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Review

Cancer Epidemiology, Biomarkers & Prevention

Risk Factors for Triple-Negative Breast Cancer among Latina Women

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Abstract

Breast cancer is the most common cancer in Latina women. Although they have a lower incidence of the disease when compared with other population groups such as non-Hispanic white and African-American women, some studies have shown that Latina women have a higher risk of mortality when compared with non-Hispanic white women. This phenomenon can be explained in part by the higher prevalence of aggressive subtypes in Latina women, particularly the triple negative. Such differences in breast cancer–intrinsic subtype distribution between population groups might be a consequence of a variety of risk factors differentially present among population groups. Here, we provide a full description of risk factors that might be associated with the high prevalence of the triple-negative subtype in Latina women. We assessed demographic (socioeconomic status), modifiable (reproductive patterns, obesity, and physical activity), and nonmodifiable (family history, germline *BRCA* mutations, and genetic ancestry) risk factors. The observed inconsistencies among different epidemiologic studies in Latinas warrant further research focused on breast cancer subtype–specific risk factors in this population.

Introduction

Breast cancer is the most common cancer and the leading cause of cancer-related death in U.S. Latina women (1); however, incidence rates in Latinas are significantly lower than those in non-Hispanic whites (NHW), African Americans (AA), and American Indian/Alaska Native (AI/AN) women (93.0 vs. 130.1, 126.5, and 100.9, respectively; ref. 2). Despite this lower incidence rate, some studies have shown that the mortality hazard is higher in Latina women compared with NHW women, even after adjustment for tumor characteristics, treatment, and socioeconomic status (3–6). This can be explained in part by cultural and socioeconomic factors (i.e., less access to the health care system, later diagnosis, less awareness, and education; refs. 7–9), as well as by biological differences, such as the higher proportion of more aggressive breast cancer–intrinsic subtypes diagnosed in Latinas.

Since the seminal work published by Perou and colleagues in 2000 (10), breast cancer is now recognized as a heterogeneous disease composed of specific intrinsic subtypes associated with different prognoses (11). The luminal group, which includes luminal A and luminal B subtypes, is mainly characterized by the high expression of the estrogen receptor (ER). Patients with these subtypes are candidates to receive hormonal treatment. Both luminal subtypes usually have the best prognosis when compared with other intrinsic subtypes; however, luminal B has a more aggressive behavior compared with luminal A (11, 12). On the other hand, the human epidermal growth factor receptor 2 (HER2)-enriched and triple-negative (TN) subtypes, both negative for the expression of ER, are associated with more aggressive disease, poor prognosis and have fewer treatment options, especially the TN subtype (13, 14).

Differences in the distribution of intrinsic subtypes between populations groups have been reported (15–17). AA women show the highest prevalence of TN subtype (18). Similarly, a relatively high prevalence of this subtype has also been reported for Latinas when compared with NHW women in studies conducted in the United States and Latin America (19, 20). Presently, there is limited information about the distribution of risk factors in minority groups and how they might contribute to the observed disparities in the prevalence of breast cancer subtypes in these populations. This review provides an overview of publications focused on the description of breast cancer risk factors and how they might contribute to the high prevalence of TN breast cancer in Latina women.

Methodology

Eligible studies

We conducted a search of the literature from the last 10 years (January 2008–December 2018) using PubMed (NIH). The eligibility criteria included original articles written in English that addressed different risk factors for TN breast cancer subtype specifically in Latina women. We did not included reviews and annual reports. We excluded studies that: (i) did not analyze risk factors according to intrinsic subtype, (ii) that analyzed risk factor for TN subtype but in terms of mortality or survival, and (iii) studies that did not include Hispanic or Latina women.

Publication search

An initial search was performed combining the Medical Subject Headings (MeSH): "breast cancer" and "risk factors" and "Hispanic OR Latinas" and "triple negative" and excluded the

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words "survival" and "mortality" to adjust the search, and retrieve 14 publications from which 6 articles were eligible. We conducted additional searches replacing "risk factors" for "socioeconomic status" (18 publications, 3 eligible); "reproductive factors" (7 publications, 3 eligible); "obesity" (7 publications, 4 eligible); "family history OR BRCA" (10 publications, 6 eligible). We also combined the MeSH words "breast cancer," "physical activity," "Hispanic OR Latinas" and "triple negative," and retrieved only one publication that was not eligible. Then we combined "breast cancer," "physical activity," "Hispanic OR Latinas" and excluded the word "Survival" to adjust the search, and retrieved 53 publications of which 2 were eligible. The combination of "breast cancer" and "genetic ancestry OR ancestry" and "Hispanic OR Latinas," and "Triple negative" retrieved 30 publications of which 5 were eligible. We also conducted a search of the literature written in Spanish using SciELO with the words "cancer de mama," "factores de riesgo," "triple negativo," and retrieved 3 articles but none were included as they did not meet eligibility criteria. The last search was carried out on May of 2019. We revised manuscripts cited within those studies to identify additional publications that fulfilled our eligibility criteria. A total of 24 unique publications were included in our review.

Breast Cancer–Intrinsic Subtypes among Latina Women

The term Hispanic or Latino is used to refer to individuals with different national identities (Mexico and countries in the Caribbean, Central and South America) and diverse place of birth (individuals born in Latin America or individuals born outside Latin America but whose ancestors were born in Latin America; refs. 21, 22). They are a heterogeneous group originated from the confluence of Indigenous American populations, Africans being brought into the continent through the slave trade, the European colonizers and more recent immigration from Asia (21, 23).

Latina women are usually diagnosed with breast cancer at younger age (56 vs. 63 years for NHW women; refs. 24–26) and at more advanced stages than NHW women (5). In addition, Latina women also present with larger tumors and are more likely to be diagnosed with more aggressive subtypes, such as HER2-enriched and TN (4, 5, 25, 27–31).

Martinez and colleagues (30) analyzed 129,488 breast cancer cases from the California Cancer Registry (CCR; 29,626 Latina women and 99,862 NHW women) and reported that even after adjusting for socioeconomic status (SES), Latina women had higher odds of being diagnosed with the TN subtype [OR = 1.29, 95% confidence interval (CI), 1.23–1.35]. Similar results were reported in a larger study that included the 17 population-based cancer registries from the Surveillance, Epidemiology and End Results (SEER) program. They found that AA and Latinas were more likely to be diagnosed with the TN subtype (AA: OR = 2.0, 95% CI, 1.8–2.2; Latinas: OR = 1.3, 95% CI, 1.2–1.5) compared with NHW women (31).

