Cancer Epidemiology 58 (2019) 1–7

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Racial/ethnic differences in the utilization of chemotherapy among stage I-III breast cancer patients, stratified by subtype: Findings from ten National Program of Cancer Registries states

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ARTICLE INFO

Keywords:
Racial/ethnic differences
Chemotherapy
Breast cancer subtype
National Program of Cancer Registries

ABSTRACT

Background: The study aimed to examine racial/ethnic differences in chemotherapy utilization by breast cancer subtype.

Methods: Data on female non-Hispanic white (NHW), non-Hispanic black (NHB), and Hispanic stage I-III breast cancer patients diagnosed in 2011 were obtained from a project to enhance population-based National Program of Cancer Registry data for Comparative Effectiveness Research. Hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) were used to classify subtypes: HR + /HER2-; HR + /HER2 + ; HR-/HER2-; and HR-/HER2 + . We used multivariable logistic regression models to examine the association of race/ethnicity with three outcomes: chemotherapy (yes, no), neo-adjuvant chemotherapy (yes, no), and delayed chemotherapy (yes, no). Covariates included patient demographics, tumor characteristics, Charlson Comorbidity Index, other cancer treatment, and participating states/areas.

Results: The study included 25,535 patients (72.1% NHW, 13.7% NHB, and 14.2% Hispanics). NHB with HR + /HER2- (adjusted odds ratio [aOR] 1.22, 95% CI 1.04–1.42) and Hispanics with HR-/HER2- (aOR 1.62, 95% CI 1.15–2.28) were more likely to receive chemotherapy than their NHW counterparts. Both NHB and Hispanics were more likely to receive delayed chemotherapy than NHW, and the pattern was consistent across each subtype. No racial/ethnic differences were found in the receipt of neo-adjuvant chemotherapy.

Conclusions: Compared to NHW with the same subtype, NHB with HR + /HER2- and Hispanics with HR-/HER2- have higher odds of using chemotherapy; however, they are more likely to receive delayed chemotherapy, regardless of subtype. Whether the increased chemotherapy use among NHB with HR + /HER2- indicates overtreatment needs further investigation. Interventions to improve the timely chemotherapy among NHB and Hispanics are warranted.

1. Introduction

Chemotherapy has improved breast cancer survival. Whether there are racial/ethnic differences in receiving chemotherapy is of public health interest. Several studies have evaluated the potential differences and yielded conflicting results. Some studies have reported that black patients were less likely to receive chemotherapy [1–4]; others did not find the disparity [5–12]. In current clinical practice, breast cancer has been classified into subtypes with different prognoses. As black women have higher likelihood to be diagnosed with more aggressive subtypes, such as tumors with hormonal receptor (HR) negative and human epidermal growth factor receptor 2 (HER2) negative (HR-/HER2-), known as triple negative breast cancer (TNBC), white women have a higher incidence of less aggressive subtypes, such as tumors with HR + /HER2-. The disproportionate distribution of tumor subtype could mask the underlying racial difference in chemotherapy use, since aggressive subtype is frequently associated with more chemotherapy use. To better understand the breast cancer related health disparity, it is

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https://doi.org/10.1016/j.canep.2018.10.015
Received 6 September 2018; Received in revised form 26 October 2018; Accepted 29 October 2018
Available online 08 November 2018
1877-7821/

necessary to examine the racial difference in chemotherapy use within each subtype.

Delayed chemotherapy initiation has been identified as a risk factor for worse breast cancer survival [13–15]. The Joint American Society of Clinical Oncology/National Comprehensive Cancer Network (ASCO/NCCN) [16] and Center for Medicare and Medicaid Services (CMS) [17] recommend breast cancer patients receive adjuvant chemotherapy within 120 days after tumor diagnosis. Several other studies have also confirmed that receiving adjuvant chemotherapy after 90 days from surgery is associated with worse survival [13,18,19], and the impact was stronger for HR-/HER2- subtype [13,14]. Previous research found that black and Hispanic patients were more likely to receive delayed chemotherapy [20], however, little is known whether the racial/ethnic difference in delayed chemotherapy initiation persists within each cancer subtype.

