Guideline-Concordant Treatment Among Elderly Women With HER2-Positive Metastatic Breast Cancer in the United States

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ABSTRACT

Background: It is crucial to identify whether women with HER2-positive (HER2+) metastatic breast cancer (MBC) are treated according to treatment guidelines and whether treatment disparities exist. This study examined guideline-concordant treatment among women with HER2+ MBC and determined the magnitude of differences in treatment between those with positive and negative hormone receptor (HR) status using a nonlinear decomposition technique. **Methods:** A retrospective observational cohort study was conducted using the SEER-Medicare linked database. The study cohort consisted of women aged ≥ 66 years diagnosed with HER2+ MBC in 2010 through 2013 ($n=241$). Guideline-concordant initial treatment after cancer diagnosis was defined based on the NCCN Clinical Practice Guidelines in Oncology for Breast Cancer. A multivariable logistic regression was performed to identify significant predictors of guideline-concordant treatment. A postregression decomposition was conducted to identify the magnitude of disparities in treatment by HR status. **Results:** Of 241 women included in the study, a total of 76.8% received guideline-concordant treatment. These women were significantly more likely to have positive HR status ($P=.0298$), have good performance status ($P=.0009$), and more oncology visits ($P<.0001$). With 1-year increments in age at cancer diagnosis, the likelihood of receiving guideline-concordant treatment reduced by 5% ($P=.0356$). The decomposition analysis revealed that 19.0% of the disparity in guideline-concordant treatment between women with positive and negative HR status was explained by differences in their characteristics. Enabling characteristics (marital status, income, and education) explained the highest (22.8%) proportion of the disparity. **Conclusions:** Nearly one-quarter of the study cohort did not receive guideline-concordant treatment. Our findings suggest opportunities to improve cancer care for elderly women with negative HR status who are unpartnered or have lower socioeconomic status. The high unexplained portion of the disparity by HR status can be due to patient treatment preferences, propensity to seek care, and organizational and physician-level characteristics that were not included in the study.

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Background

Cancer health disparity has received national attention and is considered a priority for health services research. Identifying cancer health disparities is critical to understanding why some patient groups may be more likely to not receive guideline-concordant care and die prematurely from cancer than their counterparts who received guideline-concordant care. Additionally, the US Department of Health & Human Services has revealed its action plans to eliminate health disparities related to insurance coverage, quality of care, workforce diversity, population health, and data collection, and has geared its efforts and substantial national funding to meet its goals.¹

Survival rates for breast cancer (BC), the most common cancer in US women, have been improving,² although these improvements are not observed equally in all age groups,² racial/ethnic groups,^{2,3} US regions,² or socioeconomic groups.^{3–6}

Approximately 20% of patients with BC have HER2-positive (HER2+) tumors characterized by a more aggressive phenotype, leading to shorter times to relapse and adverse disease prognosis,⁷ and significantly shortened disease-free and overall survivals compared with those without HER2+ tumors.^{8,9} Additionally, women with metastases have a 5-year survival rate of only 26%, with almost none cured.¹⁰ Despite advances in the management of HER2+ metastatic breast cancer (MBC), the response rate to first-line treatment is 50% to 80%, and 20% to 40% for second-line treatment, with most patients succumbing to their disease.^{11–15}

Although standardized guidelines for the treatment of HER2+ MBC exist, few real-world studies have identified treatment patterns and opportunities to improve care among these patients.^{16–21} Two studies have evaluated guideline-concordant care. Poorvu et al²⁰ used SEER-Medicare data for women diagnosed in 2010 through

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2011 and found that approximately 20% of patients with HER2+ disease received no systemic therapy in the first 6 months after diagnosis. However, the HER2+ tumors were not categorized into hormone receptor (HR) status, which is an important determinant of treatment and disease prognosis. Another study also used SEER-Medicare data for women diagnosed in 2007 through 2013 and reported that among 96 women with HER2+ cancer, 42 received guideline-concordant care.²¹ Moreover, performance status (PS), an essential indicator of treatment decision in patients with advanced cancer,²² was not controlled for in these studies. Yet another study reported disparities in trastuzumab utilization, with worse overall survival among disparate patients.¹⁹ However, with no HER2 status data available in SEER before 2010, women who received trastuzumab were assumed to be HER2+. Additionally, Rugo et al¹⁸ reported racial/ethnic disparities in treatment patterns among patients with HER2+ MBC; however, the data were obtained between December 2003 and February 2006, and hence do not reflect recent trends in treatment of HER2+ MBC.

