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EPIDEMIOLOGY

Predictors of timing of adjuvant chemotherapy in older women with hormone receptor–negative, stages II–III breast cancer

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Abstract Adherence to consensus guidelines for cancer care may vary widely across health care settings and contribute to differences in cancer outcomes. For some women with breast cancer, omission of adjuvant chemotherapy or delays in its initiation may contribute to differences in cancer recurrence and mortality. We studied adjuvant chemotherapy use among women with stage II or stage III, hormone receptor–negative breast cancer to understand health system and socio-demographic correlates of underuse and delayed adjuvant chemotherapy. We used Surveillance Epidemiology and End Results (SEER)-Medicare linked data to examine the patterns of care for 6,678 women aged 65 and older diagnosed with stage II or stage III hormone receptor–negative breast cancer in 1994–2002, with claims data through 2007. Age-stratified logistic regression was employed to examine the potential role of socio-demographic and structural/organizational health services characteristics in explaining differences in adjuvant chemotherapy initiation. Overall utilization of guideline-recommended adjuvant chemotherapy peaked at 43% in this population. Increasing age, higher co-morbidity burden, and low-income status were associated with lower odds of chemotherapy initiation within 4 months, whereas having positive lymph nodes, more advanced disease, and being married were associated with higher odds ($P < 0.05$). Health system–related structural/organizational characteristics and race/ethnicity offered little explanatory insight. Timely initiation of guideline-recommended adjuvant chemotherapy was low, with significant variation by age, income, and co-morbidity status. Based on these findings, future studies should seek to explore the more nuanced reasons why older women do not receive chemotherapy and why delays in care occur.

Keywords Breast cancer · Quality · SEER-Medicare · Adjuvant chemotherapy · Timing · Hormone receptor negative

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Introduction

Health disparities with regard to breast cancer outcomes among elderly, low-income, rural-dwelling, and minority women are well documented [1, 2]. The extent to which these disparities result from differences in quality of cancer treatment is unknown. Barriers to delivery of high-quality cancer treatment include poor dissemination systems, provider resistance or lack of awareness of new evidence, the fragmented nature of the health care financing system, lack of effective monitoring, poor communication, and lack of incentives to change practices [3, 4].

Clinical guidelines are intended to help standardize treatment regimens across providers. Although awareness

of differences in molecular subtypes of breast cancer and development of novel therapeutic and diagnostic tools [5–8] have yielded refined clinical guidelines for the management of breast cancer, adjuvant chemotherapy has remained the cornerstone of systemic therapy for patients with hormone receptor–negative disease since 1990 [9]. Joint American Society of Clinical Oncology/National Comprehensive Cancer Network (ASCO/NCCN) quality measures emphasize the importance of both administration of chemotherapy for such patients and initiation of therapy within 4 months of diagnosis [10]. Although consensus guidelines for breast cancer have focused on women under the age of 70, emerging evidence suggests clear benefits from adjuvant chemotherapy in older populations as well [11].

Variation in cancer treatment quality across patients may be related to both patient-level socio-demographic and health system-level structural/organizational characteristics. Adherence to guidelines and delivery of evidence-based care depends in part on diffusion of information across diverse health care organizations and providers [12, 13]. Thus, access to and receipt of chemotherapy in a timely fashion may vary based on where a patient receives care and corresponding structural/organizational factors of those institutions. It seems plausible that differences in structural/organizational factors, such as access to a National Cancer Institute (NCI)—designated cancer center, location of initial surgical care, and distance to chemotherapy providers, may vary across vulnerable populations that experience breast cancer disparities and may in part contribute to these disparities. To date, the degree to which these structural and organizational aspects of cancer care affect appropriate administration of chemotherapy for breast cancer and subsequent outcomes is unclear.

Although the interrelated effects of patient and structural/organizational characteristics of health services on quality of care have been explored in some diseases [14–18], these relationships have been much less systematically and comprehensively studied in breast cancer treatment. One study of North Carolina Medicaid beneficiaries showed that poor-quality breast cancer care was related to older age, living in a more rural county, receiving surgery at a smaller hospital, and living in a low-specialist density county [19].

We aimed to contribute to the existing evidence on the quality of breast cancer care in vulnerable subpopulations by examining trends in receipt and timing of initiation of adjuvant chemotherapy among Medicare-enrolled, stages II–III, hormone receptor–negative patients and by determining whether differences in structural/organizational factors, including distance to care and institutional affiliations, and select socio-demographic characteristics accounted for treatment differences.