The differential distribution of intrinsic subtypes between population groups has been attributed to the differences in the prevalence of a variety of demographic factors such as SES, modifiable risk factors, such as reproductive patterns, obesity and hormone exposures (Seiler and colleagues 2017), along with other nonmodifiable risk factors such as family history, germline *BRCA* mutations and genetic ancestry (refs. 32, 33; Tables 1 and 2) that we describe below.

Demographic Factors

Several studies have reported that SES could play an important role in breast cancer, given that woman with certain conditions such as low family income and low levels of education might have impaired access to the healthcare system (8, 9). According to the 2013 U.S. Census Bureau (34), approximately 23.5% of the U.S. Latinos live below the poverty level, compared with 9.3% of NHWs. Additionally, U.S. Latinos have higher barriers for healthcare access. In 2014, the highest percentage for uninsured was observed for U.S. Latinos (23.6%), followed by AAs (11.9%) and NHWs (8.2%; ref. 35).

The relation between insurance coverage and breast cancer subtypes in Latina women was analyzed by Nahleh and colleagues (24) in a case-only study that included 1,252 Mexicans with breast cancer. They reported that women without insurance coverage have a higher prevalence of more aggressive tumors such as TN subtype compared with insured patients (23% vs. 17%, $P = 0.023$).

A negative association between SES and TN disease has been reported in Latina women (30, 36). Banegas and colleagues (37) conducted a case-only study including 16,380 Latina women with breast cancer from the CCR to examine the association between breast cancer subtype distribution and survival with demographic attributes. Specifically for the TN subtype ($n = 2,549$), defined as hormone receptor (HR) negative/HER2 negative, they found that Latina women with lower SES had greater odds of being diagnosed with this subtype, compared with Latinas with higher SES (OR = 1.42, 95% CI, 1.13–1.79, $P < 0.05$). A similar association was also found for the $HR^-/HER2^+$ subtype (OR = 1.43, 95% CI, 1.07–1.92, $P < 0.05$).

Parise and colleagues (38) conducted a case-only study that included 108,372 women with TN ($n = 19,283$) and $HR^+/HER2^-$ ($n = 89,089$) breast cancer subtypes originally included in the CCR, in order to determine if age and SES could increase the risk of TN breast cancer in women from different population groups [Latina, NHW, AA, and Asian or Pacific Islander (API) women]. They found a statistically significant association between lower SES and TN disease in Latina women (high SES vs. low SES, OR = 1.29, 95% CI, 1.0–1.68) and also in NHW women (high SES vs. low SES, OR = 1.15, 95% CI, 1.04–1.27).

On the other hand, Akinyemiju and colleagues (39) conducted a study that included 47,586 breast cancer cases (34,228 NHW, 4,503 AA, 185 API, 8,670 Latinas) from the SEER 18 population-based data set to determine the association between SES and breast cancer subtypes. They reported a positive association between SES and $HR^+/HER2^-$ subtype for Latinas [high SES vs. low SES; incidence rate ratio (IRR) = 1.52; 95% CI, 1.35–1.72, $P = 0.001$], as well as for all other population groups analyzed, but failed to find an association for TN subtypes (high SES vs. low SES in Latinas, IRR = 1.09; 95% CI, 0.83–1.43, $P = 0.97$; high SES vs. low SES in NHWs, IRR = 0.98, 95% CI, 0.87 – 1.43, $P = 0.96$).

Although some of the previously mentioned studies reported an association between SES and TN subtype in Latinas, it seems that it is not specific neither for TN subtype nor for the population group. The mechanisms that might explain the association between low SES and TN subtype may be associated with the lower consumption of healthy foods and higher sedentary

Table 1. Risk factor positively associated with HR^- or TN subtypes in Latina women

Category	Associated factor	Population included	Country/ source	Sample size	TN sample size	Subtype assessment	Description	OR (95% CI)	Reference group	Model	Reference
DEMOGRAPHIC FACTORS											
Socioeconomic status	Low SES	Latinas	U.S./ California Cancer Registry	16,380 cases	2,549 cases	$ER^-/PR^-/HER2^-$	Low quantile vs. high quantile	1.42 (1.13–1.79)	$HR^+/HER2^-$ tumors	Adjusted for sociodemographic and clinical attributes	(37)
	Low SES	NHW, AA, Latina, and API women	U.S./ California Cancer Registry	108,372 cases (17,812 Latinas)	19,283 cases (4,062 in Latinas)	$ER^-/PR^-/HER2^-$	Low quantile vs. high quantile	**For Latinas:** 1.29 (1.05–1.68); **For NHWs:** 1.15 (1.04–1.27)	$ER^+/PR^+/HER2^-$ tumors	Adjusted for stage, tumor size, and tumor grade	(38)
	High SES	NHW, AA, Latina, and API women from U.S.	U.S./SEER	47,586 cases (8,670 Latinas)	5,764 cases (1,089 in Latinas)	$ER^-/PR^-/HER2^-$	High vs. low SES	**For Latinas:** IRR = 1.09 (0.83–1.43); **For NHWs:** IRR = 0.98 (0.87–1.11)	N/A	Adjusted for age	(39)
MODIFIABLE FACTORS											
Reproductive	Higher parity	Latinas	Mexico	2,074 cases	479 cases	$ER^-/PR^-/HER2^-$	≥2 vs. <2 births	1.32 (1.03–1.69)	Non-TN tumors	Adjusted for age, parity, contraceptive use, multicentricity, Bloom–Richardson grade, stage	(46)
	Contraceptive use						Use vs. no use	1.2 (1.003–1.54)		Not adjusted	
	Higher parity	Latinas	Mexico and U.S.	1,041 cases	159 cases	$ER^-/PR^-/HER2^-$	>3 vs. 1–2 children	1.68 (1.10–2.66)	Luminal A tumors	Adjusted for age at diagnosis and country (U.S. or Mexico)	(47)
	Longer duration of breastfeeding						Lifetime >12 months vs. never	2.14 (1.24–3.68)			
							Per birth >5 months vs. never	2.07 (1.20–3.58)			
	Parity	Latinas	Chile, Colombia, Costa Rica, and Mexico	288 cases and 288 controls	36 cases	$ER^-/PR^-/HER2^-$	Per child	0.99 (0.51–1.92)	Premenopausal Latina controls	Adjusted for educational level, benign breast diseases, physical activity, and waist circumference	(49)
	Age at FFTP						≥25 vs. <20 years	0.97 (0.84–1.13)			
NONMODIFIABLE											
Family history	Family history of breast cancer	NHW and Latina women	U.S.	1,387 cases and 2,452 controls	315 cases (130 in Latinas and 185 in NHWs)	ER^-	Family history yes vs. no	2.66 (1.59–4.44)	Latina controls	Adjusted for center, age, education, and known risk factors	(70)
	Breast cancer history in first- or second-degree relatives	Mexican descent women	from Mexico and U.S.	914 cases	148 cases	$ER^-/PR^-/HER2^-$	Family history yes vs. no	2.04 (1.40–2.98)	Non-TN (luminal A, luminal B, and $HER2^+$) Latinas	Adjusted for age at diagnosis and country of residence (U.S. or Mexico)	(71)

