in the biological characteristics of breast tumors between racial/ethnic groups, with consideration of variation in ancestral genetic ancestry contributions, could provide important insights into observed differences in outcome. We provide a description of published studies on the distribution of breast cancer intrinsic subtypes and molecular profiles in Hispanic/Latina women and highlight the need for more research in this population.

## Materials and Methods

### Eligible studies

All studies originally published in English and confirmed as focused on tumor subtype characterization in Hispanics/Latinas were included in this review.

### Publication search

We searched the published literature using PubMed (NIH). To identify studies we queried medical subject headings (MeSH): “breast cancer subtypes” and “Latinas” that retrieved 29 publications from which 8 were included in this paper. We also search for “breast cancer intrinsic subtypes” and “Hispanic” and this search retrieved 62 papers from which 19 were eligible for this review; 8 of them were already included from the last search. Finally we used “breast cancer subtypes distribution” and “Hispanic” and we found 59 publications, from which 4 were included in this paper. The last search was on July 11 2017. All resulted studies were retrieved and cited publications checked for related publications. We limited our electronic search to original English language publications and published since 2007 to included only studies from the last 10 years.

### Definition of breast cancer intrinsic subtypes

In 2000, Perou et. al (14) published the first paper classifying breast cancer into intrinsic subtypes based on gene expression profiles. Using a cDNA microarray of 65 surgical specimens from 42 different individuals, Perou’s group defined a list of ‘intrinsic’ genes that have consistent expression in tumors from the same patient (i.e. primary and metastasis) but differ between tumors from different patients. This analysis revealed 4 main molecular subtypes: luminal, HER2-enriched, basal-like and normal-like. ER-positive tumors, identified as luminal, are characterized by increased expression of genes from luminal cells, such as *GATA*, *X-box binding protein 1*, *trefoil factor 3* and *hepatocyte nuclear factor* (15). The luminal group is, in turn, divided into luminal A and B subtypes, with the luminal B expressing higher levels of proliferation-related genes and often expressing *human epidermal growth factor receptor-1 (HER1)*, *HER2*, and/or *cyclin E1* whereas luminal A subtype have a higher expression of genes such as the *estrogen receptor gene (ESR1)* and *GATA3* (16–19). The ER-negative group is divided into basal-like, HER2-enriched, and

normal-like. The basal-like subgroup is characterized by expression of basement membrane cytokeratins such as *CK5/6* and *CK17*, and lacks the expression of *ESR1* and its co-expressed genes. Patients with *BRCA1* mutations have been associated with the development of basal-like tumors (20–22). The HER2-enriched subtype is associated with high expression of *ERBB2* and genes in the 17q22.24 locus including *GRB7* and *MIEN1* (23–26). The normal-like subtype is still a matter of debate as some researchers have considered it as an artifact due to contamination with normal tissue adjacent to the tumor (27). Its molecular profile is characterized by the expression of genes typical of basal epithelial cells and adipose cells and low expression of genes from luminal epithelial cells (14,28,29).

The clinical implication of this new classification became apparent one year later when the same group, using a larger set of tumors, demonstrated that each of the intrinsic subtypes was associated with different prognoses (29–31). The HER2-enriched and basal-like subtypes have the poorest prognosis when compared to the luminal subtypes. Among luminal tumors, the luminal B has worst prognosis compared to luminal A, which is expected given its high expression of cell proliferation genes (32–37).

### Breast cancer in Hispanic/Latino women

The terms “Hispanic” or “Latino” are generally used to refer to people from Mexico, Cuba, Puerto Rico, Central or South America. Latinos constitute the largest, youngest and fastest-growing minority group in the United States (38). An estimated 55 million people living in the United States self-identified as Hispanic or Latino (39), representing 17% of the total population in United States in 2014, and predicted to increase to 35% by the year 2050 (40). Hispanic/Latinos is a heterogeneous group that originated from the admixture of Native American, European, and African ancestries. Hispanic/Latinos can self-identify as any race defined by the 2000 United States Census (38,41–43).