Hispanics represent a rapidly increasing population in the United States. Compared to non-Hispanic white (NHW) women, Hispanic women were less likely to be diagnosed with but more likely to die from breast cancer [21]. The literature regarding the ethnic difference in chemotherapy utilization between NHW and Hispanic women is sparse, and the limited literature has yielded inconsistent results [7,9,4]. The National Program of Cancer Registry (NPCR) data are ideal to examine racial/ethnic differences in cancer care because the data reflect all cases within a population rather than being limited to a particular healthcare setting or payer. Therefore, in this study we used NPCR Specialized Registries' data to comprehensively examine the potential racial/ethnic differences in the receipt of chemotherapy and delayed chemotherapy among population-based stage I-III breast cancer patients, stratified by tumor subtype.

2. Material and methods

2.1. Data source

Data were collected from the Enhancing Cancer Registry Data for Comparative Effectiveness Research (CER) Project, which was funded by the Centers for Disease Control and Prevention's (CDC) NPCR program in 2010. Ten population-based cancer registries of the NPCR program participated in the CER project, covering the following geographic areas: Alaska, Colorado, Idaho, Louisiana, New Hampshire, North Carolina, Rhode Island, and Texas, as well as 13 counties of the Sacramento region of California and 5 metropolitan counties of Miami in Florida. In addition to the North American Association of Central Cancer Registries (NAACCR) standard data variables, the CER project collected additional data on tumor characteristics and complete treatment information. Detailed information on the CER project can be found in a previous publication [22]. The CER project was approved by both the CDC and state Institutional Review Board (IRB).

2.2. Study population

This study included women microscopically diagnosed with American Joint Committee on Cancer (AJCC, 7th edition) stage I-III breast cancer (identified with International Classification of Diseases for Oncology 3rd Edition [ICD-O-3] topography codes C50.0 to C50.9 and morphology/histology codes 8000–9582 with exclusion of codes 9050–9055, and 9140) in 2011. Exclusion criteria included: (1) patients who had other previously diagnosed tumors (n = 4,943); (2) race/ethnicity other than NHW, non-Hispanic black (NHB), or Hispanic (n = 1,143); or (3) patients with missing information on the receipt of chemotherapy (n = 2,031). Other racial/ethnic group was not included because of small case count. There was no significant difference between patients included in the analysis and patients with missing information on chemotherapy, regarding sociodemographic and tumor characteristics.

2.3. Variables

Race/ethnicity was categorized into three groups: NHW, NHB, and Hispanics. Outcomes included the receipt of chemotherapy (including both neo-adjuvant and adjuvant chemotherapy), the receipt of neo-adjuvant chemotherapy, and the receipt of delayed chemotherapy. Neo-adjuvant chemotherapy was defined as chemotherapy administered prior to surgery or when the patient did not receive surgery, and adjuvant chemotherapy was defined as chemotherapy given after the surgery. Delayed chemotherapy was defined as received neo-adjuvant chemotherapy ≥30 days after tumor diagnosis or received adjuvant chemotherapy ≥120 days after diagnosis or ≥90 days after surgery [13,17,18]. Breast cancer was grouped into four subtypes based on HR and HER2 status: HR + /HER2-; HR + /HER2 + ; HR-/HER2-; and HR-/HER2 + . Cases with either estrogen receptor (ER) positive or progesterone receptor (PR) positive were grouped into HR positive category.