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Table 1. Risk factor positively associated with HR$^-$ or TN subtypes in Latina women (Cont'd.)

Category	Associated factor	Population included	Country/ source	Sample size	TN sample size	Subtype assessment	Description	OR (95% CI)	Reference group	Model	Reference
Genetic ancestry	Lower NA ancestry	Postmenopausal NHW and Latina women	U.S. and Mexico	1,915 cases (875 NHWs, 614 Hispanic, and 426 Mexican) and 2,265 controls (979 NHWs, 785 Hispanics, 501 controls)	841 cases (493 NHWs, 348 Hispanic)	ER$^-$	NA ancestry 0%–32% vs. >54.0%	1.80 (0.96–3.37)	Postmenopausal Latina controls	Adjusted for age, study site, and known risk factors	(92)

Abbreviations: AA, African American; API, Asian or Pacific Islander; ER, estrogen receptor; HER2, human epidermal growth factor receptor-2; HR, hormone receptor; NA, Native American; N/A, not available; NHW, non-Hispanic white; OR, odds ratio; PR, progesterone receptor; SES, socioeconomic status; TN, triple negative; U.S., United States.

behavior among low SES individuals, which can lead to obesity (37), a risk factor positively associated with ER-negative tumors and that we will discuss later in this review (40, 41). In fact, higher obesity rates in women have been associated with a lower SES (42, 43). This could suggest that low SES might be acting as an indirect risk factor for the disease as it might be contributing to higher obesity rates among women.

The lack of reproducibility in the results could also be related to differences in the study design. Having a limited number of Latinas included in the studies, along with a limited number of TN cases in each population group may compromise the power of the associations tested. Additionally, lack of reproducibility can also be due to heterogeneity of Latina women included, as the studies that used the CCR analyzed Latina women in California, which are mainly from Mexico (22), while studies analyzing the SEER database included Latina women all over the United States, therefore, are expected to have different nationalities.

Differences in the study design also include variations in methods for data collection and analysis. For example, SES determination was assigned under different criteria among the studies. For instance, Banegas and colleagues (37) used the neighborhood SES, Parise and colleagues (38) used an index that utilizes different socioeconomic variables to identify quintiles of SES [1 (lowest) and 5 (highest)]; and Akinyemiju and colleagues (39) used the census-tract SES, and as they mentioned, it may not fully recapitulate variation in individual SES. More studies are needed to address the observed inconsistencies.

Modifiable Risk Factors

Reproductive factors

Reproductive behavior and related variables are well-established risk factors for breast cancer. Among these, we found age at menarche, menopausal status, age at menopause, parity, age at first full-term birth, and duration of lactation (44). It has been established that breast cancer risk tends to increase with early age at menarche, late menopause, nulliparity, use of hormone therapy after menopause; it decreases with higher parity and longer lactation (45).

Associations between reproductive factors and breast cancer specific subtypes have been reported in case-only studies with Latina women. Lara-Medina and colleagues (46) compared clinical and pathologic characteristics of 2,074 Latina women from Mexico with TN ($n = 479$) vs. non-TN tumors ($n = 1,595$). They reported that premenopausal status was inversely associated with TN subtype (OR = 0.72, 95% CI, 0.58–0.88, $P = 0.002$), whereas hormone contraceptive use and increased parity were found positively associated for this subtype (hormone contraceptive use: OR = 1.20, 95% CI, 1.003–1.54, $P = 0.04$; increased parity: OR = 1.32, 95% CI, 1.03–1.69, $P = 0.029$). In the multivariate analysis, where only statistical significant variables from the univariate model were included, only menopausal status ($P = 0.01$) and parity ($P = 0.014$) remained statistically significant. Martinez and colleagues (47) used the *Ella* Binational Breast Cancer Study to evaluate reproductive risk factors for TN and HER2$^+$ tumors compared with luminal A subtype in 1,041 Mexican descent women (559 U.S. and 482 Mexico). They found in a model adjusted for age at diagnosis and country, that women with higher parity (>3 vs. 1–2 children) had increased odds of TN tumors (OR = 1.68, 95% CI, 1.10–2.66). In addition, they also reported that higher age at first full-term pregnancy (FFTP; >25 vs.

Table 2. Risk factor inversely associated with HR^- or TN subtypes in Latina women

Category	Associated factor	Population included	Country	Sample size	TN sample size	Subtype assessment	Description	OR (95% CI)	Reference group	Model	Reference
MODIFIABLE											
Reproductive	Premenopausal status	Latinas	Mexico	2,074 cases	479 cases	$ER^-/PR^-/HER2^-$	Pre- vs. postmenopausal status	0.72 (0.58–0.88)	Non-TN (HR^+, $HER2^+$) Latinas	Adjusted for age, parity, contraceptive use, multicentricity, Scarff–Bloom–Richardson grade, stage	(46)
	Higher age at FFTP	Latinas	Mexico and U.S.	1,041 cases	159 cases	$ER^-/PR^-/HER2^-$	>25 vs. <21 years	0.61 (0.39–0.95)	Luminal A tumors	Adjusted for age at diagnosis and country (U.S. vs. Mexico)	(47)
	HRT						Use vs. no use	0.99 (0.56–1.77)			
	Contraceptive use						Use vs. no use	0.70 (0.49–1.01)			
	Longer duration of breastfeeding	Premenopausal Latinas	Chile, Colombia, Costa Rica, and Mexico	288 cases and 288 controls	48 cases	ER^-	>12 months vs. never	0.87 (0.76–0.99)	Premenopausal Latina controls	Nonlinear model	(49)
	Parity	Latinas	Chile, Colombia, Costa Rica, and Mexico	288 cases and 288 controls	36 cases	$ER^-/PR^-/HER2^-$	Per child	0.99 (0.51–1.92)	Premenopausal Latina controls	Adjusted for educational level, benign breast diseases, physical activity, and waist circumference	
	Age at FFTP						≥25 vs. <20 years	0.97 (0.84–1.13)			
	Higher age at FFTP	NHW, AA, API women, NA, and Latina women <44 years	U.S.	1,025 cases and 941 controls	184 cases	$ER^-/PR^-/HER2^-$	35 vs. <20 years	0.4 (0.2–0.8)	Controls ages <44 years	Adjusted for 5-year age group, age at first live birth, and number of births	(50)
	Longer duration of breastfeeding						>12 months vs. never	0.5 (0.3–0.9)			
	Higher parity						Parous vs. nulliparous	0.7 (0.5–1.0)			

