

Disparities in Guideline-Concordant Initial Systemic Treatment in Women with HER2-Negative Metastatic Breast Cancer: A SEER-Medicare Analysis

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Background: Data on guideline-concordant initial systemic treatment among women with HER2-negative metastatic breast cancer (MBC) are limited. We determined the proportion of women with HER2-negative MBC who received guideline-concordant treatment and the extent to which independent variables explained differences in guideline-concordant treatment by hormone receptor (HR) status.

Methods: We conducted a retrospective cohort study using the SEER-Medicare database. We included women age >65 years diagnosed with HER2-negative MBC during 2010–2013. We used the National Comprehensive Cancer Network treatment guidelines to determine guideline-concordant initial treatment within the first 6 months of a cancer diagnosis. We conducted a multivariable logistic regression to identify the significant predictors of guideline-concordant treatment and a non-linear decomposition method to examine disparities by HR status.

Results: Among 1089 eligible women, 72.3% received guideline-concordant treatment. Compared to women who did not receive guideline-concordant treatment, women who received guideline-concordant treatment were more like to be comparatively older ($p < 0.05$), married ($p = 0.0171$), resided in areas with higher proportion of people age ≥ 25 years with at least four years of college education, and had positive HR status ($p < 0.0001$). Approximately 8% of the disparity in guideline-concordant treatment by HR status was explained by their observed characteristics. Need-related factors explained the highest proportion (66.9%) of the disparity.

Conclusion: Our findings indicate improvement of care for older women, who are single/divorced, have negative HR status, and who live in area with lower education levels. Unexplained disparities in guideline-concordant treatment by HR status can be attributed to patient preferences for treatment, physician-level factors, and perceptions.

Keywords: guideline-concordant treatment, decomposition, HER2-negative, breast cancer, SEER-Medicare database

Introduction

Metastatic breast cancer (MBC) occurs in 6–10% of newly diagnosed cases.¹ Overall survival of women with MBC can range from a few months to a few years depending on the molecular subtype,^{2,3} with almost none cured. More than 80% of the MBC cases are human epidermal growth factor receptor 2 (HER2)-negative tumors characterized by similar to poorer survival than those with HER2 positive tumors.⁴

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Prognosis has improved substantially for HER2-positive MBC because of the introduction of HER2 targeted therapies but has lagged for HER2-negative cases as development of new targeted therapies for HER2-negative cancers is only commencing.⁵

Providing cancer care per recommended treatment guidelines can help improve patient health outcomes; however, not all the patients with BC receive guideline-concordant cancer treatment.^{6,7} The National Comprehensive Cancer Network (NCCN) BC treatment guidelines recommend the use of chemotherapy and/or endocrine therapy for HER2-negative MBC.⁸ A large body of literature about guideline-concordant cancer care exist for early-stage BC cases. However, to date, very few real-world US studies have investigated guideline-concordant cancer treatment and identified opportunities to improve cancer care among women with MBC.^{6,9} Still, the literature regarding MBC, particularly in patients with HER2-negative cancers, is extremely limited.¹⁰ A study by Poorvu et al was conducted using the SEER-Medicare data for women diagnosed with MBC during 2010–2011 and reported that 24% of HER2-negative patients did not receive any systemic therapy in the first 6 months following cancer diagnosis.⁹ However, the predictors of guideline-concordant care among HER2-negative cases were not identified in the study. Another study also used the SEER-Medicare data for women diagnosed with MBC during 2007–2013 and reported that 12% of HER2-negative cases did not receive guideline-concordant care,⁶ but did not specifically identify factors that influence guideline-concordant care in HER2-negative cases. Additionally, performance status, a vital factor that impacts treatment decision in patients with advanced cancer,¹¹ was not accessed in these studies.

Hence, it is critical to examine if women with HER2-negative MBC are treated as per the guidelines, and the predictors of guideline-concordant treatment, especially in women age 65 and older who have higher cancer burden and poorer outcomes.¹² The goal of this study was to determine if women age 65 and above with HER2-negative MBC were treated as per the established treatment guidelines and to identify the factors that impact the guideline-concordant treatment. We also used a non-linear decomposition method to examine the magnitude of disparities in guideline-concordant treatment by hormone receptor (HR) status as a posthoc objective.

