Breast Cancer Res Treat (2016) 157:133–143
DOI 10.1007/s10549-016-3788-x

EPIDEMIOLOGY

Psychosocial factors related to non-persistence with adjuvant endocrine therapy among women with breast cancer: the Breast Cancer Quality of Care Study (BQUAL)

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Received: 25 January 2016 / Accepted: 5 April 2016 / Published online: 16 April 2016

Abstract Non-adherence to adjuvant endocrine therapy (ET) for breast cancer (BC) is common. Our goal was to determine the associations between psychosocial factors and ET non-persistence. We recruited women with BC receiving care in an integrated healthcare system between 2006 and 2010. Using a subset of patients treated with ET, we investigated factors related to ET non-persistence (discontinuation) based on pharmacy records (≥90 days gap). Serial interviews were conducted at baseline and every 6 months. The Functional Assessment of Cancer Therapy (FACT), Medical Outcomes Survey, Treatment Satisfaction Questionnaire (TSQM), Impact of Events Scale (IES), Interpersonal Processes of Care measure, and Decision-making beliefs and concerns were measured. Multivariate models assessed factors associated with non-persistence. Of the 523 women in our final cohort who initiated ET and had a subsequent evaluation, 94 (18 %) were non-persistent over a 2-year follow-up. The cohort was primarily white (74.4 %), stage 1 (60.6 %), and on an aromatase inhibitor (68.1 %). Women in the highest income category had a lower odds of being non-persistent (OR 0.43, 95 % CI 0.23–0.81). Quality of life and attitudes toward ET at baseline were associated with non-persistence. At follow-up, the FACT, TSQM, and IES were associated with non-persistence ($p < 0.001$). Most women continued ET. Women who reported a better attitude toward ET, better quality of life, and more treatment satisfaction, were less likely to be non-persistent and those who reported intrusive/avoidant thoughts were more likely to be non-persistent. Interventions to enhance the psychosocial well-being of patients should be evaluated to increase adherence.

Keywords Breast cancer · Adherence · Quality of life · Psychosocial factors

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Background

Adjuvant endocrine therapy (ET) is the standard of care for all women with hormone receptor positive breast cancer [1]. Endocrine therapy reduces the rates of mortality, local recurrence, and new primary breast cancers [2–8]. Studies suggest that patients may benefit from 10 years as opposed to 5 years of therapy [9, 10]. Despite these benefits, substantial variations occur in women's use of these therapies [11–13]. Some patients fail to initiate recommended therapy [12], delay initiation [14], or discontinue therapy early [11, 15, 16]. Any deviation from recommended adjuvant therapy may reduce its survival benefit [17]. Understanding the factors associated with treatment, non-persistence and discontinuation may help us to develop interventions to improve adherence to endocrine therapy [18].

Our group and others have studied the demographic, clinical, and financial factors associated with discontinuation of ET [11, 16, 19, 20]. However, many of these studies relied on large administrative databases that are often required to measure adherence. In addition, most of the prior studies on this topic did not include patient-reported outcome measures, or information about psychosocial factors and patient preferences.

The Breast Cancer Quality of Care Study (BQUAL) is a prospective cohort study of factors associated with suboptimal use of adjuvant chemotherapy and ET in women with early-stage breast cancer. We have previously shown that the perception of poor physician–patient communication, negative beliefs regarding efficacy of the medication, and fear of toxicities are associated with failure to initiate hormone therapy [12]. We now present data on the associations of demographic and clinical factors, psychosocial factors, quality of life, and patient treatment satisfaction with the risk of ET non-persistence among women who had initiated it.

Methods

Details of the BQUAL study have been described elsewhere [21]. Briefly, between 2006 and 2010, women >20 years of age with newly diagnosed, histologically confirmed, primary breast cancer, stages I–III, were recruited from three sites [Columbia University Medical Center and Mount Sinai School of Medicine (CUMC/MSSM) in New York City, Kaiser-Permanente of Northern California (KPNC), and Henry Ford Health System (HFHS)]. Complete pharmacy records were only available from KPNC, and therefore the current study is limited to patients enrolled at that site. All interviews were conducted over the telephone. Women who were non-English speaking, had less than 100 days of follow-up, had a prior history of cancer, or had no access to a telephone were excluded.

All participants were enrolled within 12 weeks of diagnosis. Baseline interviews were completed at or shortly after diagnosis. For women on hormone therapy, follow-up interviews were conducted every 6 months for the first 2 years, and annually thereafter until conclusion of the study.

For this analysis, we included patients who were confirmed to have hormone receptor positive disease on pathology report, who had at least two prescriptions for ET in the electronic pharmacy database, and who completed a baseline interview ($n = 605$). We excluded women with Stage IV breast cancer ($n = 2$), women who recurred/disenrolled/died within 2 years ($n = 23$), those who took their first and last ET prior to the baseline interview ($n = 23$), and subjects who had no interview after initiation of ET ($n = 18$). To ensure uniformity with timing, the patient-reported measures were analyzed from the first questionnaire administered after ET initiation.