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Table 2. Risk factor inversely associated with HR$^-$ or TN subtypes in Latina women (Cont'd)

Category	Associated factor	Population included	Country	Sample size	TN sample size	Subtype assessment	Description	OR (95% CI)	Reference group	Model	Reference
Obesity	Higher current BMI in premenopausal women	NHW and Latina women	U.S.	2,471 cases (846 Latinas and 1,625 NHWs)	157 in Latinas and 216 in NHWs	ER$^-$	≥30 vs. <25 kg/m^2	**For Latinas:** 0.29 (0.13–0.66); **For NHWs:** 2.47 (1.08–5.67)	ER-positive tumors	Known risk factors, parity, mammography use, family history of breast cancer, and smoking	(54)
	Higher current BMI in postmenopausal women							**For Latinas:** 0.68 (0.29–1.60); **For NHWs:** 1.6 (0.80–2.31)			
	Lower current BMI	Postmenopausal Latina	Mexico	2,074 cases	479 cases	ER$^-$/PR$^-$/HER2$^-$	<25 vs. ≥25 kg/m^2 <30 vs. ≥30 kg/m^2	0.70 (0.51–0.96) 0.54 (0.37–0.78)	Non-TN tumors	Not adjusted	(46)
	Higher young-adult BMI	Premenopausal NHW and Latina women	U.S. and Mexico	822 cases and 1,418 controls	247 cases (142 in Latinas and 105 in NHWs)	ER$^-$/PR$^-$	>23.1 vs. <20.6 kg/m^2	**For Latinas:** 0.41 (0.25–0.68), **For NHWs:** 1.23 (0.69–2.21)	Premenopausal Latina controls	Adjusted for age, study, ethnicity/English language acculturation, and average alcohol consumption	(55)
	Higher young-adult BMI	Postmenopausal NHW and Latina women	U.S. and Mexico	872 cases (447 Latinas and 425 NHWs) and 2,711 controls (1,264 Latinas and 1,447 NHWs)	286 (153 in Latinas and 133 in NHWs)	ER$^-$/PR$^-$	>23.0 vs. >20.6 kg/m^2	**For Latinas:** 0.69 (0.49–1.12); **For NHWs:** 0.60 (0.35–1.03)	Postmenopausal Latina controls	Adjusted for age, study, ethnicity/English language acculturation, family history of breast cancer in first-degree relatives, age at menarche, and use of menopausal hormone therapy	(57)
Physical activity	Being physically active	NHW and Latina women	U.S.	2,471 cases (846 Latinas and 1,625 NHWs)	157 in Latinas and 216 in NHWs	ER$^-$	Sedentary vs. vigorous	**For Latinas:** 0.55 (0.27–1.13), **For NHWs:** 0.63 (0.32–1.60)	ER+ premenopausal Latinas	Known risk factors, parity, mammography use, family history of breast cancer, and smoking	(54)
								For Latinas: 1.21 (0.55–2.65), **For NHWs:** 0.98 (0.59–1.61)	ER$^+$ postmenopausal Latinas		
		NHWs, AAs, Latinas, Tunisian–Arabs, and Polish	U.S.	1,463 cases and 4,862 controls	101 cases	ER$^-$/PR$^-$	>3 vs. <1 time per week >30 vs. <10 minutes per time 150 vs. <10 minutes per week	0.60 (0.43–0.82) 0.65 (0.47–0.90) 0.68 (0.49–0.94)	Controls	Adjusted for age, race, BMI, and pack-years of smoking	(65)
NONMODIFIABLE											
Genetic ancestry	Higher NA ancestry	Latinas	U.S.	977 cases and 722 controls	Nonspecified	ER$^-$	Risk variant at rs140068132	0.34 (0.21–0.54)	Latina controls	Not reported	(95)

Abbreviations: AA, African American; API, Asian or Pacific Islander; BMI, body mass index; ER, estrogen receptor; FFTP, first full-term pregnancy; HER2: human epidermal growth factor receptor-2; HR, hormone receptor; NA, Native American; NHW, non-Hispanic white; OR, odd ratio; PR, progesterone receptor; TN, triple negative; U.S., United States.

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<21 years) decreased odds of TN breast cancer (OR = 0.61, 95% CI, 0.39–0.95). These associations seem to be exclusive for the TN subtype, as nonsignificant association neither for higher parity nor age at FFTP was found for HER2$^+$ subtype (parity: OR = 0.87, 95% CI, 0.61–1.24; age at FFTP: OR = 0.99, 95% CI, 0.68–1.46). Other risk factors such as hormone replacement therapy (HRT) and hormone contraceptive use were not found associated with TN breast cancer (HRT: OR = 0.99, 95% CI, 0.56–1.77; hormone contraceptive use: OR = 0.70, 95% CI, 0.49–1.01).

It has been well described that Latina women tend to have more biological children, and at a younger age compared with NHW women (48). In fact, the total fertility rate in the United States is 1.87 per women whereas in Mexico it is 2.24 (2018 December 10; retrieved from https://www.cia.gov/library/publications/the-world-factbook/rankorder/2127rank.html). Taking previously mentioned results into account (46, 47) a higher parity along with a lower age at FFTP could be related to the higher prevalence of TN subtype among Latina population.

Martinez and colleagues (47) also reported that a longer duration of breastfeeding highly increased the odds of TN breast cancer compared with women who never breastfeed (lifetime duration >12 months: OR = 2.14, 95% CI, 1.24–3.68; breastfeeding duration per birth >5 months: OR = 2.07, 95% CI, 1.20–3.58). No significant association regarding duration of breastfeeding was found for HER2$^+$ subtype (OR = 0.97, 95% CI, 0.63–1.50).

