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Investigating Associations Between Health-Related Quality of Life and Endocrine Therapy Underuse in Women With Early-Stage Breast Cancer

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QUESTION ASKED: Does health-related quality of life (HRQOL) during active treatment predict whether women with hormone receptor–positive breast cancer underuse adjuvant endocrine therapy?

SUMMARY ANSWER: Our findings suggest that HRQOL measured soon after an early-stage breast cancer diagnosis can be used to identify women with hormone receptor–positive disease who may not initiate or adhere to endocrine therapy during survivorship.

WHAT WE DID: We used the Carolina Breast Cancer Study (CBCS), a large, population-based data set of women age 20 to 74 years with stage I to III hormone receptor–positive breast cancer in North Carolina. Underuse was defined as not initiating or adhering to endocrine therapy. HRQOL was self-reported by the Functional Assessment of Cancer Therapy for Breast Cancer (FACT-B) and Functional Assessment for Chronic Illness Therapy for Spiritual Well-Being (FACIT-SP), on average, 5 months after an invasive breast cancer diagnosis. FACT-B and FACIT-SP domains were used to construct subgroups using latent profile analysis, and the association between the HRQOL subgroups and underuse was examined using multivariable logistic regression models.

WHAT WE FOUND: Women with poor HRQOL during active treatment for hormone receptor–positive breast cancer may be at increased risk for underuse of endocrine therapy. Specifically, women who did not receive chemotherapy and reported poor HRQOL were five times less likely to initiate endocrine therapy. Membership in either of the two poorest HRQOL subgroups was statistically significantly associated with nonadherence to endocrine therapy. This association was observed in both non-Hispanic white and non-Hispanic black women as well as in both chemotherapy and nonchemotherapy users.

BIAS, CONFOUNDING FACTOR(S), DRAWBACKS: Although CBCS is a large cohort with broader inferences than a hospital- or clinic-based sample, only women with stage I to III breast cancer living in North Carolina who were non-Hispanic white or black were included in this study. As such, we are unable to generalize our findings to women with distant-stage breast cancer, those in other states, and those of other race or ethnicities. In addition, because endocrine therapy adherence was self-reported, we were unable to confirm the reliability of the adherence data.

REAL-LIFE IMPLICATIONS: HRQOL is modifiable and can be addressed early in the breast cancer care continuum to help reduce the risk of endocrine therapy underuse. Using self-reported HRQOL as a potential indicator for inappropriate endocrine therapy use is inexpensive and easy to do with validated HRQOL instruments, making these findings particularly appealing. This work informs and supports future interventions that aim to improve endocrine therapy initiation, adherence, and breast cancer recurrence.

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Abstract

Purpose

Endocrine therapy (ET) underuse puts women at increased risk for breast cancer (BC) recurrence. Our objective was to determine if health-related quality of life (HRQOL) subgroups were associated with underuse.

Methods

Data came from the third phase of the Carolina Breast Cancer Study. We included 1,599 women with hormone receptor–positive BC age 20 to 74 years. HRQOL was measured, on average, 5 months postdiagnosis. Subgroups were derived using latent profile (LP) analysis. Underuse was defined as not initiating or adhering to ET by 36 months postdiagnosis. Multivariable logistic regression models estimated adjusted odds ratios (ORs) between HRQOL LPs and underuse. The best HRQOL LP was the reference. Chemotherapy- and race-stratified models were estimated, separately.

Results

Initiation analyses included 953 women who had not begun ET by their 5-month survey. Of these, 154 never initiated ET. Adherence analyses included 1,114 ET initiators, of whom 211 were nonadherent. HRQOL was not significantly associated with noninitiation, except among nonchemotherapy users, with membership in the poorest LP associated with increased odds of noninitiation (adjusted OR, 5.5; 95% CI, 1.7 to 17.4). Membership in the poorest LPs was associated with nonadherence (LP1: adjusted OR, 2.2; 95% CI, 1.2 to 4.0 and LP2: adjusted OR,1.9; 95% CI, 1.1 to 3.6). Membership in the poorest LP was associated with nonadherence among nonchemotherapy users (adjusted OR, 2.1; 95% CI, 1.2 to 5.1).