Methods

Data source and patient population

The Surveillance, Epidemiology and End Results (SEER)-Medicare dataset was used in the current study [20]. We identified all women in the SEER-Medicare dataset with their first or only primary breast cancer diagnosed in the years 1994–2002, with claims data through 2007. We required that patients were (1) continuously enrolled in Medicare parts A and B fee-for-service during the one-year period prior to diagnosis and at least one year post-diagnosis, or until death, whichever occurred first; (2) non-Hispanic white, non-Hispanic black, or Hispanic patients (i.e., other groups were excluded because of their small numbers and insufficient power to examine racial/ethnic variation in quality of care); (3) 65 years and older at diagnosis; (4) stage II or III breast cancer at diagnosis; (5) not diagnosed with breast cancer at death or autopsy only, because these patients were not eligible for the outcome of interest, treatment, given their time of diagnosis at death; and (6) receiving breast conserving surgery or aggressive surgery/mastectomy as the first anti-cancer treatment. We further excluded women who received neoadjuvant chemotherapy prior to surgery, had end-stage renal disease, or were diagnosed with additional cancer within one year of the index breast cancer diagnosis, since care provided for these patients is likely different from the general breast cancer patient population. We focused our multivariate analyses on women with hormone receptor–negative cancers, defined as tumors not testing positive for estrogen or progesterone receptivity. This subgroup of patients represents women who are ineligible for endocrine therapy and for whom adjuvant chemotherapy is the cornerstone of systemic treatment, conferring a significant survival benefit [10, 21]. We refer to this group as "hormone receptor–negative" throughout, but it is important to note that also included in this definition are women with borderline or unknown hormone receptor status, since their care should be clinically similar in the absence of a positive hormone receptor test result.

Dependent variable

Initiation of any post-operative adjuvant chemotherapy within four months of diagnosis was our primary dependent variable. The 4-month time interval provides sufficient time for surgery and medical consultation and is consistent with ASCO/NCCN quality metrics [10]. Because women receive chemotherapy from various types of facilities [22], we extracted data from inpatient, carrier, outpatient, and durable medical equipment files using codes from the Healthcare Common Procedure Classification System (HCPCS), the International Statistical Classification of

Table 1 Identification of surgery and chemotherapy in Medicare claims

Treatment	Primary means of identification
Diagnostic codes	ICD-9-CM diagnosis codes: 174.0, 174.1, 174.2, 174.3, 174.4, 174.5, 174.6, 174.8, 174.9
	Other: V10.3
Aggressive surgery	ICD-9-CM procedure: 85.41, 85.42, 85.43, 85.44, 85.45, 85.46, 85.47, 85.48
	CPT/HCPCS: 19180, 19182, 19200, 19220, 19240, 19260-19272, 19303-19307
Breast conserving surgery	ICD-9-CM procedure: 85.20, 85.21, 85.22, 85.23, 85.24, 85.25
	CPT/HCPCS: 19120, 19125, 19126, 19160, 19162, 19301, 19302
Chemotherapy	ICD-9-CM procedure: 99.25, 285.3, 999.81
	CPT/HCPCS: 51720, 96400–96549, 99555, Q008–3Q0085 (oral), C9127, C9415, C9420, C9421, C9431, C8953–C8955, S9329–S9331, G0355, G0357–G0363, G9021–G9032, J8510, J8520, J8521, J8530–J8999 (oral), J9000–J9999 (IV)
	Revenue Center Code: 0331, 0332, 0335
	DRG: 410, 492
	Other: V58.1, V58.11, V66.2, V67.2, V87.41, NDC codes

Specific NDC codes that were included in searches are available upon request

CPT current procedural terminology, *DRG* diagnostic related group, *HCPCS* health care common procedure classification system, *ICD-9-CM* international statistical classification of diseases and related health problems, 9th revision, clinical modification, *NDC* national drug code

Diseases and Related Health Problems, 9th revision, clinical modification (ICD-9-CM), and National Drug Codes (NDC) (Table 1).