Available covariates that are potential confounders included age at diagnosis (years, < 50, 50–59, 60–69, 70–79, ≥80), insurance (private, Medicare only/other public, Medicaid, no insurance, unknown), residence (urban, rural, or mixed), census tract poverty (population under federal poverty level: < 10%, 10–20%, > 20%), tumor subtype, AJCC stage (I, II, III), Bloom-Richardson grade (low, intermediate, high, unknown), tumor size (≤0.5 cm, 0.6–1.0 cm, 1.1–2.0 cm, 2.1–5.0 cm, ≥5.1 cm), lymph node involvement (negative, positive, unknown), Charlson Comorbidity Index (CCI) score [23] (0, 1, ≥2), surgery (only for adjuvant chemotherapy: none, lumpectomy, mastectomy), and the geographic area. We followed two rules to identify the confounders: 1) if the coefficient of exposure (race/ethnicity) changes at least 10% by adding a covariate into the crude model, we consider this covariate as a confounder; 2) to make the adjusted racial/ethnic differences comparable across study populations, the confounders identified in overall analyses (among all patients) were adjusted in stratified analyses (among patients with different subtype). Following the above rules, we examined the confounders for the three outcomes separately. Each available covariate met the criteria of confounder for study outcomes of receipt of chemotherapy and receipt of neo-adjuvant chemotherapy; for the outcome of receipt of delayed chemotherapy, age and comorbidity did not. However, we decided to adjust for age and comorbidity in the models for receipt of delayed chemotherapy because previous investigations of delayed chemotherapy have adjusted for these covariates [17,18,20]. We also found that the results remained similar with and without adjustment of age and comorbidity. In addition, hormone therapy (yes, no) and use of trastuzumab (yes, no) met the criteria of confounder and were adjusted in the models applied to the patients with HR + tumors, and HER2 + tumors respectively.

2.4. Statistical analysis

Chi-square test was applied to compare the categorical variables among racial/ethnic groups. Because the time intervals from tumor diagnosis to chemotherapy or surgery to chemotherapy were not normally distributed, Kruskal-Wallis test was performed to compare the racial/ethnic differences in medians of the time intervals. Multivariable logistic regression was employed to examine the potential racial/ethnic differences in the receipt of chemotherapy, neo-adjuvant chemotherapy, or delayed chemotherapy. All tests were two-sided with an alpha of 0.05. All analyses were performed with SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina).

3. Results

Of the 25,535 patients included in this study, 72.1% were NHW, 13.7% NHB, and 14.2% Hispanic. Compared to NHW, NHB and Hispanic patients were more likely to be younger, living in urban and high poverty areas, and diagnosed with tumors at later stage (Table 1, P < 0.0001 for each variable when compared with NHW). Specifically,

Table 1
Characteristics of patients diagnosed with stage I-III breast cancer in 2011 (N = 25,535).

Characteristics	NHW (N = 18,402), %	NHB (N = 3,497), %	Hispanics (N = 3,636), %
All	72.1	13.7	14.2
Age			
< 50	19.4	28.6	31.9
50-59	24.3	29.1	24.5
60-69	28.5	23.0	21.9
70-79	18.1	13.2	14.6
≥80	9.8	6.1	7.1
P-value*		< 0.0001	< 0.0001
Insurance			
Private	58.5	48.1	46.6
Medicare/other public	29.2	22.9	19.4
Medicaid	6.8	20.3	18.8
None	2.1	6.4	11.5
Unknown	3.4	2.4	3.7
P-value*		< 0.0001	< 0.0001
Residence			
Urban	52.1	67.3	78.6
Rural	10.1	6.2	2.5
Urban/rural mixed	37.8	26.5	18.9
P-value*		< 0.0001	< 0.0001
Census tract-poverty			
< 10%	53.1	23.7	30.2
10-19.99%	33.3	32.0	34.9
≥20%	13.5	44.3	34.9
P-value*		< 0.0001	< 0.0001
Subtype			
HR+/HER2-	66.7	53.5	59.6
HR+/HER2+	9.0	9.6	9.9
HR-/HER2-	10.2	21.2	11.7
HR-/HER2+	3.5	4.8	5.3
Unknown	10.5	10.9	13.5
P-value*		< 0.0001	< 0.0001
AJCC stage			
I	55.1	41.9	45.1
II	33.3	40.6	39.3
III	11.6	17.4	15.6
P-value*		< 0.0001	< 0.0001
Bloom-Richardson grade			
Low	22.1	13.0	11.2
Medium	32.3	26.3	18.8
High	20.2	30.6	18.1
Unknown	25.4	30.1	52.0
P-value*		< 0.0001	< 0.0001
Tumor size			
≤0.5 cm	9.0	7.9	7.7
0.6-1.0 cm	18.5	12.7	14.9
1.1-2.0 cm	36.4	31.1	32.6
2.1-5.0 cm	29.4	36.4	35.7
≥5.1 cm	6.0	10.9	8.1
Unknown	0.8	1.1	1.1
P-value*		< 0.0001	< 0.0001
Lymph node involvement			
Negative	62.4	55.1	55.9
Positive	27.0	34.9	33.4
Unknown	10.6	10.1	10.6
P-value*		< 0.0001	< 0.0001
Charlson comorbidity index			
0	83.6	77.0	85.2
1	12.6	16.8	11.4
≥2	3.8	6.2	3.4
P-value*		< 0.0001	0.05
Participating states			
Alaska	1.0	0.1	0.3
California	7.4	4.1	6.4
Colorado	10.7	1.7	7.3
Florida	10.8	16.5	33.0
Idaho	3.9	0.0	0.6
Louisiana	8.3	19.2	1.3
North Carolina	22.3	31.2	3.0
New Hampshire	4.6	0.1	0.4
Rhode Island	3.0	0.5	1.2
Texas	28.2	26.6	46.4
P-value*		< 0.0001	< 0.0001