Romieu and colleagues (49) conducted a population-based case–control study (PRECAMA) in 288 premenopausal women with breast cancer and matched controls from 4 Latin American countries (Chile, Colombia, Costa Rica, and Mexico) aiming to examine the relationship between different reproductive factors and breast cancer subtypes. They reported that breastfeeding had a significant protective effect for both ER-positive and ER-negative tumors in a model adjusted for educational level, benign breast diseases, physical activity, and waist circumference. This effect was observed for ER-positive tumors only within the first 6 months of breastfeeding (OR = 0.74; 95% CI, 0.60–0.91) and $\geq$ 12 months of breastfeeding for ER-negative tumors (OR = 0.87, 95% CI, 0.76–0.99). Other variables were not found associated with TN, but with ER-positive subtype. Among these, higher parity (OR = 0.64, 95% CI, 0.47–0.87, $P = 0.005$) and higher age at FFTP (OR = 1.11, 95% CI, 1.04–1.19, $P = 0.003$) were included.

Similar results have been reported by Li and colleagues (50) in a population-based case–control study that assessed the relationships between various reproductive factors and risk of ER-positive, TN and HER2$^+$ breast cancer subtypes in a cohort of women ages 20 to 44 years from the United States [NHW, AA, API, Native American (NA) and Latinas]. They showed that longer duration of breastfeeding (>12 months vs. never breastfeed) decreases risk for TN breast cancer (OR = 0.5, 95% CI, 0.3–0.9, $P = 0.018$) in all population groups. No significant association was found between breastfeeding and risk for ER-positive ($P = 0.606$) and HER2$^+$ tumors ($P = 0.086$). They also reported that a higher parity was protective for both TN and ER-positive breast cancer (TN: OR = 0.7, 95% CI, 0.5–1.0, $P < 0.05$; ER$^+$: OR = 0.7, 95% CI, 0.5–0.8, $P < 0.05$), whereas higher age at FFTP was found protective exclusively for TN breast cancer (OR = 0.4, 95% CI, 0.2–0.8, $P = 0.001$).

Martinez and colleagues (47) and Lara-Medina and colleagues (46) had similar methodological designs (case-only studies) and consistently reported a higher likelihood for TN breast cancer associated with higher parity. It is important to clarify that case-only studies only point for heterogeneity between subtypes, and should not be interpreted as indicators of risk (47). On the other hand, Romieu and colleagues (49) in a case–control study did find parity as a protective factor, but only for ER$^+$ tumors. This result may indicate that women without breast cancer and higher parity will be at lower risk of developing an ER-positive tumor than nulliparous women, but not for ER-negative subtype. Regarding breastfeeding, they reported a protective effect of developing both ER-positive and ER-negative tumors for women who breastfeed for longer periods of time, although it seems that the protection effect for ER-positive tumors is higher.

It is important to highlight that the studies cited before have differences regarding women included and in the classification methods for subtyping breast tumors. Romieu and colleague (49) included premenopausal Latina women from different Latin American countries, and analyzed tumors only by ER status. Lara-Medina and colleagues (46) and Martinez and colleagues (47) included premenopausal and postmenopausal Mexican descent women, and assessed breast cancer subtypes by ER/PR/HER2 status.

The relationship between breast cancer subtype–specific risk and the reproductive history is complex. One hypothesis for the association between TN breast cancer and parity is that the higher exposure to pregnancy-related hormones, the immune-suppressive effects of pregnancy, and uterine involution-related inflammation, could play a role in promoting growth of more aggressive tumors such as TN, and this could explain in part the positive association between parity and TN reported for Mexican descent women (19). Li and colleagues (50) reported parity as a protective factor for TN breast cancer in all population groups analyzed but as they did not analyze Latinas separately, it is not possible to assess if there is a differential behavior between population groups.

Potential mechanisms have been proposed for the role of breastfeeding in the development of TN disease. Absent or short breastfeeding could result in the repeated failure of an expanded progenitor cell population that during breastfeeding naturally undergo differentiation and apoptosis; thus, the absent of breastfeeding results in a pool of cells with survival capability and at potential risk for carcinogenesis of undifferentiated tumors such as TN (51). This hypothesis could explain the association reported by Romieu and colleagues (49) but it is still unknown why Martinez and colleagues (47) reported an opposing observation for this risk factor. Either way, it is clear that reproductive patters seem to be important contributors to the observed differences in the prevalence of breast cancer–intrinsic subtypes in diverse populations (19, 46, 47).

Obesity

More than two-thirds of adults in the United States are overweight or obese, which puts them at risk for chronic diseases including cancer (52). Data from the National Health and Nutrition Examination Survey (NHANES) from 2013 to 2014 showed that the prevalence of overweight or obesity [body mass index (BMI) ≥ 25 kg/m^2] in women was higher among AAs and Latinas (57.2% and 46.6%, respectively), compared with NHW women (38.7%; ref. 53).

Obesity's contribution to breast cancer risk has been controversial, especially when menopausal status is taken into account. Only few studies have analyzed the association between obesity

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and risk of breast cancer subtypes in premenopausal and postmenopausal Latina women. Abdel-Maksoud and colleagues (54) analyzed the association between behavioral risk factors and ER-negative tumors in 2,471 cases (846 Hispanics and 1,625 NHW) from the 4-Corners Breast Cancer Study. They reported a negative association between ER-negative tumors and obesity (BMI $\geq$ 30 kg/m^2) in premenopausal Latina women compared with non-obese Latinas. This association remained statistically significant in the fully adjusted model for known risk factors (OR = 0.29, 95% CI, 0.13–0.66, $P < 0.05$). Interestingly, for premenopausal NHW women, they reported the opposite, a positive association between ER-negative tumors and obesity (OR = 2.47, 95% CI, 1.08–5.67, $P < 0.05$). No association was found between breast cancer risk and obesity for neither Latina nor NHW postmenopausal women. On the other hand, Lara-Medina and colleagues (46), as mentioned above, carried out a case-only study in Mexican women to evaluate the association between clinical characteristics and TN subtype, and reported a strong association between TN tumors and BMI in postmenopausal women. A BMI <25 or <30 kg/m^2 was inversely associated with TN breast cancer (OR = 0.70, 95% CI, 0.51–0.96, $P = 0.027$; OR = 0.54, 95% CI, 0.37–0.78, $P = 0.001$, respectively). These results together suggest that BMI may exert differential effects depending on the menopausal status.