Independent variables of interest

Structural/organizational characteristics of oncologic health services included surgical facility type/ownership, bed size, teaching status, NCI cancer center designation, and American College of Surgeons Oncology Group (ACoSOG) affiliation, each of which was available in the SEER-Medicare data. ACoSOG membership is a proxy for organizational clinical expertise in the absence of information about Commission on Cancer (CoC) accreditation; in general, most ACoSOG hospitals are CoC-accredited. Distance to providers (for surgery and nearest chemotherapy provider) was calculated using zip code centroid to zip code centroid minimum distance algorithms [23–27]. We created quartiles of distance traveled to surgical providers and nearest chemotherapy providers for multivariate models.

Patient-level characteristics included race/ethnicity, age, co-morbidity, low-income status, marital status, and clinical factors that influence treatment decisions. We used SEER registry definitions of race/ethnicity [28]. Because guidelines for adjuvant chemotherapy differ by age, we stratified analyses by age group (65–69 years old versus 70 years and older) and included age as a categorical independent variable in the models of women aged 70 years and older. Co-morbidities were assessed using the NCI combined index method [29], which has been shown to be a better predictor of non-cancer mortality among breast cancer survivors than other commonly used co-morbidity measures [29]. We created quartiles of co-morbidity scores for multivariate models.

We included several covariates previously shown to influence chemotherapy and breast cancer treatment decision making, including AJCC stage of disease and histologic grade [30, 31]; marital status as a measure of social support [32]; neighborhood racial and ethnic composition (proportions of white, black, and Hispanic residents within the zip code of residence) [33, 34]; zip code-level income and education; year of diagnosis; and low-income status (measured by having any State-Buy-In (SBI) months during the study period) [28, 35, 36]. The SBI variable indicates that the state paid for supplemental insurance through its Medicaid program for individuals who met certain low-income requirements and applied for the program; thus, because many low-income people do not apply for SBI, it is a specific, but not particularly sensitive, measure of low-income status [28].

Statistical analysis

Receipt of adjuvant chemotherapy within four months of diagnosis was examined descriptively and modeled using multivariate logistic regression. Bivariate analyses compared receipt of chemotherapy and distribution of structural/organizational factors by race/ethnicity and age, using chi-squared tests [37]. In building analytic multivariate logistic models, tests were employed to determine the most appropriate variable specification (e.g., use of the continuous versus categorical forms of co-morbidity index score) for the final analytic models [38, 39]. Corrected Huber-White standard errors were reported for all models, and tests for multicollinearity among variables were conducted [39]. A P value threshold of 0.05 was considered statistically significant.

Results

We identified 20,898 women with incident breast cancer diagnosed in 1994–2002 who met initial inclusion/exclusion criteria (i.e., all criteria except hormone receptor status). As shown in Table 2, approximately 8% of women

were non-Hispanic black, 4% were Hispanic, and 88% were non-Hispanic white. The median age at diagnosis was 76.6 years. Overall, 68% were endocrine receptor positive, of whom 98% were estrogen receptor (ER) positive and 79% were progesterone receptor (PR) positive; 6,678 women were neither ER nor PR positive. Younger women and those with hormone receptor–negative tumors more often received chemotherapy.

Structural/organizational characteristics of health services were distributed unequally across racial/ethnic subpopulations (Table 3). Hispanic women were treated more often at for-profit surgical facilities (16% compared to 7% in whites and 8% in blacks; $P < 0.001$), and black women received surgery more often at NCI Comprehensive Cancer Centers (9% compared to 2% in white women and 3% in Hispanic women; $P < 0.001$), ACoSOG-affiliated facilities (32% compared to 22% in white women and 15% in Hispanic women; $P < 0.001$), and teaching/academic health centers (62% compared to 48% in white women and 41% in Hispanic women; $P < 0.001$) (Table 3). Black women were less likely to live in a zip code where a chemotherapy facility was available ($P < 0.001$).