Conclusion

Our results suggest women with poor HRQOL during active treatment may be at increased risk for ET underuse. Focusing on HRQOL, a modifiable factor, may improve targeting of future interventions early in the BC continuum to improve ET initiation and adherence and prevent BC recurrence.

ASSOCIATED CONTENT

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INTRODUCTION

Breast cancer (BC) is a heterogeneous disease with several tumor subtypes, each of which respond differently to treatment.[1] Hormone receptor (HR) –positive subtypes account for 80% of BCs and include tumors expressing receptors for estrogen or progesterone hormones.[1-3] After primary local treatment, sustained targeted therapy against HRs using endocrine therapy (ET) improves the prognosis of patients with these tumors significantly.[1-4] ET, indicated for nearly all HR-positive BCs, is recommended as a daily pill for 5 years after primary BC treatments.[4-6]

ET is a highly effective adjuvant treatment associated with a 40% reduction in BC recurrence and 30% reduction in BC-related mortality.[7-12] Despite its clinical benefits, 10% to 30% of HR-positive women never initiate therapy, and among those who do, 50% are nonadherent by 5 years.[8-12] Underuse is concerning, because women who are inconsistent in medication use or discontinue ET before 5 years do not realize full benefits.[7,12,13] Specifically, women who underuse ET have worse BC outcomes (ie, BC recurrence and survival) compared with women who adhere to ET for 5 years.[5,13]

ET is associated with adverse effects and poor health-related quality of life (HRQOL).[14-16] Because poor HRQOL after diagnosis may persist after primary treatment, HRQOL may interfere with adjuvant treatment decisions.[17,18] Poorly managed HRQOL during active treatment may contribute to underuse, because poor HRQOL can hinder a woman's ability to cope with the adverse effects of ET as she attempts to acclimate to life after primary BC treatment.[6,13,18-21] In this study, we operationalized underuse as not initiating or not adhering to ET.[22]

Although studies have collected data on poor HRQOL while women receive ET, to our knowledge, no studies have examined associations between ET initiation and HRQOL before initiation. Some work has evaluated relationships between HRQOL and nonadherence and nonpersistence, but results have been mixed, with some studies reporting no associations and others reporting that poor HRQOL is associated with nonadherence.[18,23,24] Findings from one recent study indicated that worse psychosocial HRQOL and greater patient distress were predictive of ET nonpersistence.[24]

Evidence from previous work should be interpreted with caution, because many studies used post-ET initiation HRQOL assessments, which may be confounded by ET adverse effects, and few used BC-specific HRQOL instruments.[18,21] In addition, all studies were carried out in small cohorts of predominantly non-Hispanic white women.[14,18,23,24] The objectives of our study were to examine associations between pre-ET HRQOL and noninitiation as well as HRQOL during active treatment and nonadherence in a large, racially and socioeconomically diverse, population-based cohort of women with BC. Identifying associations between HRQOL, a modifiable factor, and inappropriate ET use offers opportunities for future interventions to reduce underuse, thus improving BC outcomes among HR-positive women.

METHODS

Data

A total of 3,000 women diagnosed with invasive BC between 2008 and 2013 in North Carolina were enrolled in the third phase of the Carolina Breast Cancer Study (CBCS-III)[25,26]; 50% of the sample was black, and 50% of women were older than 50 years.[27] CBCS-III represented women across 44 counties with private, public, or no insurance and with varying education and income levels.[25,27] Four data sources were combined for this study: CBCS-III baseline (5-month survey), medical record abstraction, pathology reports, and follow-up (25-month survey).[27] Demographics, lifestyle, and HRQOL were collected in person at a median postdiagnosis time of 5.2 months (range, 1.8 to 8.9 months).[25,28] Women completed a follow-up survey at a median of 25.1 months postdiagnosis (range, 20 to 36 months), which included adherence questions. Medical record abstraction and pathology report data included comorbidities, treatments, and tumor characteristics.[27] The institutional review board at the University of North Carolina at Chapel Hill approved our study.