Fejerman and colleagues in 2008 (44) showed the first evidence of association between genetic ancestry and breast cancer risk in Hispanic/Latinas from the San Francisco Bay area. They found an increased risk of breast cancer for every 25% increase in European ancestry (OR=1.79, CI 95% 1.28 – 2.79) that remained significant after adjusting for known risk factors for the disease (OR=1.39, CI 95% 1.06 – 2.11). Two years later they retested the association in women from Mexico to explore the possibility that the original finding was due to environmental factors. In this population, they replicated the original association finding that for every 25% increase in European ancestry (modeled as a continuous variable), there was a 20% increase in breast cancer risk (CI 95% 1.03–1.41) (45). Fejerman and colleagues (43) also showed that genetic ancestry was associated with breast cancer specific survival in a sample of Hispanic/Latinas from California. Women with more than 50% Native American ancestry had a mortality hazard that almost doubled that of Hispanic/Latinas with 50% or less of Native American ancestry.

Recently, a population-based study using SEER registries found an increase in the risk of breast cancer mortality in Hispanic/Latino women (46,47). Ooi et.al (8), also based on SEER data, found that Hispanic/Latino women have 1.1-fold greater risk of breast cancer specific

mortality compared to NHW women after adjusting for disease characteristics, treatments and some socioeconomic characteristics such as poverty and education (8).

Differences in mortality among population groups might be explained by a combination of differences in socioeconomic and biological factors (48). For example, Hispanic/Latinas are usually diagnosed at more advanced stages of the disease, possibly as a consequence of poor access to mammography screening and delayed follow-up of an abnormal mammography (46,47). Additionally, some studies have suggested that differences in language spoken, cultural beliefs and other factors contribute to inconsistencies in the screening and follow up of an abnormal mammogram even in populations with similar access to screening (49–51). Regarding biological factors, population-based studies in the U.S. have reported that Hispanic/Latino women are more likely to have ER (–) tumors, compared to NHW women (52,53), similar to what has been reported for AA women (46).

### **Distribution of intrinsic subtypes of breast cancer in Hispanic/Latino women**

Different available surrogates for molecular classification of breast cancer into intrinsic subtypes have been proposed (Table 1). The basic and most used classification includes the evaluation of hormone receptors (HR) ER and PR and the evaluation of HER2 by immunohistochemistry (IHC). The St Gallen surrogates included Ki67 to better stratify luminal tumors.

The prevalence of breast cancer intrinsic subtypes varies according to race/ethnicity (Table 2). There have been multiple studies evaluating the distribution of IHC-based tumor subtypes in Hispanic/Latinas using population-based registries from SEER (54,55). These studies report a higher prevalence of triple negative tumors in Hispanic/Latinas compared to NHW women, with percentages in Hispanic/Latinas ranging between 14% and 15% depending on the study. Using polytomous logistic regression modelling, the HR+/HER2– as the reference subtype, and NHW as the reference explanatory variable (54) they have also reported a higher risk of developing triple negative tumors and HR–/HER2+ tumors among Hispanic/Latinas (OR = 1.3, 95% CI 1.2 – 1.5 and OR = 1.4, 95% CI = 1.2 to 1.6 respectively).

Similar results have been observed in studies that used data from the California Cancer Registry (CCR) (53,56–58). The prevalence of triple negative subtype in these studies ranged between 13% and 17%. Concordant with previous reports, some of these studies also observed that Hispanic/Latina women were more likely to be diagnosed with triple negative disease (OR = 1.23 95% CI 1.14 – 1.34) when compared to NHW (56). Banegas et. al (53) used data from the CCR and analyzed the association between breast cancer subtype and patients attributes and found that foreign-born Hispanic/Latina women were significantly more likely than U.S born Hispanic/Latina women to be diagnosed with HR–/HER2+ subtype (OR=1.17, 95% CI 1.02 – 1.35). Moreover, lower socioeconomic status (SES) was also associated with a higher risk for triple negative and HR–/HER2+ subtypes. Even though this study included a large number of Hispanic/Latina women, they were all residents of California and therefore mostly of Mexican descent (53,59). This result cannot be generalized to all Hispano/Latino subpopulations.