In multivariate models, among women who had hormone receptor–negative tumors, for whom adjuvant chemotherapy is guideline-recommended, uptake of adjuvant chemotherapy was low overall (43%), even in the latest

Table 2 Descriptive statistics of full sample

Characteristic	% or mean $N = 20,898$ Total	% or mean $N = 3,360$ 65–69 years, White	% or mean $N = 336$ 65–69 years, Black	% or mean $N = 193$ 65–69 years, Hispanic	% or mean $N = 15,102$ ≥70 years, White	% or mean $N = 1,260$ ≥70 years, Black	% or mean $N = 647$ ≥70 years, Hispanic
Patient/demographic characteristics							
Married	38.5	58.6	30.1	50.8	35.9	21.5	29.2
Low income	21.6	14.0	47.0	53.9	18.5	50.3	53.8
Patient residence							
Metro	83.8	81.9	89.9	88.1	83.1	93.5	88.4
Non-metro	16.2	18.1	10.1	11.9	16.9	6.5	11.6
Clinical characteristics							
Stages							
Stage II	86.8	90.0	83.0	88.6	86.7	81.8	84.1
Stage III	13.2	10.0	17.0	11.4	13.3	18.2	15.9
ER/PR status							
ER+	66.6	69.6	49.7	59.6	67.5	54.4	63.5
ER−	16.3	17.3	27.7	17.6	15.4	21.4	15.6
ER unk/bord	17.1	13.1	22.6	22.8	17.0	24.2	20.9
PR+	53.7	57.4	37.8	52.3	54.2	42.5	52.1
PR−	27.7	27.2	32.1	25.0	27.8	37.8	25.4
PR unk/bord	18.6	18.6	25.3	22.9	14.8	24.4	22.3
NCICI score	0.30	0.17	0.38	0.27	0.31	0.43	0.37
Lymph nodes							
+Nodes	53.9	62.9	65.2	59.1	51.9	50.4	53.9
Treatment							
Received chemotherapy within 1 month of diagnosis							
	10.7	21.8	16.1	14.5	8.4	7.5	10.2
Received chemotherapy within 4 months of diagnosis							
	29.4	58.2	52.1	52.8	22.8	24.2	25.1
Ever received post-operative chemotherapy							
	35.0	62.5	59.5	59.4	28.5	30.8	30.2
Received surgery in same month as diagnosis							
	65.8	67.2	61.6	60.6	65.8	63.5	65.8

ER estrogen receptor, *NCICI* national cancer institute combined Co-morbidity index, *PR* progesterone receptor, +positive, *unk* unknown, *bord* borderline

Table 3 Distribution of health system structural/organizational factors by race/ethnicity in full sample

Organizational covariates	% or mean (SD) $N = 18,462$ White	% or mean (SD) $N = 1,596$ Black	% or mean (SD) $N = 740$ Hispanic	P value (from chi-square test or t-test)
Surgical facility characteristics				
Type/ownership				
For-profit/private	6.9%	8.4%	15.7%	<0.001
Non-profit/voluntary	78.5%	77.9%	69.7%	<0.001
Government	14.5%	13.7%	14.6%	0.682
NCI Comprehensive Cancer Center	2.3%	9.5%	3.0%	<0.001
ACoSOG-affiliated	22.3%	32.4%	14.9%	<0.001
Teaching/academic facility	48.5%	61.6%	41.1%	<0.001
Rural location	14.0%	4.9%	9.9%	<0.001
Number of beds	353 (226.2)	465 (259)	302 (219)	<0.001 ~ <0.001 #
Relational factors/access to care				
Nearest chemotherapy facility (miles)	3.2 (6.2)	1.9 (3.9)	4.2 (10.0)	<0.001 ~ <0.001 #
Nearest chemotherapy facility is located in same zip code as patient residence	84.9%	80.2%	87.4%	<0.001
Facility where patient received primary surgery is located in same zip code as patient residence	17.5%	14.9%	16.3%	0.027
Average distance traveled for primary surgery (miles)	15.6 (61.6)	11.5 (50.9)	11.5 (31.8)	0.011 ~ 0.061 #
Average distance traveled to chemotherapy provider, among those who received chemotherapy (first incidence of use) (miles)	17.5 (55.4)	11.5 (31.4)	13.3 (23.5)	0.029 ~ 0.53 #

ACoSOG American College of Surgeons Oncology Group, *NCI* National Cancer Institute

~ Indicates two-sample t-tests between white and black groups, # indicates two-sample t-tests between white and Hispanic groups

year for which data were available. Characteristics of the surgical facility where women were treated were not predictive of initiation of adjuvant chemotherapy within four months of diagnosis (Tables 4, 5). Among women aged 70 and older (Table 5), increasing distance to a chemotherapy facility and increasing distance to the surgical facility were consistently associated with lower odds of adjuvant chemotherapy within four months, although the effect was often statistically non-significant.