The primary outcome measure was ET non-persistence based on electronic pharmacy records obtained through the first 24 months after initiation. Non-persistence was defined as a ≥90-day gap following the date of anticipated completion of any ET prescription (date of prescription + days of pills prescribed + 90 days). We also evaluated the number of women who re-started hormonal therapy after a gap. Follow-up time was stopped at the time of recurrence, however only four patients recurred, and only one was classified as non-persistent prior to recurrence.

Experienced research assistants conducted the interviews. The study was approved by the Institutional Review Boards of each site and the US Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP) and Human Research Protection Office (HRPO). Written informed consent and HIPAA authorization were obtained from patients prior to study initiation.

Study variables

Demographic, tumor, and treatment measures

From the baseline survey, self-reported information included sociodemographic characteristics (age, race/ethnicity, education, annual household income, employment, marital status). Tumor characteristics abstracted from the medical record included AJCC disease stage (I, II, III, or unknown), grade, nodal status, and tumor size. The Charlson Comorbidity Index [22] score was calculated from 12 months before to 3 months after diagnosis.

Quality of life was assessed at baseline and follow-up with the Functional Assessment of Cancer Therapy: General (FACT-G), which is composed of subscales assessing Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, and Functional Well-Being, along with the breast cancer subscale (FACT-B) [23]. The item response range is 0 (not at all) to 4 (very much).

Decision-making difficulty, preferences, and considerations were assessed at baseline. The perceived level of difficulty in making the treatment decision was assessed using a 5-point Likert scale ranging from 1 = *extremely difficult* to 5 = *very easy*. [24] A measure of patient–physician communication quality was composed of 5 items and evaluated the extent to which the participant agreed (1 = *very strongly disagree* through 6 = *very strongly agree*) with statements regarding the sufficiency of information provided by the physician upon which to base a treatment decision; whether the benefits and risks of HT were explained adequately; if the doctor solicited the patient's opinion regarding treatment; and whether the physician believed the participant's comorbidities precluded adjuvant therapy. Decision-making considerations included physical considerations, the negative decisional balance, positive decisional balance, and concrete considerations [25].

The Medical Outcomes Social Support Survey (MOS) [26] was assessed at baseline to evaluate various aspects of social support (emotional, tangible, affectionate, and positive social interactions). The item response range is 1–5 (from "none of the time" to "all of the time").

Treatment satisfaction was measured with the Treatment Satisfaction Questionnaire for Medication (TSQM) and assessed at follow-up [27]. The TSQM is a 14-item validated instrument (with items scored 0–100) to assess patients' satisfaction with medication, providing scores for 4 scales (side effects, effectiveness, convenience, and global satisfaction).

Patient breast cancer-specific distress was measured using the 15-item version of the Impact of Events Scale (IES) and assessed at follow-up, which queries intrusive and avoidant thoughts about a distressing event (breast cancer) over the past 7 days. Each item has a scoring range of 0–5 [28, 29]. We also evaluated this outcome based on a total score of >24 or not based on prior studies evaluating post-traumatic stress disorder with this cut-off [30].

Patient's preferred treatment decision-making roles were assessed at follow-up using a modified version of the Interpersonal Processes of Care measures (IPC) short form [31]. The survey assesses several subdomains of communication, patient-centered decision making, and interpersonal style. The item score range is 1–5.

Endocrine symptoms (hot flashes and vaginal itching, bleeding, dryness, and discharge) were assessed with a modified version of the Memorial symptoms questionnaire [32].

Data analysis

We compared the characteristics of patients who were non-persistence to ET with those who were not using Chi-square tests. We conducted multivariate logistic regression analyses of the relationships between demographic and clinical characteristics and ET non-persistence to determine covariates for the final model. Based on these results, we developed a series of multivariate logistic regression models of the associations between each of the psychosocial assessments and non-persistence, controlling for age and income. A stepwise logistic regression including all of the covariates was performed. An exploratory analysis looking at each question was performed to determine what factors were driving the observed associations. All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

Results

We identified 601 patients with HR-positive breast cancer who met our initial inclusion criteria. Of these, 523 initiated therapy and had a baseline and subsequent interview. The cohort was primarily white (74.4 %), stage 1 (60.6 %), and on an aromatase inhibitor (68.1 %) (Table 1). Of those patients, 94 (18 %) were non-persistent. If the 18 patients were included that discontinued prior to the first interview, the total non-persistence rate was 20.7 %. The median time from diagnosis to the first assessment was 204 days; this did not differ between the groups. The median follow-up time of the cohort following ET initiation was 730 days, with a mean of 658 days (range 60–730). Of the patients who were non-persistent, the median was 320 days with a mean of 329 days (range 60–638). If non-persistence was categorized as a 45-day gap, 169 (32.3 %) patients were non-persistent and 124 (73.4 %) re-started ET.