Participants

Of the 2,998 women enrolled in CBCS, we excluded women who: did not complete adherence questions (6%), were identified as "other race" or Hispanic (3%), had distant-stage BC or no surgery (3%), or completed their first survey > 9 months postdiagnosis (5%). Limited representations of other races and Hispanics precluded us from making inferences about these groups. Our cohort was further restricted to women with HR-positive BC to ensure ET eligibility (n = 1,599). Two separate cohorts were used for initiation and adherence analyses. ET initiation analyses were limited to 953 women who did not initiate ET before their 5-month survey. Of the 1,599 women, adherence analyses were limited to 1,114 women who initiated ET and completed adherence questions.

Outcomes

Primary study outcomes were: whether a woman initiated ET and whether she adhered to ET as reported in the 25-month survey. Noninitiation was a binary variable obtained from medical records. Nonadherence was categorized as a binary variable from two self-reported questions on the 25-month survey: "At this time, are you taking hormonal therapy pills?" and "Over the past 2 weeks, how many days did you miss your hormonal pills?" Response options for the first question were: "Yes, I am taking them exactly as prescribed by my doctor," "Yes, I'm taking them, but not every day," and "No, I stopped taking those pills." If a woman responded she was taking pills as prescribed, she was considered adherent, and if she responded that she had stopped taking pills, she was considered nonadherent. Among women who reported not taking ET pills every day, self-reported pill consumption in the past 2 weeks from a modified Morisky questionnaire was used to determine adherence. Those who missed $\leq$ 2 days in the last 2 weeks were considered adherent ($>$ 80%), and those who reported missing $\geq$ 3 days in the last 2 weeks were considered nonadherent ($<$ 80%).[7] Women who were nonadherent or who discontinued treatment were grouped as nonadherent for analyses.

HRQOL Instruments

HRQOL was measured using the Functional Assessment of Cancer Therapy for BC (FACT-B) and Functional Assessment of Chronic Illness Therapy for Spiritual Well-Being (FACIT-SP). The FACT-B is BC specific and includes physical, social, emotional and functional well-being, and BC-specific concerns.[29] The FACIT-SP measures spiritual well-being.[30] FACT-B and FACIT-SP domains were assumed to be continuous, with higher scores representing better HRQOL.[27]

Key Independent Variable

The primary explanatory HRQOL variable had four levels and was derived using a cluster-based modeling approach: latent profile (LP) analysis.[31] LP analysis used FACT-B and FACIT-SP domains from the 5-month survey to identify four LPs of women who experienced distinct HRQOL patterns.

Covariates

Self-reported demographic and lifestyle covariates were: age at diagnosis, race (non-Hispanic black or non-Hispanic white), smoking status, marital status, education, and insurance at 5 months. Comorbid conditions (eg, diabetes, chronic obstructive pulmonary disease, obesity, hypertension, and heart disease) from the medical records were included. Tumor stage and grade; surgery type; and receipt of radiotherapy, chemotherapy, and trastuzumab (Herceptin; Genentech, South San Francisco, CA) were included in models.

Statistical Analyses

Unadjusted comparisons of demographic, comorbidity, tumor, and treatment characteristics across women in the four HRQOL LPs were performed using χ^2 tests. Because women who initiated ET by 5 months might have differed from women who initiated after 5 monthis (ie, earlier stage of disease, better access to care), characteristics of those who initiated before and after 5 months were compared. In sensitivity analyses, unadjusted and adjusted HRQOL scores between women with HR-positive and HR-negative BC and between women who initiated ET before or after 5 months were examined.