Plasilova et. al (60) used The National Cancer Database (NCDB) to analyze the characteristics of 38,813 breast tumors defined by the expression of HR and HER2 in women diagnosed between 2010 and 2011. They observed that among Hispanic/Latina women, the luminal A subtype was the most prevalent (67.4%) followed by triple negative (14.8%), luminal B (11.9%) and HER2-enriched (5.8%). Sineshaw et.al (61) also used the NCDB data. They analyzed 260,174 breast cancer cases from that database and found that the prevalence of triple negative subtype in Hispanic/Latina was 13.8%. This latter analysis showed that Hispanic/Latina women had 1.26 times greater odds of being diagnosed with HER2-enriched subtype (OR = 1.26, 95% CI 1.16 – 1.37) and 1.17 times greater odds of being diagnosed with triple negative subtype (OR = 1.17, 95% CI 1.11 – 1.24) using NHWs as reference population and the luminal A subtype as reference subtype.

Population-based studies such as The Life After Cancer Epidemiology (LACE) study and the 4-Corners Breast Cancer Study are valuable sources to explore ethnic differences in the distribution of breast cancer subtypes. Hines et. al. (62) reviewed pathology reports and established tissue microarrays in a sample of 188 women (69 Hispanic/Latino women and 119 NHW women) who were Colorado participants in the 4-Corners Breast Cancer Study. Five immunohistochemically markers (ER, PR, HER2, EGFR, and CK5/6) were evaluated using standard IHC staining methods. They also found that Hispanic/Latino women had a higher prevalence of ER- tumors (ER-/PR+/HER2+, ER-/PR+/HER2-, ER-,PR-/HER2+, ER-/PR-/HER2-) compared to NHW women (36.2% vs. 22.7%). Specifically, Hispanic/Latina women were reported to have a higher proportion of triple negative subtype compared to NHW (17.4% and 15.1%, respectively), but this difference was not statistically significant. Kroenke, et.al (63) analyzed 1,635 breast cancer patients from the Pathways and LACE study and found a higher prevalence of triple negative subtype (14%) when compared to the prevalence of this subtype in NHW (11.0%).

The study by Sweeney et. al (64) is the largest study to date describing the distribution of intrinsic subtypes based on PAM50 classification (27). This study included 1,319 women and observed an increased prevalence of the most aggressive intrinsic subtypes such as HER2-enriched (15.6%) and luminal B (24.0%) in Hispanic/Latina women when compared to women from other races/ethnicities.

Hispanic/Latino women have also been reported to have a relatively high proportion of HER2-positive tumors (ER+/PR+/HER2+, ER+/PR-/HER2+, ER-/PR+/HER2+, ER-/PR-/HER2+), even after adjustment for tumor characteristics such as grade, stage, ER status and risk factors such as number of children and alcohol consumption (39). Hines et. al. (62) observed that Hispanic/Latino women had a significantly higher prevalence of HER2-positive tumors (HR+/HER2+ and HR-/HER2+) compared to NHW (31.95% vs. 14.3%, respectively,  $p < 0.01$ ). Specifically they observed a higher prevalence of the HER2-enriched subtype in Hispanic/Latina compared to NHWs (14.5% vs. 5.9%). These results are concordant with those in Kwan et. al. (65), which included 2,280 women from the LACE study. These women were diagnosed with invasive breast cancer between 1997 and 2000. Breast cancer subtypes were defined by the expression of HR and HER2. They reported that HER2-enriched subtype tumors (HR-/HER2+) were more common in Hispanic/Latinas (OR = 2.19, 95% CI = 1.16 – 4.13) and Asians (OR = 2.02, 95% CI = 1.05 – 3.88) than NHWs.

Howlander et. al (54) also observed a high prevalence of HER2-enriched tumors but in an early-onset group (11.4%) compared to an older group (6.47%). Banegas et. al (53) found that foreign-born Hispanic women were significantly more likely to be diagnosed with HR–/HER2+ than HR+/HER2– breast cancer (OR=1.17, 95% CI: 1.02–1.35) compared to U.S.-born Hispanic women.