Methods

Study Design and Data Source

We used the SEER-Medicare linked dataset to conduct a retrospective observational cohort study. The SEER program provides data on newly diagnosed cancer cases from 18 population-based tumor registries that obtain data from hospitals, outpatient clinics, laboratories, private practitioners, laboratories, hospices, autopsy reports, and death certificates. The SEER program covers 26% of the US population with cancer.¹³ The Medicare files provide data on the use of inpatient, outpatient, physician, home health, durable medical equipment, and hospice care by individuals age 65 and above enrolled in CMS Medicare program. We linked the SEER cancer cases to the Medicare claims files.¹⁴ The details of the SEER-Medicare dataset are reported elsewhere.¹³ We linked the Area Health Resource File (AHRF) to the SEER-Medicare dataset to obtain the census level data on median household income, education, and number of hospitals offering oncology services.¹⁵

Study Cohort

We included women aged 66 and above at the diagnosis of first pathologically confirmed metastatic BC¹⁵ during 2010–2013 with HER2-negative status. Women diagnosed via a death certificate or autopsy were excluded. Additionally, we excluded women who were enrolled in health maintenance organizations, who were not continuously enrolled in Medicare parts A and B for 12 months before cancer diagnosis through at least 6 months following diagnosis or death, and who were not continuously enrolled in Medicare part D for at least 6 months following diagnosis or death, whichever occurred first.

Measures

Dependent Variable: Guideline-Concordant Initial Systemic Breast Cancer Treatment

The data on HER2 status are available in SEER for BC cases diagnosed from 2010 onwards. Tumor status was determined using the information for HER2 status along with HR status. The NCCN guidelines for HER2-negative MBC were used to determine receipt of guideline-concordant initial systemic treatment within 6 months following cancer diagnosis as per the woman's tumor status ([Supplemental Table 1](#)). All the versions of the NCCN guidelines published during 2010–2013 were used to identify initial treatment strategies.^{8,16–19} If a woman

received a treatment regimen that matched a systemic treatment regimen provided in the NCCN guidelines ([Supplemental Table 1](#)) per the tumor status then she was considered to have obtained guideline-concordant treatment. We identified endocrine therapies and infused or oral chemotherapies from the Medicare claims using J-codes and National Drug Codes.

We grouped our study cohort into those who received guideline-concordant initial systemic treatment and those who did not receive guideline-concordant initial systemic treatment.

Explanatory Variables

We used the Andersen behavioral model of healthcare services utilization to identify the significant predictors of guideline-concordant treatment.^{20,21} As per this model, healthcare utilization depends on the predisposition of individuals to use medical services, factors that enable or impede use, the need for care, healthcare use, and external healthcare environmental factors. Predisposing characteristics comprised age at cancer diagnosis and race/ethnicity, while enabling characteristics included marital status, census tract median household income, and census tract percentage of people age ≥ 25 years with at least 4 years of college education. Need-related factors included HR status, grade of tumor, comorbidity scores, performance status proxies, and the number of sites with cancer metastasis. We used data about co-occurring chronic conditions occurring within 12 months before BC diagnosis^{22–24} to obtain comorbidity scores. In addition, we identified claims associated with hospitalization, use of skilled nursing facility, oxygen use and related supplies, and use of wheelchair and walking aids, in the year prior to cancer diagnosis, to develop a proxy for performance status.²⁵ Healthcare use was determined by medical oncology office visits²⁶ in the follow-up period. External healthcare environmental factors comprised the location of residence, SEER region, and census level information on the number of hospitals offering oncology services.

Statistical Analyses

Descriptive statistics and Chi-square tests were conducted to describe the study cohort and to identify significant differences by receipt of guideline-concordant treatment. Multivariable logistic regression was used to identify significant predictors of guideline-concordant treatment in women with HER2-negative MBC.

HER2 status and HR status are important indicators for guiding BC care.¹⁷ Additionally, studies have indicated HR status as a crucial predictor of guideline-concordant BC care.^{6,9} Furthermore, survival is significantly different for HER2-negative patients with positive and negative HR status. Triple-negative MBC patients have poorer survival compared to patients with HER2-/HR+ MBC,²⁷ and women with triple-negative MBC are treated with aggressive cytotoxic chemotherapy regimens. A post-regression non-linear decomposition technique²⁸ was performed to quantify the disparities in guideline-concordant treatment by woman's HR status, and also to identify the extent to which explanatory variables (excluding HR status) explained these disparities. The disparity in treatment by HR status is grouped into two portions: the "explained" portion which is due to differences in the explanatory variables between two groups and the "unexplained" portion captures differences in the regression parameter estimates between two groups or differences in unobservable or unmeasured parameters (provider level, organizational level characteristics). The explained portion of the disparity by HR status is the sum of the differences between HR-positive and HR-negative women in terms of the observed characteristics weighted by the pooled regression coefficients.