Multivariable logistic regression was used to estimate adjusted odds ratios (ORs) and 95% CIs between 5-month HRQOL LPs and the likelihood of not initiating or adhering to ET, separately. The best HRQOL LP (LP4) was set as the reference group. Because race and chemotherapy may be effect-measure modifiers of associations between HRQOL and ET use, race- and chemotherapy-stratified models were estimated for noninitiation and nonadherence outcomes, separately. In sensitivity analyses, associations were examined between continuous, rather than categorical, 5-month HRQOL measures and (1) noninitiation and (2) nonadherence. As a final sensitivity analysis, nonadherence models were stratified by whether women initiated ET by their 5-month survey to determine if associations between HRQOL and nonadherence varied by initiation timing. Analyses were performed using SAS software (version 9.3; SAS Institute, Cary, NC), with two-sided statistical tests and significance of 5%.

RESULTS

5-Month HRQOL LPs

LP1 had the poorest HRQOL across all domains, and LP4 reported the best HRQOL scores across domains (Fig 1). LP2 had physical and functional scores similar to those of LP1, but LP2 had higher social and spiritual well-being scores. LP3 was similar to LP4, but spiritual and social well-being scores were lower than those of LP2.

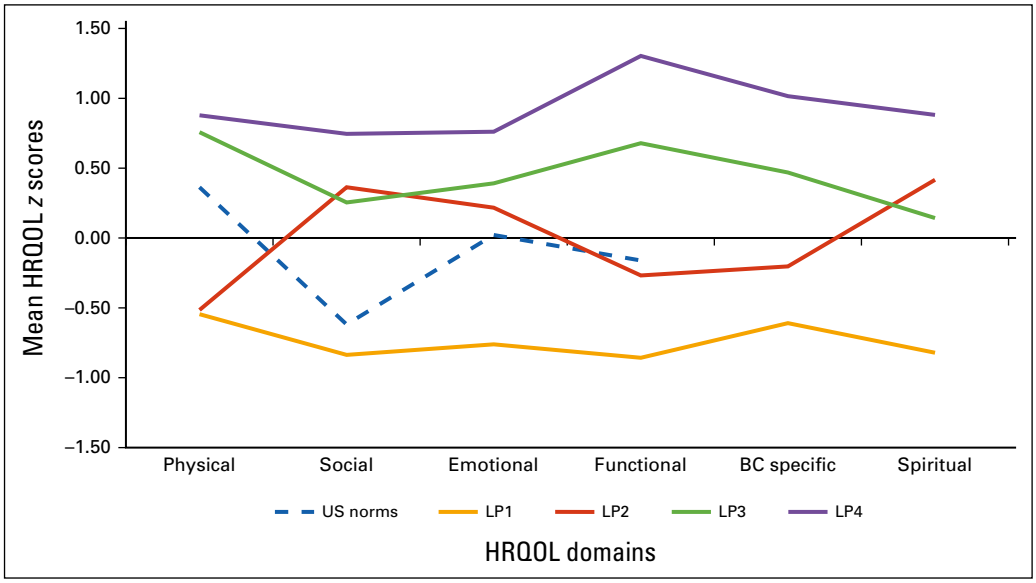

Fig 1. Mean 5-month health-related quality of life (HRQOL) scores by latent profile (LP) compared with US norms. Mean HRQOL scores were converted to *z* scores. Normed US scores are only available for physical, social, functional, and emotional Functional Assessment of Cancer Therapy for Breast Cancer domains; Data adapted.[32]

Participant Characteristics

Characteristics of the 1,599 HR-positive women stratified by the four HRQOL LPs are listed in Table 1. Fifty-seven percent of women were in the two lowest LPs. Overall, women in poorer LPs (ie, LP1 and LP2) were more likely to be young, black, unmarried, and obese; have no insurance; have stage II to III BC; and have received chemotherapy or trastuzumab. There were patient-level differences between the two lowest LPs but few differences between the two highest LPs. Compared with those in LP2, women in LP1 were more likely to be educated, unmarried, and without insurance and have earlier-stage BC and less likely to have received chemotherapy. Overall, women in LP1 received less aggressive BC treatments than those in LP2. Women in the two highest LPs (LP3 and LP4) had similar demographic, tumor, and treatment characteristics. LP3 and LP4 varied by race, with LP3 having a larger proportion of whites.