Approximately 45% of new BC cases are diagnosed in women aged ≥ 65 years, with poor survival rates.²³ Even though elderly women bear a higher BC burden and have worse outcomes,²³ they remain underrepresented in many clinical trials.^{24–27} As a result, considerable controversy persists in what constitutes a guideline-concordant treatment plan for elderly women. There is a growing need to determine whether elderly women with HER2+ MBC are treated according to guidelines and if disparities exist. The primary objective of this study was to examine guideline-concordant treatment provided to elderly patients with BC with metastatic HER2+ tumor subtype using the SEER-Medicare database. The post hoc objective was to quantify the extent to which independent variables explained disparities in guideline-concordant treatment among women by their HR status using a nonlinear decomposition technique.

Methods

Study Design and Data Source

A retrospective observational cohort study was conducted using the SEER-Medicare linked database. The SEER program, which covers 26% of the US population, obtains information on patients newly diagnosed with cancer from 18 population-based tumor registries that in turn collect information from hospitals, outpatient clinics, laboratories, private practitioners, hospices, autopsy reports, and death certificates.²⁸ The Medicare data provide information on claims from inpatient, outpatient, physician, home health, durable medical equipment, and hospice care for individuals aged ≥ 65 years who are enrolled in Medicare. The SEER cancer cases were linked to Medicare claims files.²⁹ Details of

the SEER-Medicare dataset are described elsewhere.²⁸ For this study, the Area Resource File was linked to the SEER-Medicare dataset using the state and county level information to obtain census tract data on income, education, and number of hospitals offering oncology services.³⁰

Study Cohort

The study cohort consisted of women aged ≥ 66 years at diagnosis of the first pathologically confirmed MBC (SEER site recode 46; AJCC stages IV, IV not otherwise specified [NOS], IVA, IVB, IVC)³¹ with HER2+ status in January 2010 through December 2013. Women with negative or unknown HER2 status and those diagnosed via a death certificate or autopsy were excluded, as were women who were enrolled in an HMO or were not continuously enrolled in Medicare Parts A and B during the study period of 12 months before cancer diagnosis through at least 6 months after diagnosis, death, or end of enrollment (Figure 1).

Measures

Guideline-Concordant Treatment

SEER data provide clinical information on HER2 status since 2010, which, along with HR status, was used to determine tumor status. Guideline-concordant initial treatment received within 6 months after cancer diagnosis²⁰ per tumor status was determined based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for patients with HER2+ MBC. Because women diagnosed between 2010 and 2013 were included, all versions of the NCCN Guidelines for BC published during this time frame were used to identify all possible relevant initial treatment strategies for the study cohort.^{32–37} A woman was considered to have received guideline-concordant treatment if a regimen she obtained within 6 months of her cancer diagnosis matched a treatment listed in the NCCN Guidelines (supplemental eTable 1, available with this article at JNCCN.org). Medicare claims were used to identify endocrine therapies (using J-codes and National Drug Codes [NDC]), infused or oral chemotherapies (using J-codes and NDC), and HER2-targeted therapies (using J-codes and NDC). Because the dose and duration of systemic therapy are not captured within Medicare Part B claims, evidence of the use of any systemic therapy recommended in the NCCN Guidelines was considered guideline-concordant treatment.

The primary measure of interest—receipt of guideline-concordant treatment—was categorized as guideline-concordant treatment and non-guideline-concordant treatment.

Explanatory Variables

The Andersen behavioral model of healthcare services utilization was used to evaluate significant predictors of

Figure 1. Patient flow diagram.