All analyses were conducted within statistical analysis system software SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and STATA version 15.0 (StataCorp LLC).

Results

Descriptive Characteristics

After applying the inclusion-exclusion criteria, 1089 women aged 66 and older diagnosed with first HER2-negative MBC during 2010–2013 were identified and included in the study ([Figure 1](#)). The left columns in [Table 1](#) describe the study cohort, while the right columns in [Table 1](#) provide information on the study cohort by the receipt of guideline-concordant treatments and non-guideline-concordant treatment. Fifty-seven percent were aged 75 and older, 85.1% were White, 70.8% were single or divorced or widowed, 84.7% resided in metro regions, 82.7% had HR-positive tumor, 45.3% had well or moderately differentiated tumor, 73.8% had good performance status, and 60.6% had at least one comorbidity ([Table 1](#)).

About 72.3% received guideline-concordant treatment as per the NCCN guidelines and 27.7% did not. Women who received guideline-concordant treatment were

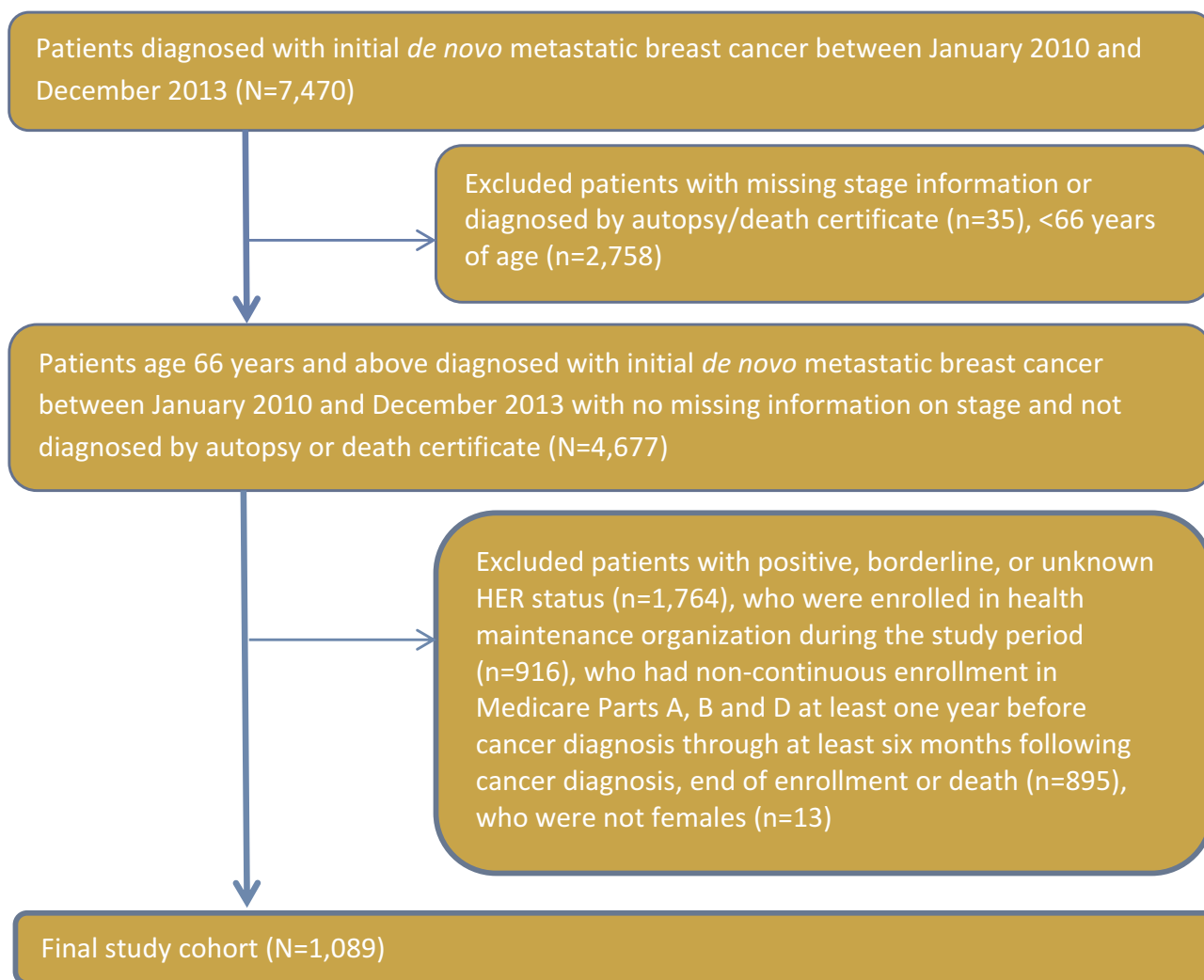


Figure 1 Patient flow diagram.

significantly more likely to be age 66–69 years, married or partnered, lived in non-metro areas, had positive HR status, had a well or moderately differentiated grade tumor, had good performance status, had no comorbidity, and had a higher number of medical oncology visits.

Among patients with HR-positive MBC who received guideline-concordant care, 76.2% received endocrine therapy only, 12.3% received both endocrine therapy and chemotherapy, while 11.5% received chemotherapy only. While among those who did not receive guideline-concordant care, all of them did not receive either chemotherapy or endocrine therapy. Among patients with HR-negative MBC who received guideline-concordant care, all of them received chemotherapy. While among those who did not receive guideline-concordant care, 85.7% received no treatment and 14.3% received endocrine therapy.

Predictors of Guideline-Concordant Treatment