ET Use

Among the 953 women who had not yet initiated ET at their 5-month survey, 16% never initiated ET. Among the 1,114 women who initiated ET according to their medical records, 19% were considered nonadherent. Factors associated with noninitiation and nonadherence included younger age, black race, higher education, public (*v* private) insurance, breast-conserving surgery (*v* mastectomy), and not receiving chemotherapy or radiotherapy.

HRQOL and ET Initiation

In adjusted and unadjusted analyses, among women who had not initiated ET at their 5-month survey, there were no significant associations between HRQOL LPs and noninitiation (Table 2). Among nonchemotherapy users, LP1 membership was significantly associated with increased adjusted odds of noninitiation (adjusted OR, 5.5; 95% CI, 1.7 to 17.4; Appendix Table A1, online only). We found no significant adjusted associations among chemotherapy users or for blacks and whites (Appendix Table A1).

HRQOL and ET Adherence

Among women who initiated ET, membership in poorer HRQOL LPs (LP1 and LP2) was significantly associated with increased likelihood of nonadherence (unadjusted OR, 2.4; 95% CI, 1.3 to 4.2 and OR, 2.0; 95% CI, 1.1 to 3.6; Table 2). After adjustment, ORs attenuated (LP1: adjusted OR, 2.2; 95% CI, 1.2 to 4.0; LP2: adjusted OR, 1.9; 95% CI, 1.1 to 3.6). Although not statistically significant, LP3 was associated with an elevated likelihood of nonadherence (adjusted OR, 1.5; 95% CI, 0.8 to 2.8).

Associations between LPs and nonadherence were not statistically significant among chemotherapy users, but among nonusers, membership in the poorest LP was associated with increased adjusted odds of nonadherence (adjusted OR, 2.1; 95% CI, 1.2 to 5.1; Appendix Table A1). Among blacks,

Table 1. Cohort Characteristics by 5-Month HRQOL LPs

Characteristic	LP1 (n = 503) No.	%	LP2 (n = 412) No.	%	LP3 (n = 483) No.	%	LP4 (n = 201) No.	%	*P*
Age at diagnosis, years									< .001*
< 35	22	4	11	3	15	3	4	2	
35-50	238	47	190	46	171	35	63	31	
50-64	167	33	137	33	181	37	75	37	
≥ 65	76	15	74	18	116	24	59	29	
Race									< .001*
Non-Hispanic white	263	52	207	50	330	68	109	54	
Non-Hispanic black	240	48	205	50	153	32	92	46	
Smoking status									< .001*
Never	237	47	227	55	265	55	122	61	
Former	143	28	112	27	149	31	60	30	
Current	123	24	73	18	69	14	19	9	
Marital status									< .001*
Not married	262	52	165	40	158	33	64	32	
Married or partnered	241	48	247	60	325	67	137	68	
Education level									< .001*
< HS	61	12	23	6	27	6	13	6	
HS and post-HS	241	48	235	57	201	42	115	57	
≥ College	291	58	154	37	255	53	73	36	
Insurance status									< .001*
None	48	10	12	3	16	3	3	1	
Private	304	60	301	73	387	80	160	80	
Public	151	30	99	24	80	17	38	19	
Diabetes	78	16	68	17	55	11	31	15	.1295
COPD	18	4	12	3	9	2	0	0	.0316†
Heart disease	28	6	29	7	21	4	7	3	.1923
Obesity	251	50	219	53	187	39	89	44	< .001*
Hypertension	237	47	190	46	186	39	99	49	.0135†
Surgery									.0058‡
Not specified	5	1	3	1	0	0	1	0	
Lumpectomy	327	65	247	60	334	69	148	74	
Mastectomy	171	34	162	39	149	31	52	26	
Chemotherapy	303	60	293	71	173	36	75	37	< .001*
Radiotherapy	363	72	290	70	340	70	150	75	.6563
Trastuzumab	75	15	72	17	37	8	12	6	< .001*
Tumor stage									
I	228	45	154	37	294	61	125	62	< .001*
II	208	41	188	46	157	33	62	31	
III	67	13	70	17	32	7	14	7	