We found one hospital-based study from United States. Singh et al. (66) analyzed the distribution of intrinsic subtypes of breast cancer in a sample of 2,120 patients from five major racial/ethnic groups: NHW, AA and Hispanics/Latinos from the U.S., Chinese (Jilin, China) and Indian (Delhi, India), and according to age (early-onset 40-years and older group 50-years and older). This study included patient race data from the Memorial Sloan Kettering Cancer Center for AA patients, New York University School of Medicine for NHW patients, The University of Texas MD Anderson Cancer Center for Hispanic/Latino patients, The first Hospital of Jilin University (China) for native Chinese patients and Rajiv Gandhi Cancer Institute & Research Centre (India) for native Indian patients. The IHC data on HR and HER2 was retrieved from each participating study to classify breast cancer into intrinsic subtypes. They found that the prevalence of triple negative breast cancer was higher in Indians (23.3%) followed by AA (22.8%), Hispanic/Latina (19.7%), Chinese (14.3%) and NHW (9.8%). Similar percentages were observed for triple negative disease in the early onset group (31.57%, 23.15%, 22.77%, 12.2% and 16.66%; respectively for the same population groups). In the older onset group, the prevalence of triple negative subtype was higher in AA (22.52%), followed by Indians (21.55) and Hispanic/Latina (14.7%).

### **Studies in Hispanic/Latina women from Latin-American countries**

All studies described above had been conducted in individuals born or residing in the United States. However, similar results have been reported for Hispanic/Latino women in Latin America. All of the studies described below are hospital-based.

Lara-Medina et. al in 2011 (67) analyzed the expression of HR and HER2 by IHC in 2,074 Hispanic/Latino breast cancer patients from the National Cancer Institute in Mexico city and were diagnosed between 1998 – 2008. They reported a high prevalence of triple negative subtype (23.1%). This percentage is similar to the prevalence reported in AA women (23% – 30%), and higher than that in NHW women (10% - 13%). This study included 20.4% of patients with a family history of breast cancer and therefore the presence of *BRCA1* mutations could be a contributing factor to the high prevalence of triple negative tumors reported.

Martinez et. al (68) assessed tumor subtype prevalence in 1,041 women of Mexican descent enrolled in a binational breast cancer study. They recruited patients in two hospitals in the U.S. (The Arizona cancer center and the M.D Anderson Cancer Center); and three in Mexico (the Universidad de Sonora, the Instituto Tecnológico de Sonora and the Universidad de Guadalajara). The prevalence of triple negative subtype was 16.7% overall but a higher proportion of ER– (HR–/HER2+ and HR–/HER2–) tumors was observed for women in Mexico compared to those in the U.S.

Srur-Rivero et. al (69) analyzed 199 breast cancer patients from the San Juan de Dios Hospital in Costa Rica diagnosed between 2009 and 2010. This hospital is a reference cancer treatment center for Costa Rica's South Central Region. Breast cancer subtypes were defined by the expression of HR and HER2. The median age at diagnosis was 53 years. The prevalence of the triple negative subtype was 17.4%.

In Brazil, de Macedo Andrade et. al (70) evaluated the expression of HR, HER2 and Ki67 following the recommendations of St. Gallen panel from 2011 (71) to assign breast tumors from 633 women into intrinsic subtypes. Data from pathology reports were obtained from the "Fundação de Assistência da Paraíba" (FAP) public hospital of Campina Grande, Paraíba, Brazil. They reported luminal B as the most prevalent subtype (44.61%), followed by luminal A (23.79%), triple negative (17.10%) and HER2-enriched (14.5%). Even though triple negative intrinsic subtype was found as the third most prevalent, the percentage reported in this study is similar to what has been reported previously in Hispanic/Latino women (53,62,67,69).

Ortiz et. al. (72) found that the two most prevalent subtypes were luminal A (61.8%) and triple negative (17.3%) in a sample of 663 patients diagnosed with invasive breast cancer between 2002 and 2005 at the I. Gonzalez Martinez Oncologic Hospital and the Auxilio Mutuo Hospital in Puerto Rico.