In general, low-income status was associated with significantly lower odds of chemotherapy initiation at four months, despite the fact that everyone in the sample was Medicare-insured (OR: 0.49, $P < 0.01$ in the 65–69 age group; OR: 0.59, $P < 0.01$ in the 70 and older age group). Having positive lymph nodes, being diagnosed as stage III (relative to stage II), being married, and being diagnosed in later years were generally associated with significantly higher odds of chemotherapy within four months. Among women aged 70 and older only (Table 5), increasing age and greater co-morbidity were associated with significantly lower odds of chemotherapy initiation at four months ($P < 0.01$ for both).

Discussion

We examined the association between structural/organizational factors in health care delivery, race/ethnicity, and age and the timing of adjuvant chemotherapy among older women with breast cancer and found low overall utilization and significant variation in timing of initiation of adjuvant chemotherapy. Although the distribution of structural/organizational factors varied significantly by racial/ethnic group, this variation did not appear to correlate with disparities in chemotherapy utilization. Rather, among hormone receptor–negative women, for whom adjuvant chemotherapy with or without trastuzumab is the sole systemic therapy option, failure to receive chemotherapy within four months was associated with increasing age, earlier year of diagnosis, being unmarried, and lower-

Table 4 Multivariate logistic regression models for breast cancer patients 65–69 years old with non-positive (i.e., negative, borderline, or unknown) hormone receptor status

Receipt of adjuvant chemotherapy within 4 months of diagnosis		
Variables	Odds ratio	95% Confidence interval
Structural/organizational variables		
Surgical facility characteristics		
Non-profit	(reference)	
Private/for-profit	1.07	(0.61–1.89)
Governmental	1.04	(0.66–1.62)
teaching facility	0.86	(0.61–1.22)
Fewer beds (<median)	1.02	(0.71–1.45)
NCI Comprehensive cancer center	0.60	(0.27–1.32)
ACoSOG-affiliated	1.04	(0.70–1.56)
Distance traveled to surgery (in quartiles)		
Same zip code	(reference)	
Surgery distance Q1	1.27	(0.75–2.14)
Surgery distance Q2	0.88	(0.54–1.43)
Surgery distance Q3	0.93	(0.56–1.53)
Surgery distance Q4	1.37	(0.81–2.33)
Distance to nearest chemotherapy provider (in quartiles)		
Same zip code	(reference)	
Chemotherapy distance Q1	1.24	(0.69–2.24)
Chemotherapy distance Q2	1.08	(0.60–1.97)
Chemotherapy distance Q3	1.14	(0.67–1.93)
Chemotherapy distance Q4	1.16	(0.65–2.05)
Clinical and patient characteristics		
Non-Hispanic white	(reference)	
Non-Hispanic black	0.84	(0.50–1.43)
Hispanic	1.58	(0.84–2.97)
NCI Combined Index Co-morbidity score (in quartiles)		
None (score = 0)	(reference)	
Co-morbidity Q1	0.95	(0.58–1.56)
Co-morbidity Q2	1.27	(0.67–2.42)
Co-morbidity Q3	0.78	(0.41–1.47)
Co-morbidity Q4	0.32[c]	(0.17–0.60)
Stage II	(reference)	
Stage III	1.93[b]	(1.13–3.30)
Node-negative	(reference)	
Node-positive	4.33[c]	(3.09–6.07)
Node status missing	1.05	(0.60–1.83)
Low-income proxy (State-Buy-In)	0.49[c]	(0.33–0.72)
Married	1.54[c]	(1.12–2.11)
Diagnosed in 1994	(reference)	
Diagnosed in 1995	1.46	(0.80–2.66)
Diagnosed in 1996	0.72	(0.37–1.38)
Diagnosed in 1997	1.16	(0.58–2.32)
Diagnosed in 1998	1.85[a]	(0.93–3.68)
Diagnosed in 1999	3.26[c]	(1.55–6.83)
Diagnosed in 2000	2.41[c]	(1.30–4.45)
Diagnosed in 2001	2.87[c]	(1.54–5.35)
Diagnosed in 2002	2.00[b]	(1.08–3.72)
Observations	1,082	

Models also control for grade, unknown hormone receptor status, timing of surgery, and zip code-level socioeconomic characteristics

NCI National Cancer Institute, *ACoSoG* American College of Surgeons Oncology Group, *Q* quartile