(continued on following page)

Table 1. Cohort Characteristics by 5-Month HRQOL LPs (continued)

Characteristic	LP1 (n = 503) No.	%	LP2 (n = 412) No.	%	LP3 (n = 483) No.	%	LP4 (n = 201) No.	%	*P*
Tumor grade									< .001*
Well differentiated	127	25	75	18	162	34	55	27	
Moderately differentiated	221	44	184	45	233	48	96	48	
Poorly differentiated or unknown	155	31	153	37	88	18	50	25	

NOTE. LP1 represented the worst HRQOL profile, relatively, and LP4 represented the best HRQOL profile, relatively.
Abbreviations: COPD, chronic obstructive pulmonary disease; HRQOL, health-related quality of life; HS, high school; LP, latent profile.
*Statistical significance: $P < .001$.
†Statistical significance: $P < .05$.
‡Statistical significance: $P < .01$.

membership in the second-lowest LP was associated with nonadherence (adjusted OR, 2.5; 95% CI, 1.1 to 6.1), but for whites, membership in LP1 was associated with nonadherence (adjusted OR, 2.4; 95% CI, 1.1 to 5.6; Appendix Table A1, online only).

Sensitivity Analyses

In unadjusted analyses using continuous, rather than categorical, HRQOL scores as predictors, we observed associations between better HRQOL and increased likelihood of noninitiation, but in multivariable models, associations became small and nonstatistically significant. In unadjusted models, better continuous HRQOL was associated with lower likelihood of nonadherence, but in multivariable analyses, continuous HRQOL was not associated with nonadherence.

Table 2. Unadjusted and Adjusted Associations Between 5-Month HRQOL LPs and ET Noninitiation and Nonadherence

	ET Noninitiation				ET Nonadherence			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
LP*	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
LP1	1.1	0.6 to 1.9	1.9	0.9 to 4.2	2.4	1.3 to 4.2†	2.2	1.2 to 4.0†
LP2	0.8	0.4 to 1.5	1.4	0.7 to 3.1	2.0	1.1 to 3.6†	1.9	1.1 to 3.6†
LP3	1.5	0.8 to 2.8	2.1	0.9 to 4.4	1.6	0.9 to 3.0	1.7	0.9 to 3.1

NOTE. Adjusted models include all covariates listed in Table 1.
Abbreviation: ET, endocrine therapy; HRQOL, health-related quality of life; LP, latent profile; OR, odds ratio.
*LP4 was the reference category for analyses.
†Denotes statistical significance at the .05 level.

There were 646 women who initiated ET before (early initiators) and 804 who initiated ET after their 5-month survey (late initiators). Compared with late initiators, early initiators had better HRQOL scores across domains, with differences ranging from 1 to 4 points per domain. In multivariable models, differences dropped to < 1 point and became nonstatistically significant.

Results from multivariable nonadherence analyses were similar when stratified by early and late initiators. The magnitude of associations between poor LPs and nonadherence was greater for early initiators (LP1: adjusted OR, 4.1; 95% CI, 1.1 to 8.8 and LP2: adjusted OR, 3.1; 95% CI, 1.4 to 11.9) compared with late initiators (LP1: adjusted OR, 1.8; 95% CI, 1.2 to 3.9 and LP2: adjusted OR, 1.3; 95% CI, 1.1 to 3.0). Regardless of initiation timing, compared with the best HRQOL LP, membership in the two poorest LPs was associated with nonadherence.