Abbreviations: HMO, health maintenance organization; MBC, metastatic breast cancer.

guideline-concordant treatment.^{38,39} This model has been widely used to understand healthcare services utilization in population-based studies. According to this model, healthcare utilization and medical care are functions of the predisposition of individuals to use services, factors that enable or impede use, the need for care, healthcare use, and external healthcare environmental factors. Predisposing factors included age at cancer diagnosis and race/ethnicity, and enabling factors included marital status, census tract median household income, and percentage of people age ≥ 25 years with at least 4 years of college education, categorized as high or low based on the median value. Need-related factors included HR status, tumor grade, comorbidity scores^{40–42} derived from co-occurring chronic conditions within 12 months before diagnosis of BC, PS proxies,⁴³ and number of sites with cancer metastasis. A proxy indicator for PS was developed by identifying claims associated with hospitalization, use of skilled nursing facility, oxygen use and related supplies, and use of wheelchair and walking aids in the year before cancer diagnosis.⁴³ A woman with at least one claim for any of these services in the year before cancer diagnosis was considered to have poor PS, whereas a woman with no claim for any of these services was considered to have good PS. Healthcare use comprised medical oncology office visits

during the follow-up period,⁴⁴ and was categorized as low (0–18) or high (≥ 19) based on the median value. Medical oncology office visits were captured from the physician files through information describing provider specialty and date of office visit. Medical oncologists were defined as physicians with a listed specialty of medical oncology or hematology/oncology. The visits were determined using Healthcare Common Procedure Coding System codes for new office visits, established office visits, and office consultations listed in a previously published study.⁴⁴ External healthcare environmental factors included location of residence, SEER region, and census-level data on number of hospitals offering oncology services, categorized as low (0–2) or high (≥ 3) based on the median value.

Statistical Analyses

Descriptive statistics were conducted to describe the study cohort. Chi-square tests were used to determine significant differences between the groups of women who received guideline-concordant treatment versus those who did not. A multivariable logistic regression with backward selection was performed to determine significant predictors of guideline-concordant treatment among women with HER2+ MBC, after controlling for all the independent variables.

Nonlinear Decomposition Technique

BC molecular subtype is a key determinant in choosing appropriate cancer treatment. The NCCN Guidelines for BC have taken HR and HER status into consideration in guiding cancer care.³³ In addition, from 2007 onward, ASCO recommended measuring HR status and HER2 expression for every primary invasive BC.⁴⁵ Studies among patients with MBC have shown disparities in guideline-concordant care by HR status.^{20,21} Compared with patients with HER2+ MBC and HR-positive status, those with HR-negative disease have worse survival⁴⁶ and hence typically require more aggressive treatment. In our study, the factors responsible for disparity in guideline-concordant care by HR status needed to be identified and quantified. Therefore, to examine the magnitude of disparities in guideline-concordant treatment by HR status and the extent to which independent variables explained these disparities, a postregression nonlinear decomposition technique was used.⁴⁷ In the report developed under contract from NCI,⁴⁸ decomposition analysis is one of the methods identified to measure cancer disparities. With the nonlinear decomposition technique, the individual contribution of independent variables that explain the disparity across groups can be identified by calculating the change in the predicted probability obtained from replacing one independent variable at a time for one group and keeping all the other variables constant for the other group. The differences in guideline-concordant treatment by HR status were

categorized into an explained portion and an unexplained portion. The explained portion provides disparities in guideline-concordant treatment by HR status that are caused by differences in the independent variables among the 2 groups. The unexplained portion provides disparities in treatment that could not be explained, either because of differences in the regression parameter estimates between the 2 groups or differences in unobservable and/or unmeasured determinants. Hence, the unexplained portion would remain even if the 2 groups had the same average levels of measured predictor variables. The explained portion of the gap is the sum of the differences between HR-positive and HR-negative women in terms of observed characteristics weighted by the pooled regression coefficients. It is calculated by multiplying the differences in the average characteristics between the 2 groups using pooled regression weights.

Analyses were conducted using SAS 9.4 (SAS Institute Inc). STATA, version 15.0 (StataCorp LLC) was used to perform nonlinear decomposition technique.

Results

Descriptive Characteristics

A total of 241 women aged ≥ 66 years at first HER2+ MBC diagnosis in January 2010 through December 2013 were included in the study (see Figure 1). Most were aged ≥ 75 years (54.7%), white (83.4%), and single, divorced, or widowed (74.3%), and had HR-positive tumors (65.6%), good PS (69.3%), and at least 1 comorbidity (63.9%) (Table 1).