Different studies have assessed risk for ER-negative tumors in premenopausal and postmenopausal Latina women and its association with current and young-adult self-reported BMI. John and colleagues (55) analyzed the association of overall adiposity with the risk of ER/progesterone receptor (PR) status in premenopausal Latina and NHW women enrolled in the population-based, case–control Breast Cancer Health Disparities Study (56). They found that Latina women with a higher young-adult BMI (>23.1 vs. <20.6 kg/m^2) had a decreased risk for ER/PR-negative tumors (OR = 0.41, 95% CI, 0.25–0.68, $P < 0.01$) and also for ER/PR-positive tumors (OR = 0.53, 95% CI, 0.33–0.84, $P < 0.01$). On the other hand, higher current BMI (>30.0 vs. <25.0 kg/m^2) among Latinas was also found associated with a lower risk for ER/PR-positive (OR = 0.63, 95% CI, 0.44–0.92, $P = 0.01$) but no ER/PR-negative tumors (OR = 0.71, 95% CI, 0.45–1.12, $P = 0.15$). All models were adjusted for age, study, ethnicity/English language acculturation (low, moderate, high, and NHW), and average alcohol consumption. A similar study conducted by John and colleagues (57) also analyzed the association of overall adiposity with the risk for breast cancer subtypes defined by ER/PR status in postmenopausal Latina and NHW women. They reported a protective effect for ER/PR-negative tumors in Latina and NHW women combined for a young-adult BMI >23 kg/m^2 (OR = 0.67, 95% CI, 0.47–0.96, $P = 0.03$), and the same trend for Latina women alone, although it was not statistically significant (>23 vs. <20.6 kg/m^2, OR = 0.69, 95% CI, 0.42–1.12, $P = 0.13$). They also reported that a higher BMI (>24.4 vs. <20.4 kg/m^2) during young-adult life in Latinas was associated with a lower risk for the ER/PR-positive (OR = 0.61, 95% CI, 0.40–0.95, $P = 0.07$) but no for ER/PR-negative subtype.

Association studies between obesity and risk for ER-negative disease in Latinas highlight differences in BMI contribution depending on the menopausal status. Evidence suggests that obesity in young-adults may act as a protective factor in premenopausal women (55), but as a risk factor in postmenopausal women (46), meaning that young-adult weight might have a long-lasting and important influence on TN breast cancer risk in Latinas. It has been suggested that the estrogen released from adipose tissue during childhood could induce breast differentiation and the expression of tumor suppressor genes, whereas the lack of breast adipose tissue during adolescence could lead to immature breast differentiation (58) and this would explain in part why obesity could act as a protective factor in young-adult women. On the other hand, obesity in postmenopausal women could act as a risk factor, mainly attributed to a higher expression of genes related to inflammation. It has been recently described that the ERK/MAPK signaling pathway is associated with TN breast cancer in obese postmenopausal women; upstream regulators of this pathway include TNF, TGFβ1, and IL1 (59, 60). Additionally, high levels of insulin and insulin-like growth factors (61), along with glucose levels, cytokines, adipokines, and chronic inflammation, might be associated with the increased risk for ER-negative subtypes (55, 62, 63); nevertheless, these findings have been found mainly in studies conducted in NHW women (54). Still further investigation is needed to elucidate the role of adiposity in ER-negative breast cancer, especially in Latinas where the direction of the association with obesity is still discussed.

The studies previously cited classified intrinsic subtypes differently. Abdel-Maksoud and colleagues (54) classified tumors by ER status, whereas John and colleagues (55, 57) used ER/PR status. Therefore, tumors defined as ER negative or ER/PR negative included not only TN subtype but also HER2-enriched tumors. Lara-Medina and colleagues (46) is the only study that truly analyzed TN tumors (ER$^-$/PR$^-$/HER2$^-$). All this together could contribute to contradictory results between the studies carried out, not only in Latinas, but also in NHW women.

Physical activity

Being physically active has been associated with reduced risk for breast cancer (64). Few studies have evaluated physical activity contribution to ER-negative breast cancer risk in Latinas. Abdel-Maksoud and colleagues (54) analyzed the association between behavioral risk factors, such as physical activity, and ER-negative tumors in 2,471 cases (846 Hispanics and 1,625 NHW) from the 4-Corners Breast Cancer Study. They reported nonsignificant association between vigorous physical activity versus sedentary, and ER-negative tumors neither in Latina nor in NHW premenopausal and postmenopausal women.

Another study by Ratnasinghe and colleagues (65) analyzed the relationship between physical activity and breast cancer subtype risk in 1,463 cases and 4,862 controls from different population groups including Latinas (NHWs, AAs, Latinas, Tunisian-Arabs, and Polishs) from the Global Epidemiology Study (GES). They found in the adjusted model (age, race, BMI, and pack-years of smoking) that women with a higher physical activity, measured as time per week, minutes per time, and minutes per week (>3 vs. <1 time per week, >30 vs. <10 minutes per time, and >150 vs. <10 minutes per week), had a lower risk of ER/PR-negative tumors (OR = 0.60, 95% CI, 0.43–0.82; OR = 0.65, 95% CI, 0.47–0.90; OR = 0.68, 95% CI, 0.49–0.94, respectively). The same trend was reported for ER-positive and ER/PR positive tumors. These results suggest that physical activity may be a protective factor for breast cancer overall independently of population groups or breast cancer subtype.

It has been proposed that physical activity can decrease breast cancer risk through modulation of steroid hormone production and circulation (66). Because TN subtype is not hormone dependent, lower blood levels of the steroid hormones would not affect

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the development of the tumor. This may explain in part why Abdel-Maksoud and colleagues (54) did not find an association between vigorous physical activity and this subtype, nor for Latinas or NHWs. Other biological mechanisms associated include the reduction of hyperinsulinemia, growth factors levels, oxidative stress, and systemic inflammation, among others (67).