DISCUSSION

To our knowledge, this is the first study to examine associations between HRQOL and ET underuse in a large, population-based, multipayer HR-positive BC cohort. Although we did not observe statistically significant associations between pre-ET HRQOL and noninitiation, adjusted ORs for LP1 to LP3 were 1.9, 1.4, and 2.1, respectively, suggesting a trend toward association between poor HRQOL and noninitiation. We observed significant associations between worse HRQOL during active treatment and nonadherence, with adjusted ORs ranging from 1.7 to 2.2.

Studies have demonstrated associations between social and provider support and ET use in BC.[33] Greater support is

associated with increased adherence.[33,34] Associations with social support are consistent with our results, because the two lowest LPs (most associated with underuse) had higher percentages of unmarried women. Provider support is important because when patients feel supported and empowered to make treatment decisions in line with personal preferences, they are more likely to adhere to therapies.[34,35] Provider support might help manage HRQOL during active treatment. One study reported that although older age at diagnosis and adverse effects were unadjusted predictors of nonadherence, once demographic, treatment, and tumor characteristics were included, only social support and patient-centered care measures (ie, patient role in decision making) remained associated with nonadherence.[35]

Chemotherapy moderated associations between HRQOL and underuse. Women who receive chemotherapy have worse HRQOL than women who do not.[16,36,-37] Chemotherapy is associated with body image concerns, fear of recurrence, and worse sexual functioning among women with BC.[16,37,38] In this study, among nonchemotherapy users, poor HRQOL was significantly associated with noninitiation and nonadherence. Women undergoing chemotherapy may attribute poor HRQOL to the aggressive treatment, whereas women not receiving chemotherapy may associate poor HRQOL with ET, making them more likely to not adhere. In addition, chemotherapy adverse effects may dissipate over time, enabling women to deal better with ET-related difficulties than those whose initial HRQOL was poor for other reasons. Alternatively, women who experienced severe chemotherapy adverse effects may view problems encountered with ET as relatively tolerable. HRQOL may be a useful screener for underuse among women who do not receive chemotherapy. More research is needed to disentangle possible explanations for our findings.

Associations between HRQOL and nonadherence were modified by race. Among whites, membership in the poorest LP was significantly associated with nonadherence, but membership in the second-poorest LP was associated with nonadherence for blacks. Women in LP1 and LP2 reported poor physical and functional scores, but social and spiritual well-being were better in LP2. Low physical and functional scores in both groups suggest these domains should be prioritized in clinical care, because they are potentially associated with increased likelihood of nonadherence. Moreover, previous studies indicate black women with BC consistently report the importance of spirituality, including religious community support, in coping with their disease.[39-43] Some studies have documented associations between greater spirituality and lower likelihood of receiving recommended care (eg, medication adherence, end-of-life care), which may partially explain our observed association between membership in LP2 (higher spiritual HRQOL) and nonadherence among blacks.[44,45] A possible explanation for this association that has been described in the literature is that spirituality and religious community affiliation may be linked to a belief in miraculous healing, which may influence treatment decisions that are not necessarily in line with clinical recommendations.[45] When black women in LP2 experience poor physical and functional HRQOL, they may rely even more on religious communities for support. As such, identifying better ways to manage HRQOL (especially physical and functional), including culturally sensitive approaches that integrate spiritual support in the clinical setting (eg, having religious leaders serve as lay health advisors), may help increase the likelihood of ET adherence in both white and black women with BC.