Within the study cohort, 76.8% received guideline-concordant initial treatment and 23.2% did not. Women who received guideline-concordant treatment were significantly more likely to be aged 66 to 74 years, be married/partnered, reside in nonmetropolitan areas, have good PS, and have had more medical oncology visits. When treatment categories were examined among patients with HR-positive disease who received guideline-concordant treatment, 36.2% received endocrine therapy only, 18.1% received endocrine therapy and HER2-targeted therapy, 22.1% received HER2-targeted therapy with or without chemotherapy, and 23.6% received all 3 therapies during the initial 6-month period after cancer diagnosis. Among patients with HR-negative MBC who received guideline-concordant treatment, 79.3% received HER2-targeted therapy with chemotherapy, and 20.7% received HER2-targeted therapy only.

Predictors of Guideline-Concordant Treatment

After controlling for other predictive factors, women who were HR-positive were more than twice as likely to receive guideline-concordant treatment than those who were HR-negative (adjusted odds ratio [aOR], 2.234; 95% CI, 1.082–4.615) (Table 2). With 1-year increments

in age at cancer diagnosis, the likelihood of receiving guideline-concordant treatment reduced by 5% (aOR, 0.948; 95% CI, 0.902–0.996). Compared with women who had poor PS, those with good PS were significantly more likely to receive guideline-concordant treatment (aOR, 3.345; 95% CI, 1.634–6.849). Furthermore, women who had more medical oncology office visits were significantly more likely to receive guideline-concordant treatment (aOR, 8.076; 95% CI, 3.509–18.591) than those with fewer medical oncology office visits.

Factors Explaining Disparities in Guideline-Concordant Treatment by HR Status

There was a 10.5% difference in the proportion of women with HR-positive versus HR-negative status who received guideline-concordant treatment (Table 3). From the decomposition analysis, it was observed that of this difference, 2.0% was explained by the observed characteristics included in the study. Therefore, 19.0% of the disparity in guideline-concordant treatment between women with positive and negative HR status was explained by differences in these characteristics. Enabling factors explained the highest (22.8%) proportion of this disparity, followed by external healthcare environmental factors at 5.3%, need-related factors at 3.2%, and healthcare use at –9.7%. From the findings regarding enabling factors, it could be interpreted that if these factors were similar between women with positive and negative HR status, then the disparity in guideline-concordant treatment would decrease by 22.8%. The negative coefficient of healthcare use indicates that if medical oncology office visits for women with positive and negative HR status were similar, then the disparity would increase by 9.7%. Additionally, a large portion of the differences in guideline-concordant treatment by HR status remained unexplained (81.0%).

Discussion

The seminal report *Ensuring Quality of Cancer Care* published in 1990 by the Institute of Medicine identified the need for research on cancer health disparities to optimize cancer care.⁴⁹ Although this report created fervor, BC disparities still exist in the United States, which could be partly attributed to treatment disparities. Of several initiatives that have been designed to quantify and improve cancer care quality,^{50–52} a number of efforts have been targeted to non-MBC care.^{53–56} To the best of our knowledge, this study is the first of its kind to examine guideline-concordant treatment among elderly women with HER2+ MBC after controlling for a comprehensive list of confounders, including PS. In addition, we examined the extent to which predisposing, enabling, need-related, and external healthcare environmental factors and healthcare use explained disparities in guideline-concordant treatment by women's HR status.