Women age 70 years of age and older with HER2-negative MBC were significantly less likely to receive guideline-concordant treatment compared to those 66–69 years of age (Table 2). The adjusted odds ratios (AOR) for women in the age groups 70–74, 75–59, and age 80 and above were 0.581 (95% confidence interval (CI) = 0.352–0.960, $p=0.0339$), 0.593 (95% CI = 0.355–0.990, $p=0.0456$), and 0.410 (95% CI = 0.259–0.651, $p=0.0002$), respectively (Table 2). Women whose annual household income was >\$60,000 were 51% less likely to receive guideline-concordant treatment compared to those with an annual household income of ≤\$45,000. Compared to women who were single or widowed or divorced, those who were

Table I Description of Medicare FFS Beneficiaries with Metastatic HER2-Negative Breast Cancer by Receipt of Guideline-Concordant Initial Systemic Treatment SEER-Medicare 2010–2013 Cases

Variables	Total Cohort		Guideline-Concordant Treatment		Non-Guideline-Concordant Treatment		p-value
	N = 1089	%	N = 787 (72.3%)	%	N = 302 (27.7%)	%	
Age at Diagnosis							<0.0001
66–69	203	18.6%	169	83.3%	34	16.7%	
70–74	266	24.4%	202	75.9%	64	24.1%	
75–79	225	20.7%	168	74.7%	57	25.3%	
80+	395	36.3%	248	62.8%	147	37.2%	
Race/Ethnicity							0.8381
Whites	927	85.1%	671	72.4%	256	27.6%	
Others	162	14.9%	116	71.6%	46	28.4%	
Marital Status							0.0010
Married/Partnered	318	29.2%	252	79.3%	66	20.7%	
Single/Divorced/Widowed	771	70.8%	535	69.4%	236	30.6%	
Location of Residence							0.0336
Metro	922	84.7%	655	71.0%	267	29.0%	
Non-metro	167	15.3%	132	79.0%	35	21.0%	
SEER Region							0.2950
North East	284	26.1%	199	70.1%	85	29.9%	
South	266	24.4%	198	74.4%	68	25.6%	
North Central	158	14.5%	107	67.7%	51	32.3%	
West	381	35.0%	283	74.3%	98	25.7%	
Census Tract Household Income							0.5412
LE \$45,000	237	21.8%	177	74.7%	60	25.3%	
\$45,001–\$60,000	369	33.9%	268	72.6%	101	27.4%	
GT \$60,000	483	44.5%	342	70.8%	141	29.2%	
Census Tract Education							0.9947
0–22.0	300	27.6%	217	72.3%	83	27.7%	
22.1–30.3	278	25.5%	201	72.3%	77	27.7%	
30.4–37.7	247	22.7%	177	71.7%	70	28.3%	
GT 37.7	264	24.2%	192	72.7%	72	27.3%	
Hormone Receptor Status							<0.0001
Positive	901	82.7%	697	77.4%	204	22.6%	
Negative	188	17.3%	90	47.9%	98	52.1%	
Grade of Tumor							0.0038
Well/Moderately differentiated	493	45.3%	375	76.1%	118	23.9%	
Poorly/Very poorly differentiated	361	33.1%	238	65.9%	123	34.1%	
Unknown	235	21.6%	174	74.0%	61	26.0%	
Number of Metastatic Sites*							0.9633
0–1	785	72.1%	567	72.2%	218	27.8%	
2–4	304	27.9%	220	72.4%	84	27.6%	
Performance Status							0.0212
Good	804	73.8%	596	74.1%	208	25.9%	
Poor	285	26.2%	191	67.0%	94	33.0%	