Several studies have been conducted in Colombia. Our group analyzed the distribution of breast cancer intrinsic subtypes in 301 patients from the National Cancer Institute in Colombia (INC) diagnosed between 2008 and 2012 (73). The INC has a double role in cancer control in Colombia: 1) It advises the Ministry of Health on all national cancer related issues (policies, strategies, surveillance for cancer control and prevention); and 2) it is the national comprehensive reference center for cancer treatment. The mean age at diagnosis was 56.6 years. Using the different surrogates proposed by the St. Gallen panel of experts in 2011 (71) and in 2013 (74) we found that following the recommendations of the St. Gallen 2013 surrogates, the luminal B subtype was the most prevalent (37.2%). Although using the 2011 St. Gallen surrogates the most prevalent subtype was luminal A (36.21%), an enrichment of luminal B was noticed when compared to the basic classification that included the evaluation of HR and HER2 (30.23% vs. 15.95%, respectively). The high prevalence of luminal B subtype is concordant with the findings reported by Macedo Andrade et. al (70). We also observed high proportion of triple negative tumors (20.6%). We found a higher proportion of African ancestry in patients with triple negative tumors, which is consistent with the literature (11,48,75,76). Gomez et. al. (77) analyzed the distribution of breast cancer intrinsic subtypes in 328 clinic-based patients from Medellin, Colombia diagnosed between January 2009 and December 2010. The mean age at diagnosis for this study was 52.9 years. They followed St. Gallen 2011 surrogates (71) and found that the luminal B represented more than 50% of the intrinsic subtypes identified.

In Peru, Vallejos et. al (78) analyzed 1,198 breast cancer patients diagnosed between January 1, 2000 and December 21, 2002 in the Instituto Nacional de Enfermedades Neoplásicas in Lima and retrieved the expression of HR and HER2. They observed a high prevalence of



more aggressive intrinsic subtypes such as triple negative (21.3%) and HER2-enriched (16.2%).

Despite the heterogeneity in the reported prevalence of different molecular subtypes among Hispanic/Latino women, most studies suggest a high prevalence of the more aggressive subtypes (i.e. ER (-) and luminal B) (Table 2). This heterogeneity may be related in part to the differences in the classification methods used, biases associated with clinic/hospital-based studies (as opposed to registry based studies), and to differences in the genetic ancestry from the Hispanic/Latino women analyzed (79,80).

## Discussion

Hispanic/Latinas represent a heterogeneous population group with variation in European, Indigenous American and African ancestry proportions (40) as well as lifestyle and environmental exposures.

There are multiple risk factors that have been associated with differences in the distribution of breast cancer intrinsic subtypes between population groups, including lifestyles and reproductive factors (81–86). Hispanic/Latina women and AA share some of these risk factors, for example, these two population groups tend to have children at an earlier age, have a higher body mass index and have low physical activity, all characteristics previously associated with the risk of developing triple negative tumors.

The prevalence of breast cancer intrinsic subtypes change according to the age of the patients included in the studies. Different studies have reported that the age at diagnosis of breast cancer in AA is earlier which is also associated with the development of triple negative tumors. A similar pattern is observed in Hispanic/Latina women, who are diagnosed at a younger age, compared to NHW (50 years vs. 61 years, respectively) (6,47,58). Some of the previously mentioned studies analyzed the age at diagnosis in women from different races/ethnicities (54,55,58,62,66) and found that Hispanic/Latina women were usually diagnosed at younger ages when compared to NHW. When the prevalence of intrinsic subtypes were analyzed according to age groups and ethnicity, some authors did not find statistical significant difference in the distribution of intrinsic subtypes according to age groups (58,66). These results suggest that the high prevalence of triple negative subtype in Hispanic/Latinas is not fully explained by differences in the age groups analyzed in the different studies.