Table 1. Patient Characteristics

Variables	Total Cohort n (%)	Guideline-Concordant Treatment n (%)	Non-Guideline-Concordant Treatment n (%)	P Value
Total	214 (100)	185 (76.8)	56 (23.2)	
Age at diagnosis, y				.0250
66–74	97 (45.3)	83 (85.6)	14 (14.4)	
75–79	56 (18.2)	41 (73.2)	15 (26.8)	
≥80	88 (36.5)	61 (69.3)	27 (30.7)	
Race/Ethnicity				.1290
White	201 (83.4)	158 (78.6)	43 (21.4)	
Other ^a	40 (16.6)	27 (67.5)	13 (32.5)	
Marital status				.0100
Married/Partnered	62 (25.7)	b	b	
Single/Divorced/Widowed	179 (74.3)	b	b	
Location of residence				.0500
Metropolitan	189 (78.4)	b	b	
Nonmetropolitan	52 (21.6)	b	b	
SEER region				.8050
Northeast	48 (19.9)	b	b	
South	76 (31.6)	b	b	
North Central	35 (14.5)	b	b	
West	82 (34.0)	b	b	
Census tract household income (\$USD)				.9990
≤\$50,000	99 (41.1)	76 (76.8)	23 (23.2)	
>\$50,000	142 (58.9)	109 (76.8)	33 (23.2)	
Census tract education				.6810
High (>27.1)	119 (49.4)	90 (75.6)	29 (24.4)	
Low (0–27.0)	122 (50.6)	95 (77.9)	27 (22.1)	
Hormone receptor status				.0670
Positive	158 (65.6)	127 (80.4)	31 (19.6)	
Negative	83 (34.4)	58 (69.9)	25 (30.1)	
Tumor grade				.4080
Well/Moderately differentiated	66 (27.4)	53 (80.3)	13 (19.7)	
Others	175 (72.6)	132 (75.4)	43 (24.6)	
Number of metastatic sites ^c				.1320
0–1	170 (70.5)	126 (74.1)	44 (25.9)	
2–4	71 (29.5)	59 (83.1)	12 (16.9)	
Performance status				.0004
Good	167 (69.3)	139 (83.2)	28 (16.8)	
Poor	74 (30.7)	46 (62.2)	28 (37.8)	
Comorbidity				.1810
0	87 (36.1)	71 (81.6)	16 (18.4)	
≥1	154 (63.9)	114 (74.0)	40 (26.0)	
Oncology visits				<.0001
0–18	122 (50.6)	b	b	
≥19	119 (49.4)	b	b	
Hospitals offering oncology services				.0250
0–2	122 (50.6)	101 (82.8)	21 (17.2)	
≥3	119 (49.4)	84 (70.6)	35 (29.4)	

^aIncludes African American, American Indian/Alaskan Native, Asian or Pacific Islander, other unspecified, or unknown.^bCells are suppressed because of small sample size that is in compliance with the SEER-Medicare data use agreement.^cMetastasis to brain, liver, lung, or bone.

Table 2. Predictors of Guideline-Concordant Care from the Logistic Regression^a

Variable	aOR	95% CI	P Value
Age at diagnosis	0.948	(0.902–0.996)	.0356
Marital status			
Married/Partnered	2.193	(0.846–5.681)	.1060
Single/Divorced/Widowed	Ref		
HR status			
Positive	2.234	(1.082–4.615)	.0298
Negative	Ref		
Performance status			
Good	3.345	(1.634–6.849)	.0009
Poor	Ref		
Oncology visits			
0–18	Ref		
≥19	8.076	(3.509–18.591)	<.0001

Abbreviation: aOR, adjusted odds ratio.

^aA multivariable logistic regression with backward selection was performed controlling for age at cancer diagnosis, race/ethnicity, marital status, location of residence, SEER region, census tract household income, census tract education, hormone receptor status, tumor grade, number of metastasis sites, performance status, comorbidity, oncology visits, and the number of hospitals offering oncology services. Findings from the fitted model are reported.

We found that 77% of elderly women with HER2+ MBC received guideline-concordant initial cancer treatment according to NCCN Guidelines, a marginally lower estimate than was reported earlier (80%).²⁰ However, our estimate was substantially higher than that reported in another study of HER2+ patients by Rocque et al²¹ (77% vs 44%). However, such inconsistency could be because of the way HER2+ status was determined in that study—because no HER2 status data were available before 2010, the authors categorized all women diagnosed before 2010 as an HER2-unknown group and considered them to be guideline-concordant if they received treatment for either HER2+ or HER2-negative MBC. A surprising finding was that nearly one-quarter of the study cohort did not receive initial cancer treatment according to recommended guidelines, thereby highlighting opportunities for improvement in the delivery of cancer care in older patients with cancer. The process of treatment decision-making in older patients with cancer is highly complex and multidimensional and comprises trade-offs resulting from increased risk of adverse events and functional decline after cancer treatment.⁵⁷ In addition, an array of considerations can influence treatment decision-making, including patient-, physician-, and health system-related factors. A comprehensive geriatric assessment of older patients with cancer prior to oncologic decision-making can help clinicians detect previously unidentified health problems and provide the foundation for a treatment regimen specific to the needs of the patient.⁵⁸