Of the 94 patients who were non-persistent with ET, 48 (41 %) re-started it at some point. The median time to re-starting ET was 152 days. Baseline characteristics were the same in those who re-started therapy compared to those who did not (data not shown). Compared to women in the lowest household income group (<$50,000), women who had a household income of >$90,000 were half as likely to interrupt their ET (OR 0.47, 95 % CI 0.26–0.85). No association with ET non-persistence was observed for other baseline characteristics, type of hormone therapy (aromatase inhibitor vs. tamoxifen), or receipt of chemotherapy. In a multivariate analysis of clinical and demographic factors, only household income remained associated with ET non-persistence (OR 0.43, 95 % CI 0.23–0.81) (Table 1). Covariates

Table 1 Baseline characteristics of women with early-stage breast cancer who continued and were non-persistent with endocrine therapy

	Total	Continued	Non-persistent	Univariate analysis		Multivariate analysis*	
	N (%)	*N* (%)	*N* (%)	OR (95 % CI)	*p* value	OR (95 % CI)	*p* value
Total		429 (82.0)	94 (18.0)				
Age							
<60	264 (50.5)	215 (81.4)	49 (18.6)	1.0 (Ref)		1.0 (Ref)	
>60	259 (49.5)	214 (82.6)	45 (17.4)	0.92 (0.59–1.44)	0.72	0.79 (0.47–1.35)	0.39
Race							
White	394 (75.3)	330 (83.8)	64 (16.2)	1.0 (Ref)		1.0 (Ref)	
Black	38 (7.3)	29 (76.3)	9 (23.7)	1.60 (0.72–3.54)	0.24	1.42 (0.63–3.19)	0.39
Other	91 (17.4)	70 (76.9)	21 (23.1)	1.55 (0.89–2.70)	0.12	1.49 (0.84–2.65)	0.17
Marital status							
Unmarried	218 (42.3)	174 (79.8)	44 (20.2)	1.0 (Ref)			
Married	298 (57.8)	252 (84.6)	46 (15.4)	0.72 (0.46–1.14)	0.16		
Income							
< $50,000	151 (30.2)	115 (76.2)	36 (23.8)	1.0 (Ref)		1.0 (Ref)	
$50,000–89,999	177 (35.4)	141 (79.6)	36 (20.3)	0.91 (0.55–1.53)	0.73	0.83 (0.48–1.44)	0.50
> $90,000	172 (34.4)	152 (88.4)	20 (11.6)	0.47 (0.26–0.85)	0.01	0.43 (0.23–0.81)	0.009
Education							
≤High school	121 (23.1)	97 (80.2)	24 (19.8)	1.0 (Ref)			
>High school	402 (76.9)	332 (82.6)	70 (17.4)	0.85 (0.51–1.43)	0.54		
Employment							
Unemployed	290 (55.5)	240 (82.8)	50 (17.2)	1.0 (Ref)		1.0 (Ref)	
Employed	233 (44.5)	189 (81.1)	44 (18.9)	1.12 (0.71–1.75)	0.63	1.18 (0.72–1.61)	0.51
Grade							
Well diff	152 (31.1)	130 (83.5)	22 (14.5)	1.0 (Ref)			
Moderate diff	260 (53.3)	207 (79.6)	53 (20.4)	1.51 (0.88–2.60)	0.13		
Poor diff	76 (15.6)	62 (81.6)	14 (18.4)	1.33 (0.64–2.78)	0.44		
Unknown	35 (6.7)	30 (85.7)	5 (14.3)	0.99 (0.35–2.81)	0.98		
Stage							
I	317 (60.6)	260 (82.0)	57 (18.0)	1.0 (Ref)		1.0 (Ref)	
II/III	206 (39.4)	169 (82.0)	37 (18.0)	0.99 (0.63–1.58)	0.99	1.01 (0.63–1.61)	0.98
Nodes							
Negative	360 (68.8)	296 (82.2)	64 (17.8)	1.0 (Ref)			
Positive	157 (30.0)	132 (84.1)	25 (15.9)	0.88 (0.53–1.45)	0.61		
Missing	6 (1.2)	1 (16.7)	5 (83.3)				
Her2							
Negative	465 (89.9)	377 (81.1)	88 (18.9)	1.0 (Ref)			
Positive	52 (10.1)	47 (90.4)	5 (9.6)	0.46 (0.18–1.18)	0.11		
Comorbidities							
0–1	482 (92.2)	399 (82.8)	83 (17.2)	1.0 (Ref)		1.0 (Ref)	
>2	41 (7.8)	30 (73.2)	11 (26.8)	1.76 (0.85–3.66)	0.13	1.76 (0.82–3.75)	0.15
Year of diagnosis							
2006–2007	210 (40.6)	172 (81.9)	38 (18.1)	1.0 (Ref)			
2008–2010	307 (59.4)	256 (83.4)	51 (16.6)	0.90 (0.57–1.43)	0.66		
Hormone therapy							
Tamoxifen	167 (31.9)	139 (83.2)	28 (16.8)	1.0 (Ref)			
AI	356 (68.1)	290 (81.5)	66 (18.5)	1.13 (0.70–1.84)	0.62		
Chemotherapy							
No	294 (56.2)	237 (80.6)	57 (19.4)	1.0 (Ref)	0.34		