(Continued)

Table I (Continued).

Variables	Total Cohort		Guideline-Concordant Treatment		Non-Guideline-Concordant Treatment		p-value
	N = 1089	%	N = 787 (72.3%)	%	N = 302 (27.7%)	%	
Comorbidity							0.0206
0	429	39.4%	325	75.8%	104	24.2%	
1	241	22.1%	179	74.3%	62	25.7%	
2+	419	38.5%	283	67.5%	136	32.5%	
Oncology Visits							<0.0001
0-8	368	33.8%	215	58.4%	153	41.6%	
9-25	323	29.7%	226	70.0%	97	30.0%	
GT 25	398	36.5%	346	86.9%	52	13.7%	
Hospitals Offering Oncology Services							0.6072
0-1	361	33.2%	270	74.8%	91	25.2%	
2-3	228	20.9%	160	70.2%	68	29.8%	
4-6	263	24.2%	188	71.5%	75	28.5%	
GT 6	237	21.7%	169	71.3%	68	28.7%	

Note: *Number of metastatic sites refers to metastasis to brain, liver, lung, or bone.

Abbreviations: FFS, fee for service; LE, less than or equal to; GT, greater than.

married or partnered were 53% more likely to receive guideline-concordant treatment (AOR=1.528, 95% CI=1.079–2.164, $p=0.0171$). Women with triple-negative MBC were significantly less likely to receive guideline-concordant treatment compared to women diagnosed with HR-positive tumor (AOR=0.250; 95% CI=0.171–0.366, $p<0.0001$). Women who had higher medical oncology office visits were significantly more likely to receive guideline-concordant treatment compared to those with lower medical oncology office visits.

Decomposition Analysis by Hormone Receptor Status

The percentage-point-difference in the proportion of women who received guideline-concordant treatment by their HR status was 29.5 (Table 3). By decomposing this difference, out of a 29.5-percentage-point difference, a 2.22-percentage point difference was explained by the observed characteristics, which represents 7.52% of the total disparity in guideline-concordant treatment between women with positive and negative HR status. Need-related factors explained the highest proportion (66.89%) of the disparity. This was followed by healthcare use factors at 55.72%, external healthcare environmental factors at 9.31%, predisposing factors at 3.19%, and enabling factors at -35.11%. The findings of need-related factors can be

interpreted as: if women with positive and negative HR status were similar in terms of their need-related factors, then the disparity in guideline-concordant treatment would decrease by 66.89%. The negative value for enabling characteristics suggests that if enabling factors of two groups of women were alike, then the disparity will increase by 35.11%. Over ninety percent (92.48%) of the difference in guideline-concordant treatment by HR status remained unexplained.

Discussion

To our knowledge, this is the first study that examined guideline-concordant initial systemic treatment among women age 65 and older with HER2-negative MBC and its predictors after controlling for several confounders, including performance status. We also discovered some insights into the magnitude of disparities in guideline-concordant treatment by women's HR status using an advanced non-linear decomposition method. Approximately 72% of the study cohort with HER2-negative MBC received NCCN guideline-concordant initial systemic treatment. Also, 77.4% of women with HR-positive tumors and 47.9% with HR-negative tumors received guideline-concordant care. The overall estimate is lower than that reported previously for HER2-negative MBC cases (72% vs 88%)⁶ but somewhat