Among predisposing factors, age at cancer diagnosis was significantly associated with receipt of guideline-concordant treatment. Increasing age was a significant predictor of nonreceipt of guideline-concordant treatment in the multivariable analysis. This finding is similar to that reported earlier and may be attributed to several factors, including physician treatment choice and patient treatment preferences, which SEER-Medicare does not capture.²⁰ Because cancer treatment may affect patient morbidity and quality of life, physicians may be conservative in choosing aggressive cancer treatment for relatively older patients compared with their younger counterparts. Furthermore, although elderly women are underrepresented in clinical trials, several subgroup analyses from recent trials have shown a good safety profile for recent targeted therapies, including pertuzumab and trastuzumab emtansine for elderly patients.^{59–61} Hence, age alone should not be a contraindication for cancer treatment.

Among need-related factors, negative HR status and poor PS were significant predictors of nonreceipt of guideline-concordant treatment. Our finding regarding negative HR status, consistent with that reported previously,^{21,62} indicates divergence from recommended care for women with negative HR status. Given that patients with HR-negative disease have poorer prognosis with shorter survival¹⁹ and benefit less from cancer treatment⁴⁶ compared with those with positive HR status, physicians may be less likely to provide guideline-concordant treatment to these patients. Moreover, endocrine therapy, which has been the preferred first-line therapy for HR-positive disease, generally has fewer adverse effects and relatively more convenient routes of administration (eg, oral, intramuscular). Hence, patients with positive HR disease are more likely to receive guideline-concordant care than those with negative HR disease.

Additionally, our finding about PS could be attributed either to physicians selecting less-aggressive treatments for elderly patients with poor PS or to preferences of patients seeking to avoid aggressive treatments. Our finding was similar to what was reported by a non-US study among patients with HER2+ MBC,⁶³ thereby suggesting specific recommendations for this subgroup.

Nonlinear decomposition analysis showed that 19% of the disparity in guideline-concordant treatment between women with positive and negative HR status was explained by characteristics adjusted in the analyses. This method provides essential and crucial insights about guideline-concordant treatment in women with BC. Enabling factors, including marital status, household income, and education, accounted for the highest

Table 3. Nonlinear Decomposition of Guideline-Concordant Treatment by HR Status

Guideline-Concordant Treatment		
HR-positive disease	80.4%	
HR-negative disease	69.9%	
Difference	10.5%	
Total explained	2.0%	
Variable	% of Explained Difference	% Contribution to the Explained Portion
Predisposing factors (age at breast cancer diagnosis, race/ethnicity)	−2.6%	−13.7%
Enabling factors (marital status,* census tract median household income,** and education)	22.8%	119.9%
Need-related factors (tumor grade, comorbidity, performance status,** number of sites of cancer metastasis)	3.2%	17.0%
Healthcare use (medical oncology office visits*)	−9.7%	−51.0%
External healthcare environmental factors (location of residence, SEER region, hospitals offering oncology services)	5.3%	27.8%
Total difference explained	19.0%	100%
Total difference unexplained	81.0%	

Abbreviation: HR, hormone receptor.

*P value of <.20 was used because of a relatively smaller sample size of HR-negative versus HR-positive patients.

*P<.20; **P<.10.

proportion of explained disparities in the recommended treatment between women with HR-positive and HR-negative cancers. A higher proportion of HR-negative patients were unmarried/single/divorced and had lower socioeconomic status (SES) compared with HR-positive patients (data not shown in tabular form), which explained 23% of the disparity in guideline-concordant treatment. Our finding indicates that if women with negative HR status had the same marital and SES as those with positive HR status, then the disparity in guideline-concordant treatment would be reduced by almost 23%. Our findings thereby suggest opportunities to address cancer care for women with negative HR status.