Abbreviations: NHW: non-Hispanic white; NHB: non-Hispanic black; AJCC: American Joint Committee on Cancer; HR: hormone receptor; HER2: human epidermal growth factor receptor 2.

* P-values were calculated from the comparisons with Non-Hispanic white.

NHB women had the highest prevalence of Medicaid coverage, HR-/HER2- subtype diagnosis, and having at least one comorbidity. The majority of Hispanic women were from Florida and Texas.

Overall, 42.4% of patients received chemotherapy as part of their first course of cancer-related treatment, which was highest for NHB (53.7%), followed by Hispanics (48.0%) and NHW (39.1%) (P < 0.0001) (Table 2). Hispanics were most likely (29.8%) and NHW were least likely (20.3%) to receive neo-adjuvant chemotherapy (P < 0.0001). NHW (17.3%) had lower frequency of receiving delayed chemotherapy than NHB (29.3%) and Hispanics (31.6%), and the difference remained for the use of both neo-adjuvant or adjuvant chemotherapy (P < 0.0001).

The percentage of neo-adjuvant chemotherapy use varied by breast cancer subtype, which was higher for HR- tumors and lower for HR + tumors (data shown in Table 3). The median time (1st quartile, 3rd quartile) to chemotherapy use differed by race/ethnicity (P < 0.0001), but was similar across cancer subtypes.

To evaluate whether the racial/ethnic disparities in chemotherapy utilization vary by breast cancer subtype, an interaction term of race/ethnicity and subtype was examined in the logistic regressions. With adjustment of the confounders, the interaction was significant for any chemotherapy utilization (P = 0.009), which indicated the disparities varied by subtype, but it was not significant for the receipt of neo-adjuvant chemotherapy and delayed chemotherapy. However, to report the racial/ethnic differences in chemotherapy utilization in each subtype, we continued the stratified analyses by breast cancer subtype.

With adjustment for the covariates, NHB were more likely to use chemotherapy than NHW only when diagnosed with HR+/HER2- tumors (adjusted odds ratio [aOR]: 1.22; 95% confidence interval [CI]: 1.04–1.42) (Table 4). Hispanics had higher odds of using chemotherapy than NHW for all subtypes combined (aOR: 1.17; 95% CI: 1.04–1.31) and for HR-/HER2- subtype (aOR: 1.62; 95% CI: 1.15–2.28). There were no statistically significant differences in receiving neo-adjuvant chemotherapy between NHB and NHW, as well as between Hispanic and NHW, after adjusting for the covariates. NHB (aOR: 1.59; 95% CI: 1.37–1.84) and Hispanics (aOR: 1.53; 95% CI: 1.31–1.77) had significantly higher odds of receiving delayed chemotherapy compared with NHW, and the results were consistent across each subtype.