Table 2 Adjusted Odds Ratios and 95% Confidence Intervals from Logistic Regression on Guideline-Concordant Initial Systemic Treatment Among Medicare FFS Beneficiaries with Metastatic HER2-Negative Breast Cancer SEER-Medicare 2010–2013 Cases

Variables	Guideline-Concordant Care		
	AOR	95% CI	p-value
Age at Diagnosis			
66–69	Reference		
70–74	0.581	[0.352, 0.960]	0.0339
75–79	0.593	[0.355, 0.990]	0.0456
80+	0.410	[0.259, 0.651]	0.0002
Race/Ethnicity			
White	Reference		
Others	1.395	[0.989, 2.169]	0.1388
Location of Residence			
Metro	Reference		
Non-metro	1.537	[0.945, 2.500]	0.0834
Census Tract Household Income			
LE \$45,000	Reference		
\$45,001–\$60,000	0.679	[0.426, 1.081]	0.1027
GT \$60,000	0.487	[0.265, 0.894]	0.0203
Census Tract Education			
0–22.0	Reference		
22.1–30.3	1.162	[0.735, 1.836]	0.5214
30.4–37.7	1.570	[0.891, 2.767]	0.1190
GT 37.7	2.058	[1.111, 3.810]	0.0217
Marital Status			
Married/Partnered	1.528	[1.079, 2.164]	0.0171
Single/Divorced/Widowed	Reference		
Hormone Receptor Status			
Positive	Reference		
Negative	0.250	[0.171, 0.366]	<0.0001
Grade of Tumor			
Well/Moderately differentiated	Reference		
Poorly/Very poorly differentiated	0.724	[0.510, 1.026]	0.0697
Unknown	0.886	[0.598, 1.312]	0.5447
Oncology Visits			
0–8	Reference		
9–25	1.592	[1.136, 2.233]	0.0070
GT 25	4.868	[3.292, 7.197]	<0.0001

Abbreviations: GT, greater than; LE, less than equal to; AOR, adjusted odds ratio; CI, confidence interval.

similar to that found in another study (72% vs 76%), and also by type of HR status.^{9,29} More than a quarter of the study cohort with HER2-negative MBC and more than half with triple-negative MBC did not receive initial guideline-recommended cancer treatment, which indicates several opportunities for the improvement of cancer care.

Age at cancer diagnosis, a predisposing factor, significantly predicted receipt of guideline-concordant treatment in women age 65 and above with HER2-negative MBC. The adjusted odds ratios of the receipt of guideline-concordant care decreased with an increase in age, a finding consistent with that published earlier.⁹ Perhaps, with increase in age, women age 65 and above may be less

Table 3 Nonlinear Decomposition of Guideline-Concordant Initial Systemic Treatment Among Medicare FFS Beneficiaries with Metastatic HER2-Negative Breast Cancer with Positive and Negative Hormone Receptor Status SEER-Medicare 2010–2013 Cases

	Guideline-Concordant Treatment	
% of HR-positive cases with guideline-concordant care	77.4%	
% of HR-negative cases with guideline-concordant care	47.9%	
Difference	29.5	
Total “Explained” (%)	2.22	
Variables	% of “Explained” Difference	% Contribution to the “Explained” Portion
Predisposing factors (Age at breast cancer diagnosis*, Race/Ethnicity)	0.24%	3.19%
Enabling factors (Marital status, Census tract median household income** and education*)	−2.64%	−35.11%
Need-related factors (Grade of tumor*, Comorbidity, Performance status, Number of sites of cancer metastasis)	5.03%	66.89%
Healthcare use (Medical oncology office visits***)	4.19%	55.72%
External healthcare environmental factors (Location of residence, SEER region, Hospitals offering oncology services)	0.70%	9.31%
Total Difference Explained	7.52%	100%
Total Difference Unexplained	92.48%	

Notes: *p<0.1; **p<0.05; ***p<0.001. We used the p-value of <0.1 due to relatively smaller sample size of HR-negative cases compared to HR-positive cases.

likely to receive aggressive cancer treatments given their overall health status, which may reduce their likelihood of receiving guideline-concordant initial cancer care. Similar to an earlier study,⁹ we found that an enabling factor, being married or partnered, significantly predicted receipt of

guideline-concordant cancer treatment. This suggests that social support may aid in facilitating cancer care.

