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ORIGINAL ARTICLE

Associations between adjuvant endocrine therapy and onset of physical and emotional concerns among breast cancer survivors

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Abstract
Background Breast cancer survivors often receive long-term adjuvant endocrine therapy (AET) to reduce recurrence risk. Adherence to AET is suboptimal, which may be due to the experience of symptoms and/or concerns. Few studies have comprehensively assessed self-reported concerns between those who currently, previously or have never received AET. The study objective is to describe self-reported physical and emotional concerns of breast cancer survivors who are current, prior, or never-recipients of AET.

Methods Secondary analysis was performed on a subset of survey data collected in the 2010 LIVESTRONG Survey. Breast cancer survivors (n = 1,013, mean 5.4 years post-diagnosis) reported on 14 physical and eight emotional concerns that began after diagnosis and were experienced within 6 months of participation in the survey. Bivariate analyses examined the prevalence of each concern by AET status. The relationships between AET and burden of physical or emotional concerns were modeled with logistic regression.

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Results More than 50 % of the participants reported currently experiencing cognitive issues, fatigue, fear of recurrence, emotional distress, and identity/grief issues. Thyroid dysfunction and stigma concerns were more common among participants with prior AET ($p<0.01$), while fear of recurrence, emotional distress, and concern about appearance were more common among those currently receiving AET ($p<0.01$). Fatigue, sexual dysfunction, and pain were more common among prior and current AET recipients ($p<0.01$). In adjusted models, receipt of AET was associated with a higher number of physical, but not emotional concerns. A higher number of concerns was associated with younger age, having children, receipt of chemotherapy, longer duration of cancer treatment, and shorter time since diagnosis ($p<0.01$).
Conclusions Breast cancer survivors who received AET were at risk of developing a variety of physical and emotional concerns, many of which persisted after treatment. These findings suggest the importance of developing individualized, supportive resources for breast cancer survivors.

Keywords Breast cancer survivor · Adjuvant endocrine therapy · Quality of life · Adverse effects

Introduction

Over 200,000 women are newly diagnosed with breast cancer annually in the USA [1]. Of these, approximately 75 % are hormone receptor positive [2] who often receive long-term (i.e., 5 or more years of) adjuvant endocrine therapy (AET) upon completion of primary therapy (e.g., surgery, radiation, chemotherapy) to further reduce their cancer recurrence risk [3, 4]. AET has been associated with a range of physical and psychosocial symptoms, including cognitive dysfunction, musculoskeletal symptoms, sexual dysfunction, urinary symptoms, vasomotor symptoms, adjustment disorder or other psychosocial distress, insomnia and fatigue [3, 5–7].

These symptoms can become persistent and bothersome in a subset of patients, potentially resulting in increased health care utilization [8] as well as decreased quality of life [9], ability to function [10], and adherence to AET [5, 6, 11]. For example, roughly a third of breast cancer survivors need to discontinue their first line adjuvant aromatase inhibitor agents due to the development of AET-related adverse effects, of which about a quarter are musculoskeletal symptoms [6]. Early discontinuation and adherence rates of less than 80 % are independent predictors of mortality [12]. Therefore, increased insight into the nature and course of symptoms will facilitate the development of targeted and cost-effective supportive care efforts.

Most studies have documented symptom experiences of breast cancer survivors during AET, but little is known about how this compares to those who have never or previously taken AET. Some studies have reported on the long-term concerns of breast cancer survivors [13–15], but little is known about the degree to which these symptoms persist upon completion of AET. A unique source of data regarding symptoms experienced by breast cancer survivors is the 2010 LIVESTRONG Survey, which was designed to comprehensively assess physical, emotional, and practical concerns that may develop in survivors after completion of primary cancer treatment (http://www.livestrong.org/pdfs/3-0/LSSurvivorSurveyReport). Here, the term "concerns" refers to physical and emotional symptoms and issues that have previously been associated with the post-treatment cancer survivorship experience [9, 16–21].

Using this comprehensive data set, the current study is to our knowledge the first to compare a full range of self-reported physical and emotional concerns among breast cancer survivors who are currently taking, have previously taken, or have never taken AET. This comparison can provide insight into which concerns may be related to AET and the prevalence of persistent physical and emotional concerns following completion of AET.