4. Discussion

Using a large population-based sample of stage I-III breast cancer patients, this study examined racial/ethnic differences in the utilization of chemotherapy. We found that NHB with HR+/HER2- subtype and Hispanics with HR-/HER2- subtype were more likely to receive chemotherapy compared to their NHW counterparts. NHB and Hispanics also had higher odds of receiving delayed chemotherapy, regardless of tumor subtype. No significant racial/ethnic differences in neo-adjuvant chemotherapy use was observed.

To our knowledge, this is the first study investigating the racial/ethnic differences of chemotherapy use by breast cancer subtype,

Table 2
Chemotherapy utilization among stage I-III breast cancer patients by race/ethnicity (N = 25,535).

Characteristics	NHW, % (N = 18,402)	NHB, % (N = 3,497)	Hispanics, % (N = 3,636)	All, %
Receive any chemotherapy[a]	39.1	53.7[††]	48.0[††]	42.4
Receive neo-adjuvant chemotherapy[b]	20.3	26.5[††]	29.8[††]	22.9
Receive any delayed chemotherapy[b]	17.3	29.3[††]	31.6[††]	21.7
Neo-adjuvant chemotherapy 30 days after tumor diagnosis[c] or later	46.0	62.0[††]	59.0[††]	52.0
Adjuvant chemotherapy 90 days after surgery[d] or later	6.3	11.9[††]	10.7[††]	7.9
Adjuvant chemotherapy 120 days after tumor diagnosis[d] or later	8.1	13.9[††]	17.4[††]	10.4

Abbreviations: NHW: non-Hispanic white; NHB: non-Hispanic black.
[a] Among all patients.
[b] Among patients who received chemotherapy.
[c] Among patients who received neo-adjuvant chemotherapy.
[d] Among patients who received adjuvant chemotherapy.
[††] P < 0.0001 for the comparison with non-Hispanic white.

although intensive racial/ethnic disparity research has been conducted for breast cancer without the specification of subtypes. Previous studies yielded different results, which varied according to the timing of study, patient sociodemographic status, and tumor characteristics. Studies including patients diagnosed with breast cancer in the year 2000 or before were more likely to find the higher percentage of chemotherapy use among white patients [1,3,4], whereas data after 2000 were less likely to identify a significant racial difference [5,6,9,7,8]. In addition, less racial differences in chemotherapy use have been found among patients aged 70 years or older [1,3], those with equal access to health care, such as all Medicaid insured patients [12], those with equal access to local comprehensive health care system, such as Kaiser Permanente Northern California [6], and those with more aggressive tumors, such as hormone receptor negative tumors [11]. Similar to the findings using the National Cancer Data Base (NCDB) [5], 42.4% of our patient population received chemotherapy; when all tumor subtypes were grouped together, no racial difference was observed between NHW and NHB. These findings may reflect the improved access to cancer care among NHB patients, since chemotherapy has been widely accepted as a cornerstone of systemic treatment for breast cancer.

After stratification by subtype, we found that among patients with HR+/HER2- tumors, NHB had higher odds of using chemotherapy than NHW. HR+/HER2- is the subtype with the best prognosis, for which hormonal therapy is an option and the benefit of chemotherapy is more

Table 3
Frequency of receiving neo-adjuvant chemotherapy and adjuvant chemotherapy, and median time from tumor diagnosis to chemotherapy and from surgery to adjuvant chemotherapy among breast cancer patients, stratified by race/ethnicity and breast cancer subtype.