It is important to emphasize that the studies included in this review are based on different sources of information. Some studies are based on data from population registries (53–55,57,58,60–64,87,88) and, others are hospital/clinic based (66,68–70,72,73,77,78). The population-based studies tend to report lower prevalence of the more aggressive tumors (ranging between 12 to 17%) compared to hospital/clinic-based studies (ranging between 12 to 23%) (Table 2), which is to be expected when the hospitals included in the studies are reference centers and therefore tend to receive patients that could not be adequately served by local hospitals/clinics. However, population-based studies show that Hispanic/Latinas have higher prevalence of more aggressive subtypes such as triple negative and HER2-

enriched tumors compared to NHWs (53,57,62,63) (Table 2) and, therefore, further research should be conducted to unveil possible behavioral/environmental or genetic factors that might be contributing to this observation.

Increasing evidence has demonstrated differences in gene expression profiles between AA patients compared to non-AA patients (89–92). In fact, gene expression profiles might change according to the ancestral genetic architecture of the individual's genome (93). However, there is a lack of information regarding gene expression profiles in Hispanic/Latinas of different national and ancestral backgrounds. More studies of gene expression including Hispanic/Latino patients are needed in order to assess possible biological heterogeneity that might be relevant in terms of treatment efficacy and outcome.

## Abbreviation list

<b>ER</b>	Estrogen Receptor
<b>PR</b>	Progesterone Receptor
<b>HER2</b>	Human Epidermal Growth Factor Receptor 2
<b>SEER</b>	Surveillance, Epidemiology and End Results
<b>NHW</b>	Non-Hispanic White
<b>AA</b>	African-Americans
<b>API</b>	Asian/Pacific Islanders
<b>IHC</b>	Immunohistochemistry
<b>CCR</b>	California Cancer Registry
<b>SES</b>	Socioeconomic Status
<b>NCDB</b>	The National Cancer Database
<b>LACE</b>	The Life After Cancer Epidemiology study

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**Table 1**

Available surrogates for molecular classification of breast cancer

Intrinsic Subtype	Definitions		
	HR and HER2	St. Gallen 2011	St. Gallen 2013
Luminal A	ER+ and/or PR+, HER2-	ER+, HER2-, Ki67 <14%	ER+, PR>20%, HER2-, Ki67<20%
Luminal B	ER+ and/or PR+, HER2+	ER+, HER2+, Ki67>14%	ER+, HER2- and/or PR < 20% or Ki67 > 20%
			ER+, HER2+
HER2-enriched	ER-, PR-, HER2+	ER-, PR-, HER2+	ER-, PR-, HER2+
Triple Negative	ER-, PR-, HER2-	ER-, PR-, HER2-	ER-, PR-, HER2-

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**Table 2**

Prevalence of breast cancer intrinsic subtypes in different populations

Race/ethnicity	Reference	Source	Subtypes definition	Prevalence of breast cancer intrinsic subtypes			
				Luminal A	Luminal B	HER2-enriched	Triple Negative
NHW	Plasilova (60)	The National Cancer Database (NCDB)	HR and HER2	74.80%	9.70%	4.10%	11.40%
AA				59.60%	11%	5.60%	23.70%
API				70.10%	11.70%	6.90%	11.20%
US Latinas				67.40%	11.90%	5.80%	14.80%
Other/Unknown	Sineshaw (61)	The National Cancer Database (NCDB)	HR and HER2	71.80%	11.00%	5.10%	12.10%
NHW				66.80%	8.90%	3.80%	10.20%
AA				51.70%	10.00%	5.00%	21.10%
API				63.50%	10.60%	6.10%	10.10%
US Latinas	Kurian (57)	California Cancer Registry	HR and HER2	58.20%	10.60%	5.20%	13.10%
Other/Unknown				57.30%	10.40%	4.90%	11.00%
NHW				71.60%		16.90%	11.50%
AA				53.00%		22.40%	24.60%
API	Howlader (54)	SEER registries	HR and HER2	62.80%		27.20%	10.00%
US Latinas				59.30%		24.00%	16.70%
NHW				75.50%	9.80%	4.00%	10.70%
AA				60.20%	11.40%	6.00%	22.50%
API	Chen (55)	SEER registries	HR and HER2	71.10%	12.30%	6.90%	9.70%
US Latinas				68.20%	11.40%	5.70%	14.70%
NHW				76%	9.40%	3.90%	10.70%
AA				60.70%	10.90%	5.70%	22.60%
API	Bancgas (53)	California Cancer Registry	HR and HER2	71.80%	11.90%	6.60%	9.70%
American Indian/Alaska Native				71.40%	12.10%	4.70%	11.90%
US Latinas				68.70%	11.60%	5.70%	14%
US Latinas				62.60%	13.80%	8.10%	15.60%
NHW	Clarke (58)	California Cancer Registry	HR and HER2	62%	9%	4%	9%