Non-Hispanic white and black women residing in North Carolina were included in this study, limiting generalizability to women in other states and of other races or ethnicities. However, CBCS-III is a large cohort, which provides broader inference, with a population-based sample as opposed to a hospital- or clinic-based sample. In addition, women who initiated ET by 5 months were excluded from initiation analyses. We conducted sensitivity analyses to determine if these women differed in HRQOL and found that once patient characteristics were accounted for, no significant HRQOL differences between women who initiated ET before or after 5 months existed. Women who initiated ET by their 5-month survey were included in adherence analyses. Because ET may negatively affect HRQOL, including these women could potentially have confounded associations between HRQOL and nonadherence. Therefore, sensitivity analyses were conducted including stratifying models by whether a woman initiated before or after her 5-month survey. Because results were similar, all HR-positive women were included in adherence analyses to increase generalizability of results to women with HR-positive BC. Finally, because ET adherence was self-reported, reliability of adherence data was not confirmed.

In conclusion, our findings suggest HRQOL measured soon after diagnosis can be used to identify women who may not initiate or adhere to ET during survivorship. HRQOL is modifiable and can be addressed early in the BC continuum to help reduce underuse. Women with poor HRQOL during

active treatment should receive targeted HRQOL support to reduce the risk of inappropriate adjuvant treatment decisions.[46,47] Those experiencing poor physical and functional well-being may be at greater risk for underuse, because lower scores in these domains were most associated with underuse. Furthermore, BC subgroups such as nonchemotherapy users and blacks may especially benefit from additional physical and functional HRQOL management. Because blacks present with more aggressive BC subtypes at younger ages and report worse physical and functional HRQOL, they might be more susceptible to underuse.[1,48-54] Reducing ET underuse among black women may offer an opportunity to help reduce racial disparities in BC outcomes. Using self-reported HRQOL as a potential indicator for inappropriate ET use is inexpensive and easy to do with validated HRQOL instruments, making these findings particularly appealing. Women most vulnerable to underuse should be identified early in the BC continuum and provided ongoing HRQOL management to support ET use and improve BC outcomes.[12,55]

Authors' Disclosures of Potential Conflicts of Interest

Disclosures provided by the authors are available with this article at jop.ascopubs.org.

Author Contributions

Conception and design: All authors
Financial support: Andrew F. Olshan
Provision of study materials or patients: Andrew F. Olshan
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Appendix

Table A1. Adjusted Associations Between 5-Month HRQOL LPs and ET Noninitiation and Nonadherence Stratified by Chemotherapy and Race

	ET Noninitiation		ET Nonadherence	
Cohort	**OR**	**95% CI**	**OR**	**95% CI**
Black women only*				
LP1	1.3	0.5 to 3.8	1.9	0.8 to 4.6
LP2	1.2	0.4 to 3.6	2.5	1.1 to 6.1†
LP3	1.6	0.5 to 4.7	1.8	0.8 to 4.5
White women only*				
LP1	2.6	0.8 to 8.1	2.4	1.1 to 5.6†
LP2	1.4	0.4 to 4.7	1.4	0.6 to 3.5
LP3	2.1	0.7 to 6.6	1.4	0.6 to 3.3
Chemotherapy users*				
LP1	1.1	0.3 to 3.2	1.8	0.7 to 4.4
LP2	1.4	0.4 to 4.5	1.5	0.6 to 3.7
LP3	1.4	0.4 to 4.9	1.3	0.5 to 3.4
Nonchemotherapy users*				
LP1	5.5	1.7 to 17.4‡	2.1	1.2 to 5.1†
LP2	1.0	0.3 to 3.2	2.0	0.8 to 5.1
LP3	2.8	0.9 to 7.9	1.8	0.8 to 3.9

NOTE. Adjusted models include all covariates listed in Table 1.

Abbreviations: ET, endocrine therapy; HRQOL, health-related quality of life; LP, latent profile; OR, odds ratio.

*LP4 was the reference category for analyses.

†Denotes statistical significance at the .05 level.

‡$P < .0001$.