	All		HR+/HER2-		HR+/HER2+		HR-/HER2-		HR-/HER2+	
	Receive any chemotherapy among all patients, % (proportion)									
All	42.4	(10,822/25,535)	32.5	(5,295/16,312)	65.6	(1,542/2,352)	76.3	(2,330/3,053)	77.4	(782/1,010)
NHW	39.1	(7,199/18,402)	30.1	(3,692/12,274)	64.4	(1,067/1,657)	73.4	(1,383/1,885)	76.9	(499/649)
NHB	53.7	(1,878/3,497)	41.6	(778/1,870)	69.6	(233/335)	80.6	(597/741)	77.5	(131/169)
Hispanics	48.0	(1,745/3,636)	38.1	(825/2,168)	67.2	(242/360)	82.0	(350/427)	79.2	(152/192)
P[a]	< 0.0001		< 0.0001		0.15		< 0.0001		0.80	
	Receive neo-adjuvant chemotherapy among all chemotherapy recipients, % (proportion)									
All	22.9	(2,429/10,603)	18.1	(945/5,224)	21.0	(316/1,508)	29.1	(668/2298)	28.8	(221/767)
NHW	20.3	(1,429/7,040)	16.2	(590/3,635)	18.6	(195/1,047)	25.8	(351/1362)	26.9	(131/487)
NHB	26.5	(492/1,856)	21.5	(166/772)	23.1	(53/229)	30.1	(178/592)	32.6	(42/129)
Hispanics	29.8	(508/1,707)	23.1	(189/817)	29.3	(68/232)	40.4	(139/344)	31.8	(48/151)
P[a]	< 0.0001		< 0.0001		0.001		< 0.0001		0.30	
	Median time (quartile 1 – quartile 3) from tumor diagnosis to receipt of neo-adjuvant chemotherapy, days									
All	30	(20-45)	31	(20-47)	31	(19.5-45)	28	(20-43)	29	(21-42.5)
NHW	28	(19-39)	29	(20-39)	28	(19-40)	26	(18-37)	28	(20-39)
NHB	36	(22-56)	40	(24-61)	35	(23-55)	34	(22-56)	33	(24-52)
Hispanics	33	(21-50)	33	(20.5-54)	35	(21.5-48)	35	(21-54)	30.5	(22-43)
P[b]	< 0.0001		< 0.0001		0.01		< 0.0001		0.10	
	Median time (quartile 1 – quartile 3) from surgery to receipt of adjuvant chemotherapy, days									
All	42	(30-59)	44	(33-61)	41	(29-56.5)	40	(28-55)	41	(29-58)
NHW	42	(30-56)	43	(32-59)	40	(29-55)	38	(28-51)	39	(28-54.5)
NHB	45	(32-65)	46	(35-65)	44	(32-64)	43	(29-63)	50	(28-70)
Hispanics	45	(32-65)	47	(33-66)	46	(29-61)	42	(31-63)	45	(35-63)
P[b]	< 0.0001		0.004		0.003		< 0.0001		0.0007	
	Median time (quartile 1 – quartile 3) from tumor diagnosis to receipt of adjuvant chemotherapy, days									
All	70	(53-91)	73	(56-95)	70	(51-91)	64	(48-84)	68	(49-89)
NHW	69	(52-88)	71	(55-92)	68	(50-87)	63	(47-81)	64.5	(47-82.5)
NHB	76	(58-98)	77	(57-101)	81.5	(61-109)	69.5	(51-91)	76	(53-97)
Hispanics	77	(57-106)	79	(60-110)	75.5	(56.5-98)	72.0	(51-91)	79	(54-109)
P[b]	< 0.0001		< 0.0001		< 0.0001		< 0.0001		0.0001	

Abbreviations: HR: hormone receptor; HER2: human epidermal growth factor receptor 2; NHW: non-Hispanic white; NHB: non-Hispanic black.
[a] Chi-square test was applied to compare the racial/ethnic differences (NHW, NHB, and Hispanics) in using chemotherapy or neo-adjuvant chemotherapy.
[b] Kruskal-Wallis test was applied to compare the racial/ethnic differences in medians of the time intervals from tumor diagnosis to chemotherapy or surgery to chemotherapy.

Table 4
Adjusted odds ratio[a] (95% confidence interval) of receiving chemotherapy and delayed chemotherapy for race/ethnicity, stratified by breast cancer subtype.