Table 1 continued

	Total	Continued	Non-persistent	Univariate analysis		Multivariate analysis*	
	N (%)	*N* (%)	*N* (%)	OR (95 % CI)	*p* value	OR (95 % CI)	*p* value
Yes	229 (43.8)	192 (83.8)	37 (16.2)	0.80 (0.51–1.26)			

* Logistic regression analysis

Table 2 Mean scores on baseline questionnaires, with multivariate analysis of differences in response between those who continued endocrine therapy and those who were non-persistent

	Range of scores	Total	Continued	Non-persistent	Multivariate analysis[a]
		Mean ± SD	Mean ± SD	Mean ± SD	OR (95 % CI)
Quality of life					
Physical score	0–28	23.4 ± 5.0	23.8 ± 4.6	21.4 ± 6.2	0.96 (0.92, 1.00)*
Social score	0–28	24.7 ± 3.9	24.9 ± 3.7	23.7 ± 4.5	0.96 (0.91, 1.01)
Emotional score	0–24	20.9 ± 3.1	21.0 ± 2.9	20.1 ± 3.9	0.97 (0.92, 1.04)
Functional score	0–28	22.1 ± 5.1	22.5 ± 4.7	20.4 ± 6.3	0.96 (0.92, 1.00)
FACTG	0–108	91.1 ± 13.8	92.3 ± 12.4	85.6 ± 17.8	0.98 (0.97, 1.00)*
Breast cancer concerns score	0–36	26.9 ± 5.0	27.2 ± 4.9	25.7 ± 5.6	0.93 (0.89, 0.98)*
Decision-making difficulty	0–1				
Difficult (reference)		0.14 ± 0.35	0.13 ± 0.33	0.21 ± 0.41	–
Neither difficult nor easy		0.15 ± 0.36	0.16 ± 0.37	0.11 ± 0.31	0.45 (0.19, 1.04)
Easy		0.65 ± 0.48	0.66 ± 0.48	0.61 ± 0.49	0.64 (0.35, 1.16)
Did not respond		0.06 ± 0.24	0.06 ± 0.23	0.07 ± 0.26	0.79 (0.29, 2.12)
Decision-making preferences	0–1				
Doctors should make decision (reference)		0.26 ± 0.44	0.25 ± 0.43	0.31 ± 0.46	–
Patients should make decision		0.38 ± 0.49	0.39 ± 0.49	0.34 ± 0.48	0.80 (0.46, 1.40)
Doctors and patients should make decision together		0.36 ± 0.48	0.36 ± 0.48	0.35 ± 0.48	0.70 (0.40, 1.23)
Decision-making considerations					
Physical concerns	0–1	0.55 ± 0.50	0.53 ± 0.50	0.67 ± 0.47	1.68 (1.02, 2.76)*
Negative balance	0–5	1.62 ± 1.37	1.59 ± 1.36	1.80 ± 1.40	1.14 (0.95, 1.36)
Positive balance	0–3	2.31 ± 0.97	2.30 ± 0.99	2.35 ± 0.92	1.04 (0.80, 1.35)
Concrete concerns	0–3	0.66 ± 0.97	0.60 ± 0.93	0.93 ± 1.12	1.31 (1.04, 1.65)*
Attitude toward hormonal therapy	1–4	3.0 ± 0.49	3.02 ± 0.48	2.84 0.52	0.51 (0.32, 0.81)*
Social support	1–5				
Emotional/informational		4.29 ± 0.6	4.32 ± 0.6	4.19 ± 0.6	0.73 (0.50, 1.06)
Tangible		4.36 ± 0.8	4.38 ± 0.7	4.25 ± 0.9	0.86 (0.65, 1.13)
Affectionate		4.61 ± 0.7	4.62 ± 0.7	4.57 ± 0.7	0.95 (0.69, 1.30)
Positive social interaction		4.34 ± 0.7	4.37 ± 0.7	4.23 ± 0.8	0.79 (0.58, 1.08)
Overall social support		4.37 ± 0.6	4.39 ± 0.6	4.29 ± 0.6	0.80 (0.56, 1.58)

* $p < 0.05$

[a] Unadjusted logistic regression

for the multivariate psychosocial variable models included age and variables that were significant at $p < 0.05$ in the univariate analysis. Of the 94 patients who were non-persistent, 38 (40 %) reported a reason, and of these, 33 % reported that the non-persistence was due to side effects. ET symptoms, were not associated with non-persistence (Table 2).