Nonmodifiable Risk Factors

Family history and BRCA1/2 mutations

Family history. Family history of breast cancer increases a woman's risk of developing the disease (68). It accounts for about 5.5% of the excess lifetime risk in women with one affected first-degree relative and 13.3% in women with two or more first-degree relatives affected (69). It has also been associated with an increased risk for ER-negative breast cancer. Hines and colleagues (70) conducted a case–control study that included 2,492 NHWs (1,571 controls and 921 cases) and 1,343 Latinas (881 controls and 466 cases) from the 4-Corners Breast Cancer Study, to examine the relationship between family history of breast cancer and the pathologic characteristics of ER-positive and ER-negative tumors among Latina and NHW women. They reported that Latinas with a family history of the disease had a significantly higher proportion of ER-negative tumors compared with those without family history ($P < 0.02$), and an increased risk of ER-negative tumors in a model adjusted for center, age, and known risk factors, compared with controls (OR = 2.66, 95% CI, 1.59–4.44). No significant association was reported for ER-negative tumors in NHWs or for ER-positive tumors neither in Latina nor NHW women. Similarly, another case-only study based on the Ella Binational Breast Cancer Study analyzed 914 Mexican descent women with family history of breast cancer and compared the odds of TN versus other subtypes, according to family history of the disease. They found that 21.6% of women with TN tumors had a family history, compared with 13.5% of the women with other subtypes. The OR for TN tumors versus other subtypes for women with breast cancer in first-degree relatives was 2.04 (95% CI, 1.40–2.98; ref. 71), in a model adjusted for age at diagnosis and country of residence (USA or Mexico).

BRCA1/2 mutations. Mutation in the *BRCA1/2* genes account for 20% to 25% of inherited breast cancers and 10% to 15% of all breast cancer cases (72). The lifetime risk of developing breast cancer for a woman with a *BRCA1/2* mutation is ~87% (73). *BRCA1/2* mutations in Latinas have been found with varying proportion depending on the specific population studied (73, 74). The types and distribution of mutations differ by race/ethnicity, even within the same population group (73, 75, 76), and it may be one of the biological contributors to the differences in tumor subtype distribution among women from different population groups.

It has been reported that 60% to 80% of breast tumors from *BRCA1* mutation carriers have a TN phenotype (77, 78). The studies conducted in Latinas cited below are case-only and have analyzed the prevalence of the TN subtype in *BRCA1* mutation carriers (Table 3).

Lagos-Jaramillo and colleagues (33) analyzed 154 breast cancer patients (80 Latinas and 74 NHWs) that underwent genetic cancer risk assessment and *BRCA1/2* testing at the City of Hope Cancer Screening and Prevention Program. They reported a prevalence of 38.75% (31/80) *BRCA1* mutations for Latinas and 27.02% (20/74) for NHWs. Moreover, among the *BRCA1* cases, 74% (23/31) of Latinas had TN disease compared with 70% (14/20) of NHWs. Moreover, they found that Latinas positive for *BRCA1* mutations were more likely to have ER-negative tumors than *BRCA1*-negative Latina women (81% vs. 39%, $P < 0.001$). Another study carried out in Colombian women from the Instituto de Cancerología Las Americas in Medellin that included patients with breast and/or ovarian cancer referred to the oncogenetics service found that 100% (6/6) of *BRCA1* mutation carriers had a TN subtype (79). Villarreal-Garza and colleagues (80) conducted a case-only study that included unselected 96 breast cancer samples from the Mexican National Cancer Institute (INC) to analyze the frequency of *BRCA* mutations in Mexican breast/ovarian cancer patients and its association with clinicopathologic characteristics. They found that 11.5% (11/95) had *BRCA1* mutations, from which 81.8% (9/11) were TN tumors. Gonzalez-Rivera and colleagues (81) conducted a case-only study in 105 unselected TN breast cancer patients from 7 hospitals in Spain and 1 from Peru, to describe the status and frequency of germline mutations in seven breast cancer predisposition genes (*BRCA1*, *BRCA2*, *PALB2*, *BARD1*, *RAD50*, *RAD51C*, and *RAD51D*), and reported a frequency of 12.4% of *BRCA1* mutations among this population.

Recent evidence suggests that breast cancer risk in *BRCA1/2* carriers increases with the number of first-degree and second-

Table 3. TN prevalence among BRCA1 mutation carriers in Latina women

Recruitment strategy	Population included	Country	Mutation assessment technology	Sample size	No. of *BRCA1*-positive patients (%)	No. of TNBC among *BRCA1*-positive patients (%)	Reference
Selected patients	NHW and Latina women	U.S.	BRCA testing	80	31 (38.7)	23 (74)	(33)
	Latinas	Colombia	25-gene hereditary cancer panel (myRisk, Myriad)	85	6 (7)	6 (100)	(79)
	Latinas <50 years	Mexico	HISPANEL assay[a]	190 (only TNBC patients)	43 (22.6)	43 (100)	(83)
Unselected patients	Hispanic and Latinas	Mexico	HISPANEL assay[a]	96	11 (11.4)	9 (81.8)	(80)
		Spain and Peru	Targeted next-generation sequencing (of BRCA1, BRCA2, PALB2, BARD1, RAD50, RAD51C, and RAD51D)	105 (only TNBC patients)	13 (12.4)	13 (100)	(81)

Abbreviations: NHW, non-Hispanic white women; No., number; TNBC, triple-negative breast cancer; U.S., United States.
[a]HISPANEL assay: 114 *BRCA* mutation panel based on data from Hispanics from the United States, Spain, and South America.

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degree relatives diagnosed ($P < 0.001$ for *BRCA1*; $P = 0.02$ for *BRCA2*; ref. 82). Villarreal-Garza and colleagues (83) conducted a study in young Mexican women (<50 years old) with TN breast cancer treated at the National Cancer Institute in Mexico City ($n = 190$) and found that 23.2% ($n = 44$) of the patients had mutations either in *BRCA1* (43 patients) or *BRCA2* (1 patient) genes. Forty-five percent ($n = 20$) of the *BRCA*-positive patients reported a first-degree or second-degree relative affected with breast cancer (83).

The strong association between family history of breast cancer and TN subtype in Latina women is likely due to the presence of mutations in the susceptibly genes *BRCA1/2*. Many studies have evaluated the prevalence of *BRCA1/2* mutations among specific population groups in Latin America (84); nevertheless, only few have assessed the association between *BRCA1/2* mutations and breast cancer risk for intrinsic subtypes (83). More studies that include TN tumors in their analysis are needed, since it is well known that *BRCA1/2* mutation carriers are more likely to develop this subtype (85). Not all TN cases are explained by mutations in *BRCA1/2*. Studies that included different population groups have shown that other genes such as *BARD1*, *PALB2*, and *RAD51D* are also associated with higher risk of TN subtype (77, 86, 87). Gonzalez-Rivera and colleagues (81) found 2 mutations in *BARD1* and 1 in *RAD51D* in 105 unselected TN breast cancer patients from Spain and Peru. In general, studies in Latinas have analyzed the distribution of mutations in breast cancer susceptibility genes and its association with the risk for the disease, but have failed to assess the risk specifically for the TN subtype (84).