To our knowledge, no study has used a decomposition technique to study treatment disparities in patients with BC, and hence it was difficult to compare our findings from decomposition analyses. However, our findings are interesting in the context of existing literature about social support and SES being associated with cancer treatment. Several studies have identified lack of social support^{20,64,65} and poorer SES^{62,64,66,67} as the most common barriers to treatment of BC. However, none of these studies focused specifically on women with HER2+ metastatic disease. Cancer treatment often requires the availability of family members to facilitate care. Lack of family, friends, or living children may serve to limit access to

cancer care. We did not anticipate identifying SES as a barrier to guideline-concordant treatment in women with negative HR status, because all women were covered by Medicare Parts A and B. However, the literature endorses that even insured patients with cancer can experience financial toxicity from substantial out-of-pocket expenses,⁶⁸ which may affect their receipt of recommended care.

A notable finding was that 81% of the difference in guideline-concordant treatment by HR status remained unexplained. It is likely that some portion of this difference could be attributed to severity of comorbid conditions, contraindications to cancer therapies, patient treatment preferences, propensity to seek care, physician treatment choice, and provider belief in the importance of guideline-concordance treatment, factors that are not captured in the SEER-Medicare database. The literature has also shown that several factors, including logistics of transportation and travel time to specialty physicians⁶⁹—also not captured by the SEER-Medicare database—may cause disparities in access to healthcare.

A few limitations are worth noting. Some patient-level variables, including annual household income, education level, and access to hospitals offering oncology services, are not available in the SEER-Medicare database, and therefore census tract information was used.⁷⁰ Data on severity of comorbidities and patient symptoms, which may affect the selection of cancer treatment, were

not captured. However, PS was determined using a claims-based algorithm and was controlled for in the analyses. The study findings are generalizable only to elderly patients with cancer enrolled in Medicare. It is likely that many patients who did not receive guideline-concordant care received hospice care, and hospice use was not examined in our study. Moreover, a considerable number of women were excluded from the study because of their enrollment in an HMO or because of noncontinuous enrollment in Medicare Parts A and B during the study period, which may have affected our study findings and hence generalizability of our findings to all elderly women diagnosed with HER2+ MBC. Lastly, because of a smaller sample size of HR-negative patients, we used $P < .20$ for decomposition analysis. Future studies with larger sample size of HER2+ MBC patients are needed to validate our study findings.

Conclusions

Almost one-quarter of the study cohort did not receive guideline-concordant treatment. Our data from

decomposition analysis suggest opportunities to address cancer care for elderly women with negative HR status.

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Guideline-Concordant Treatment Among Elderly Women With HER2-Positive Metastatic Breast Cancer in the United States

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eTable 1: Treatment Algorithms Based on NCCN Guidelines for HER2-Positive Metastatic Breast Cancer

eTable 1. Treatment Algorithms Based on NCCN Guidelines for HER2-Positive Metastatic Breast Cancer

HR-negative disease	<p>(a) HER2-targeted therapy + chemotherapy</p> <p>(i) Trastuzumab + taxane (docetaxel or paclitaxel) OR</p> <p>(ii) Pertuzumab + trastuzumab + taxane (docetaxel or paclitaxel) OR</p> <p>(iii) Trastuzumab + chemotherapy^a OR</p> <p>(iv) Other first-line therapies ([trastuzumab + paclitaxel ± carboplatin] OR [trastuzumab + vinorelbine] OR [trastuzumab + capecitabine]) OR</p> <p>(b) Trastuzumab only</p>
HR-positive disease	<p>(a) Aromatase inhibitors (anastrozole OR letrozole OR exemestane) OR</p> <p>(b) Selective endocrine receptor modulators (tamoxifen OR toremifene) OR</p> <p>(c) Selective endocrine receptor downregulator (fulvestrant) OR</p> <p>(d) Other endocrine therapy (megestrol acetate OR fluoxymesterone OR ethinyl estradiol) OR</p> <p>(e) Trastuzumab only OR</p> <p>(f) HER2-targeted therapy + chemotherapy</p> <p>(i) Trastuzumab + taxane (docetaxel or paclitaxel) OR</p> <p>(ii) Pertuzumab + trastuzumab + taxane (docetaxel or paclitaxel) OR</p> <p>(iii) Trastuzumab + chemotherapy^a OR</p> <p>(iv) Other therapies ([trastuzumab + paclitaxel + carboplatin] OR [trastuzumab + vinorelbine] OR [trastuzumab + capecitabine])</p>

^aThese included other chemotherapy agents for which claims were found: doxorubicin, gemcitabine, cyclophosphamide, fluorouracil.