At baseline, low scores on global and the BC subscale of the FACT were associated with non-persistence. In a multivariate analysis controlling for income and age,

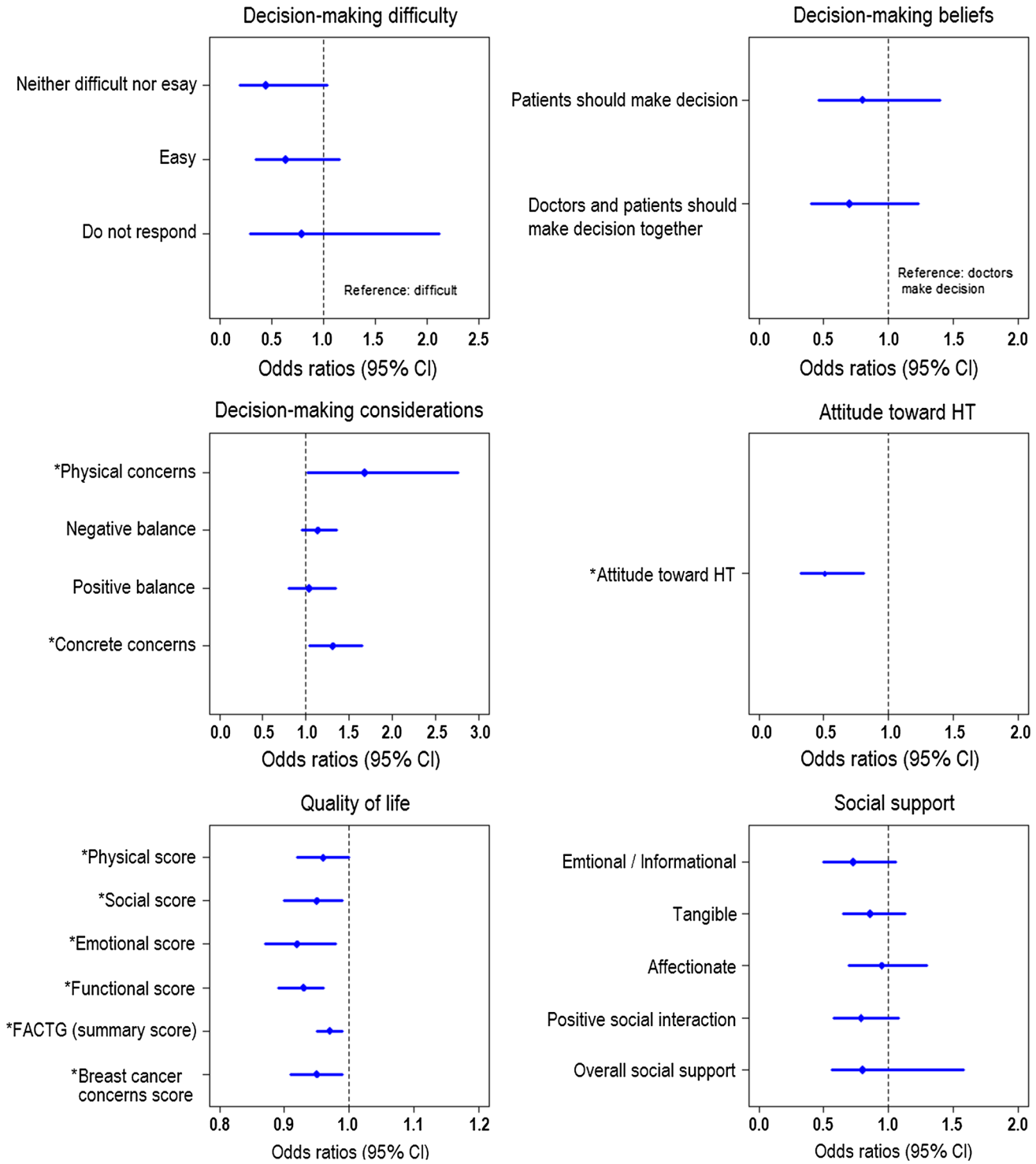

Fig. 1 Multivariate analysis from baseline questionnaires comparing those who continued endocrine therapy and those who were non-persistent. *$p < 0.05$

non-persistence was associated with overall quality of life (OR 0.98, 95 % CI 0.89–0.98). In addition, patients with more positive attitudes about ET were less likely to be non-persistent (OR 0.51, 95 % CI 0.32–0.81). Physical and concrete decision-making concerns were associated with non-persistence, but decision-making preferences and decision-making difficulty were not. Social support total and subscale scores were not associated with subsequent ET non-persistence (Table 2; Fig. 1).