It is worth mentioning that the studies assessing *BRCA1/2* mutations in Latin America might be confounded by study design, some included unselected patients whereas others included only patients who fulfilled criteria for Hereditary Breast and Ovarian Syndrome (HBOC). Another confounding factor is screening technology as some used commercial screening panels, others used Sanger sequencing or whole sequencing of *BRCA1/2* genes.

Genetic ancestry

Population-based studies usually classify subjects into racial/ethnic groups (Hispanic, AA, NHW, API, AI/AN, and others) by self-identification. As differences in breast cancer risk (88, 89) and gene-expression profiles (90) have been shown according to ancestry, breast cancer genetic epidemiology studies started to categorize individuals based on their genetic ancestry (88, 91).

Several studies have reported a strong association between genetic ancestry and risk of breast cancer in Latina women. Fejerman and colleagues (88) conducted a case–control study in U.S. Latinas (440 cases and 597 controls) to identify an association between genetic ancestry and breast cancer risk. They reported an increased risk for breast cancer for every 25% increase in European ancestry (OR = 1.79, 95% CI, 1.28–2.79, $P < 0.001$), and this association remained statistically significant after adjustment for known risk factors (OR = 1.39, 95% CI, 1.06–2.11, $P = 0.013$). In this study, no significant association was reported between genetic ancestry and tumor characteristics such as HR status. Other studies have replicated this association (89, 92).

Few studies have evaluated the association between genetic ancestry and risk of breast cancer subtypes in Latinas. Serrano-Gomez and colleagues (93) analyzed the distribution of breast cancer–intrinsic subtypes and its association with clinicopathologic variables and genetic ancestry in 301 Latinas from Colombia. They reported a suggestive association between the African ancestry fraction and ER-negative disease ($P = 0.0211$). Other case–control study that analyzed the influence of risk factors and genetic ancestry on breast cancer risk in postmenopausal women (1,854 NHWs and 2,326 Latinas) from the United States and Mexico found a suggestive association between NA ancestry with ER-negative tumors in U.S. Latinas (NA ancestry: 0%–32% vs. >54.0%, OR = 1.80, 95% CI, 0.96–3.37, $P = 0.07$), in a model adjusted for age, study site, and known risk factors. This may indicate that a lower NA ancestry could be a risk factor for ER-negative tumors. This association was not statistically significant in NHW women neither for ER-negative ($P = 0.28$) nor for ER-positive tumors ($P = 0.25$; ref. 92). Consistent results were reported by Fejerman and colleagues in an admixture mapping (94) and genome-wide association study (GWAS; ref. 95) in Latinas. They found a region at 6q25, approximately 50 kb upstream the estrogen receptor 1 gene *(ESR1)* that is associated with protection from breast cancer in Latina women. The protective variant (rs140068132), with an OR of 0.60 (95% CI, 0.53–0.67), originates from NA and is practically absent in most other population groups. Additionally, it seems to be more protective for ER-negative tumors (OR = 0.34, 95% CI, 0.21–0.54), although it is also protective for the ER-positive subtype (OR = 0.63, 95% CI, 0.49–0.80). Prevalence of this variant in Latinas is variable, depending on the proportion of NA ancestry fraction of the region (95). These results suggest that Latin American countries with a low reported NA ancestry, such as Brazil, Chile, and Colombia, would have a higher risk of developing an ER-negative subtype, compared with higher NA ancestry countries, such as Peru and Mexico (96). More and larger studies are needed to better understand how ancestral background and environmental/behavioral interact to contribute to the risk of specific tumor subtypes, not only in Latina women but in all populations.

Conclusions and Perspectives

In this review, we provided a description of risk factors for ER-negative, ER/PR-negative, and TN breast cancer reported in Latina women. The prevalence of TN breast cancer in Latinas is higher than in NHW women (20). The proportion of the TN subtype in U.S. Latinas ranged between 10% and 18%, whereas in NLW women, it ranged between 8% and 15%. Moreover, this proportion of TN breast cancer is higher in Latinas from Latin America, ranging between 20% and 24% (17, 37, 88, 97–102). It is worth mentioning that the age-adjusted incidence of TN breast cancer is similar between NHW women (12 per 100,000) and Latinas (10 per 100,000; ref. 18). This, added to the fact that more than 50% of the U.S. Latino population is under 50 years old compared with approximately 40% of the non-Hispanic white population in the same age group could act as a confounded factor related with high prevalence of TN breast cancer in Latinas (103).

It is noteworthy that studies in nonmodifiable risk factors (family history and *BRCA* mutations, and genetic ancestry) showed the most concordant results, whereas studies in modifiable risk factors showed contradictory results. It is possible that this lack of concordance could be explained in part to the differences in tumor classification criteria; some studies analyzed ER-negative tumors, other ER/PR-negative and others TN tumors (ER/PR/HER2 negative). Additionally, studies are heterogeneous in the population included. Some studies that analyzed U.S. Latina could be biased due to the fact that acculturation process may change lifestyles behaviors; therefore, the modifiable risk

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factors (reproductive behaviors, feeding habits, and SES) for the disease compared with Latinas from Latin America. For this reason, it would be important to consider other factors such as time living in the United States, and residency in Hispanic enclaves, to control the analyses. Moreover, some of these studies included a low number of Latina women, and this could limit the power of the associations tested.

There are only few studies in Latina women from Latin America, and most of them are hospital-based registries; if we consider that some hospitals receive patients mainly from high SES or low SES, the spectrum of the lifestyle behaviors could change between hospitals and might modify the associations reported. Furthermore, these studies include women from different countries from Latin America (mainly Mexico and Colombia) that differ in their genetic ancestry, culture heritage, and Western influence. All this together contributes to the lack of concordance between the studies cited.

In conclusion, studies suggest that modifiable and nonmodifiable risk factors could play an important role in the development of breast cancer in Latina women, specifically TN subtypes, but the mechanisms responsible for some of the associations reported here are still unknown. More studies are needed to elucidate these mechanisms in order to clarify their roles as either risk or protective factors.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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