[a] Significant at 10%,
[b] significant at 5%,
[c] significant at 1%

Table 5 Multivariate logistic regressions for breast cancer patients 70 years and older with non-positive (i.e., negative, borderline, or unknown) hormone receptor statuses

Receipt of adjuvant chemotherapy within 4 months of diagnosis		
Variables	Odds ratio	95% Confidence interval
Structural/organizational variables		
Surgical facility characteristics		
Non-profit	(reference)	
Private/for-profit	1.17	(0.88–1.55)
Governmental	0.83	(0.66–1.05)
Teaching facility	0.94	(0.79–1.13)
Fewer beds (<median)	1.03	(0.86–1.23)
NCI Comprehensive Cancer Center	0.84	(0.54–1.31)
ACoSOG-affiliated	1.07	(0.87–1.31)
Distance traveled to surgery (in quartiles)		
Same zip code	(reference)	
Surgery distance Q1	0.88	(0.68–1.13)
Surgery distance Q2	0.85	(0.66–1.09)
Surgery distance Q3	0.86	(0.66–1.11)
Surgery distance Q4	0.79[a]	(0.61–1.04)
Distance to nearest chemotherapy provider (in quartiles)		
Same zip code	(reference)	
Chemotherapy distance Q1	0.86	(0.64–1.15)
Chemotherapy distance Q2	0.74[b]	(0.55–1.00)
Chemotherapy distance Q3	0.8	(0.61–1.05)
Chemotherapy distance Q4	0.92	(0.69–1.23)
Clinical and patient characteristics		
Non-Hispanic white	(reference)	
Non-Hispanic black	1.04	(0.77–1.40)
Hispanic	1.49[a]	(0.99–2.24)
Aged 70–74 years	(reference)	
Aged 75–79 years	0.45[c]	(0.38–0.54)
Aged 80–84 years	0.18[c]	(0.15–0.23)
Aged 85 years and older	0.04[c]	(0.03–0.05)
NCI combined index co-morbidity score (in quartiles)		
None (score = 0)	(reference)	
Co-morbidity Q1	0.92	(0.71–1.19)
Co-morbidity Q2	0.79	(0.59–1.06)
Co-morbidity Q3	0.64[c]	(0.49–0.85)
Co-morbidity Q4	0.59[c]	(0.44–0.77)
Stage II	(reference)	
Stage III	1.50[c]	(1.21–1.86)
Node-negative	(reference)	
Node-positive	4.00[c]	(3.34–4.79)
Node status missing	1.03	(0.78–1.36)
Low-income proxy (State-Buy-In)	0.59[c]	(0.48–0.73)
Married	1.14[a]	(0.98–1.34)
Diagnosed in 1994	(reference)	
Diagnosed in 1995	1.08	(0.75–1.57)
Diagnosed in 1996	1.11	(0.76–1.63)
Diagnosed in 1997	1.53[b]	(1.02–2.28)
Diagnosed in 1998	1.81[c]	(1.25–2.62)
Diagnosed in 1999	2.15[c]	(1.45–3.20)
Diagnosed in 2000	2.66[c]	(1.87–3.77)
Diagnosed in 2001	2.52[c]	(1.77–3.59)
Diagnosed in 2002	2.56[c]	(1.80–3.65)
Observations	4,823	

Models also control for grade, unknown hormone receptor status, timing of surgery, and zip code-level socioeconomic characteristics

NCI National Cancer Institute, *ACoSoG* American College of Surgeons Oncology Group, *Q* quartile

[a] Significant at 10%, [b] significant at 5%, [c] significant at 1%

income status. Overall, it was reassuring that chemotherapy utilization appeared more likely among patients with lymph node–positive and high-grade disease and lower among those with serious co-morbidity.

Age was strongly associated with receipt of chemotherapy within four months of diagnosis, consistent with prior studies [36, 40–42]. Due to insufficient accumulation of clinical trial evidence about the effects of adjuvant chemotherapy in older women, clear guidelines were lacking for breast cancer patients older than 70 during this period [10]. However, many experts have argued that underrepresentation of older women in clinical trials should not preclude their receiving potentially life-prolonging breast cancer treatments [43, 44]. Moreover, clear evidence now exists indicating benefit from adjuvant chemotherapy within this patient subgroup and particularly those with hormone receptor–negative disease [11, 21, 42, 45, 46]. Our data serve to highlight the need to develop guidelines for older patients with breast cancer and provide an important benchmark for further research in this area.