Table 3 Mean scores on follow-up questionnaires, with multivariate analysis of differences in response between those who continued endocrine therapy and those who were non-persistent

	Range of scores	Total Mean ± SD	Continued Mean ± SD	Non-persistent Mean ± SD	Multivariate analysis[a] OR (95 % CI)
Quality of life					
Physical score	0–28	23.4 ± 5.0	23.8 ± 4.6	21.4 ± 6.2	0.92 (0.89, 0.96)*
Social score	0–28	24.7 ± 3.9	24.9 ± 3.7	23.7 ± 4.5	0.94 (0.89, 0.99)*
Emotional score	0–24	20.9 ± 3.1	21.0 ± 2.9	20.1 ± 3.9	0.93 (0.87, 0.99)*
Functional score	0–28	22.1 ± 5.1	22.5 ± 4.7	20.4 ± 6.3	0.93 (0.89, 0.97)*
FACTG	0–108	91.1 ± 13.8	92.3 ± 12.4	85.6 ± 17.8	0.97 (0.96, 0.99)*
Breast cancer concerns score	0–36	26.9 ± 5.0	27.2 ± 4.9	25.7 ± 5.6	0.95 (0.91, 0.99)*
Treatment satisfaction	0–100				
Effectiveness		80.0 ± 20.7	80.8 ± 20.0	76.1 ± 23.7	0.99 (0.98, 1.00)
Side effects		17.8 ± 22.0	17.5 ± 21.0	19.1 ± 26.0	1.00 (0.99, 1.01)
Convenience		95.5 ± 10.9	96.1 ± 10.1	92.7 ± 13.8	0.98 (0.96, 1.00)
Global satisfaction		80.5 ± 21.0	81.8 ± 20.0	74.3 ± 24.3	0.99 (0.98, 1.00)*
Impact of events					
Intrusive thoughts	1–40	6.7 ± 7.0	6.3 ± 6.5	8.2 ± 8.8	1.03 (1.00, 1.06)*
Avoiding thoughts	0–40	7.9 ± 8.0	7.5 ± 7.6	10.1 ± 9.4	1.04 (1.01, 1.06)*
Global score	0–80	14.6 ± 13.1	13.8 ± 12.2	18.4 ± 16.0	1.02 (1.01, 1.04)*
Interpersonal processes of care	1–5				
Doctors don't explain clearly		1.9 ± 0.7	1.8 ± 0.7	2.0 ± 0.8	1.40 (1.02, 1.92)
Doctors find out your concerns		4.4 ± 0.6	4.4 ± 0.6	4.4 ± 0.6	0.89 (0.61, 1.30)
Doctors clearly explain results		4.5 ± 0.7	4.5 ± 0.7	4.5 ± 0.6	1.11 (0.79, 1.57)
Work out treatment together		4.4 ± 0.8	4.3 ± 0.8	4.4 ± 0.8	1.04 (0.79, 1.39)
Doctors treat you with respect		4.4 ± 0.6	4.4 ± 0.7	4.4 ± 0.6	1.03 (0.73, 1.46)
Doctors discriminate against you due to race		1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.4	1.04 (0.61, 1.78))
Office staff disrespected you		1.2 ± 0.4	1.2 ± 0.4	1.2 ± 0.4	1.02 (0.56, 1.83)

* $p < 0.05$

[a] Unadjusted logistic regression

At follow-up (first assessment after ET initiation), in a multivariate analysis controlling for income and age, non-persistence was associated with overall quality of life (OR 0.97, 95 % CI 0.95–0.99), as well as with each of the general subscales (physical, social, emotional, and functional) and the breast cancer concerns subscale (Table 3; Fig. 2). In addition, lower scores on global treatment satisfaction were also associated with subsequent non-persistence (OR 0.99, 95 % CI 0.99–1.00). Interpersonal processes of care (i.e., patient–physician communication) were not associated with non-persistence.

Higher scores on the impact of events questionnaire were also associated with ET non-persistence (Table 3; Fig. 2). In the multivariate analysis, intrusive thoughts (OR 1.04, 95 % CI 1.01–1.07), avoidance (OR 1.03, 95 % CI 1.01–1.06), and the summary score (OR 1.02, 95 % CI 1.01–1.04) were each associated with ET non-persistence. We also found that patients with a score >24 had a higher odds of non-persistence (OR 1.92, 95 % CI 1.14–3.23) compared to those with scores ≤24.

In a stepwise multivariate analysis that included the global scores of each of the measures, income and age, only income and the Impact of Events Scale (OR 0.98, 95 % CI 0.97–0.99) remained statistically significantly associated with non-persistence.