Race/ethnicity	Reference	Source	Subtypes definition	Prevalence of breast cancer intrinsic subtypes				
				Luminal A	Luminal B	HER2-enriched	Triple Negative	
AA				47%	11%	6%	20%	
API				55%	12%	8%	9%	
US Latinas				52%	11%	7%	13%	
NHW				76.50%	8.80%	4.90%	9.80%	
AA				58.90%	11.40%	6.80%	22.80%	
US Latinas	Singh (66)	Hospital-based	HR and HER2	59.00%	11.80%	9.50%	19.70%	
Chinese				65.60%	9.60%	10.50%	14.30%	
Indian				50.10%	12.20%	14.30%	23.30%	
NHW				70.60%	8.40%	5.90%	15.10%	
US Latinas	Hines (62,88)	4-Corners Breast Cancer Study	HR and HER2	50.70%	17.30%	14.50%	17.40%	
NHW				75.30%	11.10%	3.10%	10.50%	
AA				59.40%	9.00%	3.20%	28.40%	
API	Kwan (65)	The Life After Cancer Epidemiology (LACE) study	HR and HER2	71.40%	15.90%	6.40%	6.30%	
US Latinas				68.50%	14.20%	6.60%	10.70%	
Other				68.50%	13.00%	5.50%	13.00%	
NHW				52.00%	32.90%	3.90%	11.00%	
AA				31.40%	34.40%	4.50%	29.70%	
API	Kroenke (63)	The Life After Cancer Epidemiology (LACE) study and Pathway study	HR and HER2	47.70%	36.80%	6.60%	8.90%	
US Latinas				45.50%	35.80%	4.70%	14.00%	
Other				39.30%	39.70%	4.00%	17.10%	
NHW				55.20%	20.90%	12.50%	8.20%	
AA				43.20%	8.70%	11.60%	30.40%	
API	Sweeney (64)	The Life After Cancer Epidemiology (LACE) study and Pathway study	PAM50	55.20%	21.50%	12.40%	5.00%	
US Latinas				44.20%	24.00%	15.60%	11.60%	
Latinas from Mexico	Lara-medina (67)	National Cancer Institute in Mexico	HR and HER2	76.90%				23.10%
Latinas from Costa Rica	Snur-Rivero (69)	Hospital-based Costa Rica	HR and HER2	62.30%	9.00%	9.50%	17.10%	
Latinas from Brazil	de Macêdo Andrade (70)	Hospital-based Brazil	St Gallen 2011	23.79%	44.61%	14.50%	17.10%	

Race/ethnicity	Reference	Source	Subtypes definition	Prevalence of breast cancer intrinsic subtypes			
				Luminal A	Luminal B	HER2-enriched	Triple Negative
Latinas from Puerto Rico	Ortiz (72)	Hospital-based Puerto Rico	HR and HER2	61.80%	13.30%	7.50%	17.30%
Latinas from Colombia	Serrano-Gómez (73)	National Cancer Institute in Colombia	HR and HER2	52.49%	15.95%	10.30%	20.60%
			St Gallen 2011	36.21%	30.23%	8.64%	20.60%
Latinas from Colombia	Gómez (77)	Hospital-based Colombia	St Gallen 2013	26.25%	37.21%	8.64%	20.60%
			St Gallen 2011	22.30%	56.40%	9.10%	12.20%
Latinas from Mexico	Martinez (68)	Clinical-based	HR and HER2	59.80%		23.60%	16.60%
Latinas from Peru	Vallejos (78)	Hospital-based Peru	HR and HER2	49.3%	13.20%	16.2%	21.3%

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