	All	HR + /HER2-	HR + /HER2 +	HR-/HER2-	HR-/HER2 +
Receive any chemotherapy					
NHB	1.12 (1.00, 1.26)	**1.22 (1.04, 1.42)**	0.89 (0.61, 1.31)	1.02 (0.78, 1.35)	0.93 (0.50, 1.76)
Hispanics	**1.17 (1.04, 1.31)**	1.10 (0.95, 1.28)	1.18 (0.81, 1.72)	**1.62 (1.15, 2.28)**	1.45 (0.78, 2.70)
Receive neo-adjuvant chemotherapy					
NHB	1.06 (0.91, 1.24)	1.10 (0.85, 1.42)	1.16 (0.72, 1.87)	0.91 (0.69, 1.19)	1.44 (0.83, 2.52)
Hispanics	1.11 (0.94, 1.31)	1.13 (0.88, 1.46)	1.23 (0.77, 1.96)	1.01 (0.73, 1.40)	1.06 (0.61, 1.84)
Receive delayed chemotherapy					
NHB	**1.59 (1.37, 1.84)**	**1.37 (1.10, 1.71)**	**2.20 (1.47, 3.30)**	**1.61 (1.21, 2.14)**	**1.95 (1.12, 3.37)**
Hispanics	**1.53 (1.31, 1.77)**	**1.51 (1.21, 1.88)**	**1.55 (1.01, 2.38)**	**1.53 (1.10, 2.13)**	1.50 (0.87, 2.58)

Abbreviations: HR: hormone receptor; HER2: human epidermal growth factor receptor 2; NHB: non-Hispanic black.

[a] Multivariable logistic model adjusted for subtype, age, insurance, residence, census tract-poverty level, AJCC stage, Bloom-Richardson grade, tumor size, lymph node involvement, Charlson comorbidity index, states/areas at diagnosis. Subtype was not adjusted for in the models stratified by subtype. Surgery was adjusted for in the models including adjuvant chemotherapy as outcomes. Hormone therapy was adjusted for in the models applied to the patients with HR + . Use of trastuzumab was adjusted for in the models applied to the patients with HER2 + . Non-Hispanic white patients were used as reference group.

controversial. For this subtype, NCCN guidelines recommend chemotherapy to be given only to those patients with positive lymph node or with high Oncotype DX recurrence risk score [24]. In current clinical practice, physicians recommend against chemotherapy to low recurrent risk HR + /HER2- patients to avoid chemotherapy overtreatment [25,26]. Due to high missing rate of recurrence risk score in the data, we were not able to identify the patients who received unnecessary chemotherapy. However, our findings indicate the potential racial difference in the overtreatment of HR + /HER2- tumors. Future studies are warranted to investigate whether NHB patients with HR + /HER2- subtype experience increased overtreatment or the higher chemotherapy use in this patient population is associated with improved survival.

Hispanic women represented about 15% of patients in our study. Similar to one previous study [7], we found that Hispanic patients were more likely to receive chemotherapy compared to NHW patients, in particular among patients with HR-/HER2- tumors, where a statistically significant 62% higher odds was observed. HR-/HER2-, known as TNBC, is the most aggressive breast cancer subtype where chemotherapy is the only systemic treatment option. A previous study showed that compared to NHW women, low-acculturated Hispanics had even higher odds of using chemotherapy than high-acculturated Hispanics [7]. Understanding how the psychosocial factors interact with clinical factors including tumor subtype to increase the chemotherapy use among Hispanic patients could lend more evidence to improve cancer care and survival for this minority patient population.

Neo-adjuvant chemotherapy has been accepted to downsize tumors for facilitating surgery, or to reduce the extent of surgery to achieve adequate resection. Given these benefits, the use of neo-adjuvant chemotherapy has increased over time from 12.2% in 2003 to 24.0% in 2011 [27]. In our study population, 22.9% patients received neo-adjuvant chemotherapy, which is similar to the findings using national data [5,27]. Data regarding the racial difference in receipt of neo-adjuvant chemotherapy is limited. One study using NCDB data reported that black and Hispanic patients are more likely to receive neo-adjuvant chemotherapy than white patients [28]. In our study, although the percentage of neo-adjuvant chemotherapy was higher among NHB and Hispanic patients compared to NHW patients, the differences can be explained by the advanced stage and more aggressive tumor characteristics.