With regards to need-related factors, women with triple-negative tumors had lower odds of the receipt of guideline-concordant treatment compared to those with HR-positive tumor, adding support to an earlier study.⁹ Over the past two decades, treatment options in triple-negative tumors have been limited to conventional cytotoxic chemotherapy with considerable toxicity,^{30–32} whereas HR-positive patients have multiple options including hormonal therapy which is comparatively less toxic. Hence, due to the lack of effective less-toxic therapies for triple-negative MBC,^{33,34} this older group may be less likely to receive guideline-concordant treatment. However, recent evidence has emerged regarding the efficacy of targeted immune checkpoint inhibitors when combined with chemotherapy as the first-line treatment of triple-negative MBC.^{35,36} With the approval of the combination of chemotherapy and immunotherapy for triple-negative MBC, a higher proportion of women with the disease may receive guideline-concordant care in near future, however, this may not be highly evident in the older group due to drug-related toxicities.

From the decomposition analysis, we found that about 8% of disparity in guideline-concordant treatment between women with HR-positive and HR-negative tumors was explained by the covariates included in the regression model. Need-related factors which consisted of tumor grade, comorbidities, performance status, and several sites of cancer metastasis contributed the highest portion of explained disparities. Consistent with the previous literature,³⁷ we found that a higher percentage of women with HR-negative tumors had poorly, undifferentiated or unknown grade than those with HR-positive tumors (data not shown), which explained 5% of disparity. This finding signifies that if women with HR-negative tumors had the same tumor grade as women with HR-positive tumors then the disparity may decrease by 5%, thereby indicating opportunities of improvement in women with poor or undifferentiated HR-negative tumors. Additionally, healthcare use in terms of medical oncology office visits contributed to a substantial amount of the disparity in guideline-concordant between the two groups. To our knowledge, no study specifically examined medical oncology office visits in women with HER2-negative MBC. Therefore, it is important that further research explore this finding regarding the ambulatory visits and predicting factors of use among these two cohorts. We also found that

approximately 92% of the disparity in guideline-concordant treatment by women's HR status was unexplained. Some of this unexplained difference may be due to patient's severity of comorbidities, and patient and physician treatment choices that are not available in the database. This is a critical area for further research, as treatment varies by HR status.

This study has a strong conceptual framework and used an advanced decomposition method to identify disparities in guideline-concordant initial treatment by HR status among women with HER2-negative MBC. This study also leveraged SEER-Medicare data to conduct a comprehensive analysis. However, secondary data analyses have inherent limitations. Some limitations of the study include use of census level information on patient's household income, education level, and access to oncology hospitals,³⁸ and limited generalizability of the study findings to older BC patients enrolled in Medicare. Additionally, the SEER-Medicare does not provide information on patient's severity of comorbidities and patient preferences and physician preferences which may impact treatment choices. However, we controlled for performance status proxy in the analyses. Furthermore, we did not measure any gaps in the treatment after the patients initiated their treatment, which may ultimately affect their clinical outcomes. However, measuring outcomes was not the objective of this study.

Conclusion

More than a quarter of older women with HER2-negative MBC did not receive guideline-concordant treatment as per the NCCN treatment guidelines and the non-receipt of guideline-concordant treatment was higher in older women age 70 and above and those with negative hormone receptor status. In decomposition analysis, approximately 8% of the disparity in guideline-concordant treatment was explained thereby identified opportunities of cancer care improvement for older women, especially with negative HR status.

Data Sharing Statement

Data sharing not available due to restrictions. The SEER-Medicare data needs to be requested for the specific research aims and cannot be shared due to restrictions. The Area Health Resource File is a publicly available database.

Ethical Approval Statement

Since the study was conducted using a de-identified secondary database, the University of Rhode Island (USA) Institutional Review Board committee considered this

study as exempt from human subjects research. The Area Health Resource File data are freely available to the researchers from the website: <https://data.hrsa.gov/topics/health-workforce/ahrf>. The researchers need to apply for the SEER-Medicare data to perform the research. More information about the SEER-Medicare data is available on: <https://healthcaredelivery.cancer.gov/seermedicare/>.

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Author Contributions

All authors (AV, MG, SK) made significant contribution to the work reported, whether it is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas. All the authors equally took part in drafting, revising or critically reviewing the article, provided final approval of the version to be published, have agreed on the journal to which the article has been submitted, and also agree to be accountable for all aspects of the work.

Disclosures

No conflict of interests or disclosures.

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