Discussion

Despite the survival benefits of adjuvant hormonal therapy, we found that 18 % of breast cancer patients in our study who initiated adjuvant ET were non-persistent during the first 2 years of therapy. Women who reported better quality of life, a better attitude toward ET, and greater treatment satisfaction were less likely to interrupt their ET use. Women who reported increased distress, as measured by both increased intrusive and increased avoidant thoughts about breast cancer, were more likely to have non-persistence in ET. Global scores on social support measures, decision-making difficulty, and perceived quality of

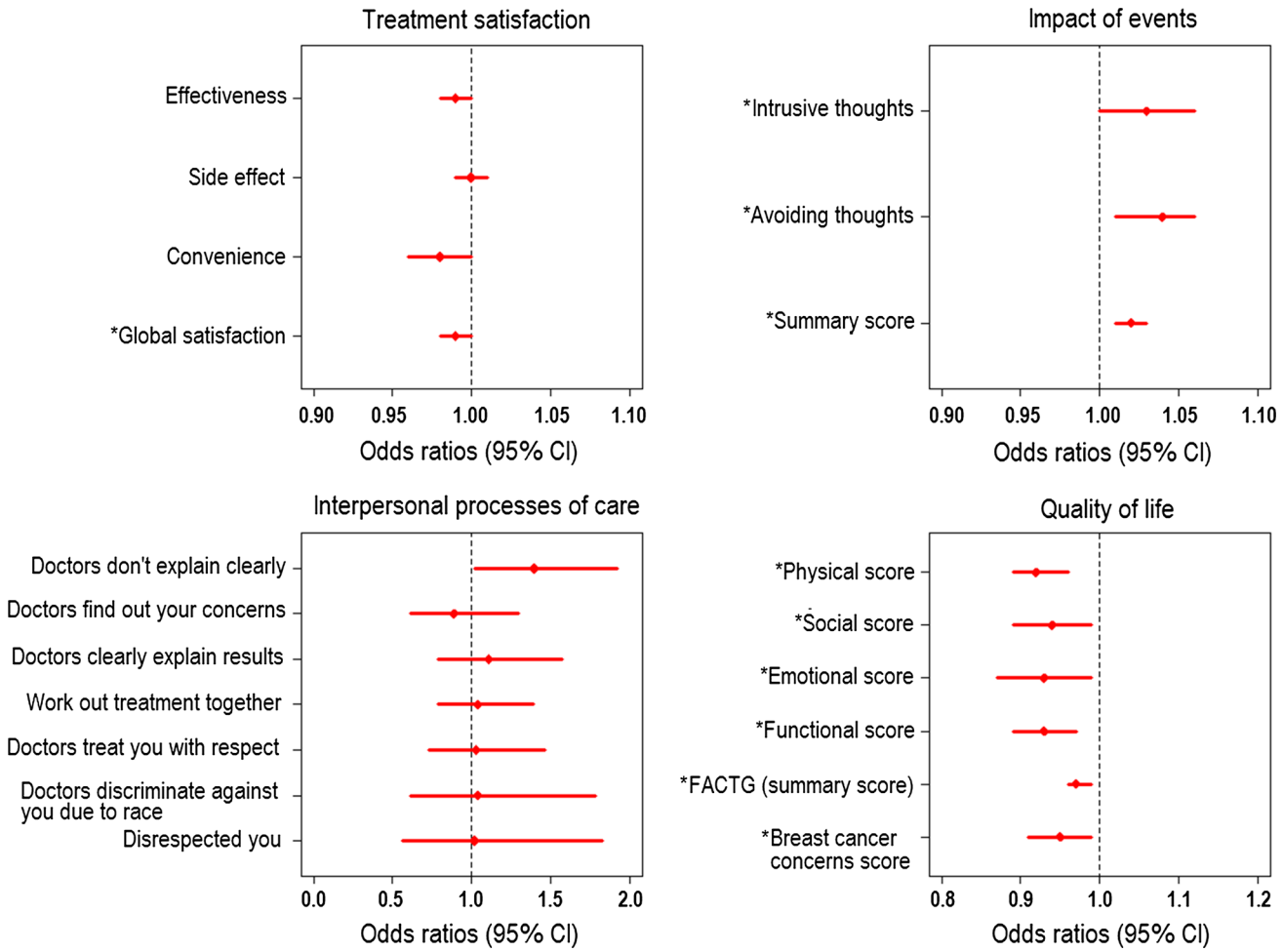

Fig. 2 Multivariate analysis from follow-up questionnaires comparing those who continued endocrine therapy and those who were non-persistent. *$p < 0.05$

communication were not independently associated with risk of ET non-persistence.

We were not surprised to see the association between lower quality of life scores at baseline and follow-up and ET non-persistence. For women with breast cancer, quality of life is known to be associated with age, stage at diagnosis, and social support [33]. In a prior retrospective study, many women attributed their early discontinuation of ET to adverse effects and decreased quality of life [34]. We did not see an association between some common ET symptoms and non-persistence; however, the subset of patients who reported reasons for discontinuation commonly reported that it was due to side effects. Symptoms prior to initiation of therapy and during therapy may contribute to poor quality of life. An association between the number of symptoms experienced prior to, or after, treatment initiation and subsequent non-adherence has been previously reported [16, 35]. These results suggest that efforts to improve quality of life may be a productive avenue for improving adherence to hormone therapy.