Our study found significant racial/ethnic disparities in delayed chemotherapy, i.e., receiving neo-adjuvant chemotherapy ≥30 days after tumor diagnosis, adjuvant chemotherapy ≥120 days after tumor diagnosis or ≥90 days after surgery. Median time to chemotherapy, regardless of neo-adjuvant or adjuvant chemotherapy, was longer for NHB and Hispanic patients than NHW patients. NHB had 59% and Hispanics had 53% higher odds of receiving delayed chemotherapy compared to NHW patients, after adjusting for measured factors. Our findings were consistent with previous studies [20,29]. We further found that the racial/ethnic disparities in receiving delayed chemotherapy were consistent for all subtypes. As delayed chemotherapy is associated with worse breast cancer outcomes, particularly for those with aggressive subtypes [13,14], identifying the reasons of delayed chemotherapy among NHB and Hispanic patients is warranted to mitigate the survival difference.

The primary strength of this study is the use of population-based data, which are not limited to healthcare settings and show the diverse racial/ethnic composition and geographic variations, thus the findings have greater generalizability. Another strength is the completeness of treatment information, including chemotherapy and hormonal therapy. While data routinely collected by cancer registries may not have complete information on adjuvant treatment due to limited resource [30], the CER project provided funds to collect data on the first course of treatment from all sources including non-hospital settings such as physician's offices and out-patient clinics which may be missed in registry routine data collection.

Despite its strengths, our study has some limitations. One limitation is the potential underestimation of patients' comorbid conditions. Since the CER study only collected comorbid conditions from hospitals, the information may not have been complete for patients who were diagnosed and received treatment for these conditions at non-hospital settings. However, with thorough examination of medical records, a previous study reported that the prevalence of the comorbid conditions are low among breast cancer patients [31]. In addition, if present, this underestimation was random for each racial/ethnic group, thus the disparities we observed should not result from the underestimation of comorbid conditions. Another limitation is that we did not evaluate specific chemotherapy agent, particularly oral chemotherapy. The access to oral or intravenous chemotherapy agent could vary by race/ethnicity. However, only 0.4% patients took oral chemotherapy (Capecitabine), from which the influence should be minimal. The other limitation is the lack of information on types of facilities where patients received treatment. One previous study found that facility type could explain a small portion of, but not all, the racial difference in delayed adjuvant chemotherapy [29]. Future studies could investigate whether racial/ethnic disparities continue to exist for each tumor subtype after adjusting for facility type.

5. Conclusions

In conclusion, we found NHB and Hispanic breast cancer patients with certain tumor subtypes used more chemotherapy than NHW, which is encouraging and can be considered as improved equality of health care access over the past twenty years. However, NHB and

Hispanic patients are still less likely to receive timely chemotherapy, which is an indicator of under-treatment experienced by minority patients. Our study warrants the investigation of the factors contributing to the disparity and the further intervention to improve the timely use of chemotherapy for all women regardless of race or ethnicity.

Conflict of interest

None.

Funding

This work was supported in part under CDC Cooperative Agreements of the National Program of Cancer Registries: #U58/DP000792 in conjunction with the participating states and a CDC Comparative Effectiveness Research contract to ICF: #200-2008-27957.

Role of funding source

The findings and conclusions are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or Louisiana State University Health Sciences Center.

Authors contributions

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Jessica King – data analysis.

Xiao-Cheng Wu, MPH, MD - study design, data acquisition, and revising article.

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Acknowledgments

We would like to acknowledge the project investigators at the participating central cancer registries, as well as other organizations, and individuals, including the registrars, that supported the collection of the data to enhance NPCR for Comparative Effectiveness Research: Alaska Cancer Registry (Judy Brockhouse); Cancer Registry of Greater California (Dee W. West); Colorado Central Cancer Registry (Randi K. Rycroft); Cancer Data Registry of Idaho (Christopher J. Johnson); Florida Cancer Data System (Monique N. Hernandez); Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention (Christie R. Eheman, Timothy S. Styles); ICF International (Kevin B. Zhang) Louisiana Tumor Registry and Epidemiology Program (Vivien Chen, Xiao-Cheng Wu); Rhode Island Cancer Registry (David Rousseau); New Hampshire State Cancer Registry (Maria O. Celaya); CDC-NPCR Contractor, DB Consulting (Jennifer M. Wike); North Carolina Cancer Registry (Melissa Pearson); and Texas Cancer Registry (Anne M. Hakenewerth).

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