The lack of a racial/ethnic disparity in the current study contrasts with findings of other work documenting significant racial/ethnic differences in chemotherapy use for breast cancer patients in select geographic regions with mixed insurance status [32, 47], but is in line with results from patients in single insurer systems, such as the military health system and Medicare [41, 48]. As such, the lack of racial/ethnic effect in the current study may be explained by the insured status of the underlying SEER-Medicare sample. Our findings may suggest that the structure and organization of health services used by minority groups with insurance do not affect receipt of adjuvant chemotherapy; alternatively, features of SEER-Medicare sampling, problems with measurement of structural/organizational variables, and/or omission of unobservable variables could explain this finding. For instance, although SEER is one of the largest national cancer registry programs in the world, SEER largely samples black and Hispanic cancer patients from specific areas (e.g., many black patients live in Detroit and Atlanta) which may not be representative of the experiences of rural-dwelling black and Hispanic persons in the United States [20]. Our subanalyses comparing health system organizational/structural factors by race/ethnicity (Table 3) support this premise, as black women in this study were more likely to be treated at larger hospitals, NCI Comprehensive Cancer Centers, and academic facilities, which have been associated with improved treatment quality and/or health outcomes [18, 49–51] and which are reflective of more urban health facilities. Given the low numbers of Hispanic women in our sample, our findings may not be representative of their experiences as a whole, regardless of urban/rural residence.

Among women aged 70 and older, increasing distance to chemotherapy providers was associated with lower odds of receiving adjuvant chemotherapy at various time periods, but this effect was not always statistically significant. If distance to care presents an obstacle to elderly women, public health programs focused on providing reliable transportation options may benefit women. Given the limitations of using straight-line distances between zip code centroids, it is possible that our measures were too imprecise to detect the true effect of distance on care delivery. As such, future research should explore in more depth issues around geographic access to care as it relates to treatment planning and perceived burden of seeking oncology services among older women.

Despite the high predictive power of many variables related to tumor characteristics, co-morbidities, marital status, and income, we were unable to directly measure intent, treatment choice, or other behavioral factors that may have affected receipt of care. The decision to pursue or forgo adjuvant chemotherapy for older patients with breast cancer is complex, requiring consideration of toxicity, benefits, competing co-morbid conditions, and logistical burdens patients may face during treatment. As such, reasons for underuse of adjuvant chemotherapy are multifaceted and cannot be completely understood in a retrospective observational study of this nature. Nevertheless, older women in good health could benefit from chemotherapy [11] and thus may be systematically undertreated and unnecessarily missing out on life-sustaining therapy. Moreover, because patients receiving neoadjuvant chemotherapy were excluded from this analysis, pre-operative use of chemotherapy is unlikely to contribute to the low levels of adjuvant chemotherapy utilization.

This study has several strengths, including its use of a large, population-based cancer registry linked with Medicare claims data and longitudinal examination of trends in breast cancer care. We have also addressed one important potential source of omitted variable bias—insurance status—by limiting our study to insured Medicare beneficiaries continuously enrolled in parts A and B fee-for-service. Despite controlling for insurance status, however, we found significantly lower odds of chemotherapy initiation within four months among low-income women, suggesting that low-income women may experience financial barriers to care that extend beyond insurance status. Future studies should employ patient interviews or focus groups with low-income women comparable to those in this study to elucidate these additional barriers; for example, lower-income, older women may be more likely to stay in the workforce than more affluent, older women, and workforce participation may conflict with keeping chemotherapy appointments.

This study extends our understanding of breast cancer treatment by (1) documenting low utilization of adjuvant chemotherapy over time among important patient subpopulations, including older, low-income, unmarried women, (2) illustrating substantial variation in timeliness of initiation of chemotherapy (which may be related to subsequent health outcomes [52]), and (3) showing potential age-related disparities in treatment among healthy elderly women with good functional status. Combined with recent data on the likely benefit of standard adjuvant chemotherapy in the older breast cancer population [11], it is possible that outcomes may be improved for a substantial number of older patients. Future studies should seek to explore the more nuanced reasons why older women do not receive chemotherapy and to better identify women at risk for under-treatment and delays in care. Moreover, older women may need better access to information about risks/benefits of adjuvant chemotherapy and improved access to chemotherapy providers (e.g., through better referral processes and transportation to chemotherapy facilities).

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