In our study, high levels of breast cancer-specific emotional distress were associated with subsequent non-persistence in ET. We have previously shown that nearly 25 % of patients report levels of breast cancer-specific distress high enough to be consistent with PTSD shortly after diagnosis, and that the risk for PTSD symptoms was higher among black and Asian women than among white women [30]. In a retrospective analysis using electronic billing claims, non-adherence to hormone therapy was lower among patients with a history of claims for psychotherapy consultations or therapeutic support consultations than among women without such a history [36]. Although ET interruption was not associated with overall baseline social support, it was associated with specific questions on the scale dealing with understanding and sharing worries and problems. Early identification of emotional distress and therapeutic interventions to improve psychological well-being should be evaluated to improve the quality of breast cancer care.

Unlike prior studies that showed that improved patient–physician communication may enhance medication

adherence [37, 38], our study did not find an association between ET non-persistence and any of the domains of interpersonal processes of care. A study by Liu et al. [39] reported that low-income breast cancer survivors with higher scores on "patient-centered" communication and greater self-efficacy scores on patient–physician communication at 18 months were more likely to continue to be on hormonal therapy at 36 months than patients with poorer scores.

Cancer treatment decisions confront both providers and patients with complex issues and challenges. These challenges are particularly pointed for women confronting the long-term adherence required for optimal curative treatment of breast cancer with ET. It has been suggested that patients mentally conduct a cost–benefit analysis; those who perceive a higher necessity for their medication have higher adherence, while those with more concerns are less adherent [40, 41]. Women in our study who had a positive attitude toward ET were significantly less likely to be non-persistent. Consistent with that view, adherence to ET has been reported to be associated with belief in the efficacy of the medication [42, 43] and with belief in the benefits of taking prescribed medications more generally [40, 44–46]. We found that higher satisfaction with treatment was associated with decreased risk of subsequent ET non-persistence. Specifically, we found that increased confidence about efficacy and belief that the good things outweighed the bad, were associated with decreased risk of non-persistence.

As we found in a prior analysis [19], women in the highest income bracket were significantly more likely to be adherent than women in the lowest income group. Low-income groups have traditionally been found to be vulnerable with regard to quality of health care, but we were surprised that income had such a strong association with non-persistence among patients who were part of an integrated healthcare system that minimized financial barriers to oral therapy. Income may be an inadequate proxy for overall financial resources, especially among the elderly, for whom net worth appears to be a more accurate predictor of the use of healthcare services [47]. In a previous study, we found that low net worth was associated with hormone therapy discontinuation, and partially explained the association between black race and non-compliance [20].

A study strength was that subjects were recruited prospectively at the time of breast cancer diagnosis or shortly thereafter; thus, the data were collected prior to the interruption of ET. In addition, our estimates of ET interruption were determined from electronic pharmacy records, which may have been more valid and less biased than self-report, which was utilized in most other studies. In the present study, we did not find associations between non-initiation of ET and several sociodemographic factors that previously were reported to influence compliance [15, 43, 48]. It is possible that there was insufficient statistical power due to modest sample sizes for some analyses. That concern notwithstanding, our study is one of the larger prospective studies to examine the association between patients' perceptions and ET non-persistence.

This study had some important limitations. Because the patients were enrolled in an integrated healthcare plan, we could not explore issues related to access, which may limit the generalizability of the findings. We were also not able to assess the reasons for discontinuation among the 2 % of patients who discontinued prior to their first evaluation. It is possible that some patients may have filled their ET prescriptions outside of KPNC, but such behavior is known to be infrequent [48]. We only included patients who were English speaking and had access to a telephone and the majority of the patients were white, which may have implications for the generalizability of our results. Reassuringly, half of the patients who had ET non-persistence re-started treatment at some subsequent point during follow-up, however we do not know the reasons why they re-started. Finally, we performed multiple analyses; therefore, it is possible that some of the significant results, especially the exploratory analyses, were due to chance.

In conclusion, in this prospective cohort study of women with early-stage breast cancer, we found that the majority of women continued their hormone therapy, however patients under greater emotional duress, those who do not have positive attitudes about ET and those with lower quality of life appeared to be at the highest risk of discontinuing. A better understanding of modifiable psychological factors that can result in early discontinuation may inform targeted educational interventions to improve adherence.

Acknowledgments This study was supported by the Department of Defense Breast Cancer Center of Excellence Award (BC043120) to Drs. Neugut/Hershman; the NCI R01 (CA105274) to Dr. Kushi; the Department of Defense (DAMD-17-01-1-0334) to Dr. Bovbjerg; and the NCI R01 (CA124924 and 127617) and U10 (CA 84131) to Dr. Mandelblatt. Drs. Hershman is the recipient of funding from the Breast Cancer Research Foundation.

Compliance with ethical standards

Conflict of interest All authors report no conflicts of interest. All of the authors are responsible for the data analysis and interpretation. No additional individuals were involved in the analysis.

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