Methods

Participants

Breast cancer survivors completed the online, anonymous, and cross-sectional LIVESTRONG Survey between June 2010 and March 2011 (approved by the Western Institutional Review Board). Males as well as cases of metaplastic and inflammatory breast cancer were excluded ($n=69$), in addition to those who were still in primary treatment ($n=201$) and who responded "yes" to the question "Living with cancer as a chronic condition" ($n=67$), as these respondents may be considered to have metastatic disease. Women ($n=1,013$) in the sample were categorized as currently taking, have previously taken, or have never taken AET, based on responses to two questions: 1) indicating that "hormonal therapy" was one of their cancer treatments and 2) whether they were currently taking "medication to prevent a recurrence." *Never-recipients* were respondents who answered "no" to both questions, while *current recipients* answered "yes" to both. *Prior recipients* were respondents who answered "yes" to having received hormonal therapy as part of treatment but "no" to currently taking medication to prevent a recurrence. There were several respondents who were excluded, as their AET status could not be determined ($n=18$).

Procedure

This is a secondary analysis of a subset of the survey data collected in the 2010 LIVESTRONG Survey. Upon request

(available at research@livestrong.org), we were granted access to the de-identified data set. Additional details are available in the LIVESTRONG report (http://www.livestrong.org/pdfs/3-0/LSSurvivorSurveyReport).

Measures

Our analysis focused on sociodemographic and medical characteristics, as well as physical and emotional concerns (http://www.livestrong.org/pdfs/3-0/LSSurvivorSurveyReport). LIVESTRONG developed survey questions through a process that engaged cancer survivors as well as experts in survey methodology and oncology. The survey examines sociodemographic characteristics (age, race/ethnicity, marital status, parity status, education, employment, income, and health insurance status), medical characteristics (type of treatment facility, time since diagnosis, time since last treatment, duration of treatment, and types of primary treatment received), and physical and emotional concerns. The concerns queried in the survey were included because they were identified as important according to one or more of the following criteria: appeared in prior publicly available, validated surveys focused on survivorship (specifically, the Quality of Life in Adult Cancer Survivors [QLACS] scale [22]); identified as late effects of cancer by expert advisors or in the peer-reviewed literature (e.g., [23]); and/or were concerns identified by survivors reaching out to LIVESTRONG for assistance. Draft survey items underwent initial analysis with a pilot test and focus groups composed of cancer survivors, as well as expert review. Participants could endorse up to 14 physical and eight emotional concerns that had surfaced since completing primary cancer treatment and continued to be experienced within 6 months of survey participation (http://www.livestrong.org/pdfs/3-0/LSSurvivorSurveyReport). If a respondent endorsed any of the items related to a specific concern (via choosing "yes" or "no"), they were counted as having the concern.

Statistical analysis

Associations of AET experience with categorical demographic variables and with physical and emotional concerns were tested using chi-square tests. Associations of AET with continuous variables including age and a number of physical or emotional concerns were tested by ANOVA or Kruskal–Wallis test. The number of concerns was bounded between 0 and 14 for physical concerns and between 0 and 8 for emotional concerns. The number was dichotomized as "Low Number" or "High Number" using the median number of concerns (Low: <3 vs. High: ≥3, for both physical and emotional sums) as the cut point. Multiple logistic regression models were fit to explore the relationship between a high versus low number of physical and emotional concerns experienced and demographic, disease duration and treatment-related factors. The set of predictors to be included in each model was determined a priori and no model selection methods were used. Modeling assumptions were verified and all tests were two-sided. The three study groups were first compared on background demographic and cancer history-related characteristics, and then compared on the prevalence of specific physical and emotional concerns and the total number of concerns endorsed within each domain using chi-square tests. Due to the high number of statistical tests, we used a more conservative criterion of $p \leq 0.01$ to indicate statistical significance. The analysis for this paper was generated using SAS software, Version 9.2 of the SAS System for PC.

Results

Comparison of sociodemographic and medical characteristics as well as physical and emotional concerns among breast cancer survivors who are currently taking, have previously taken, or have never taken AET: The respondents' characteristics are shown in Table 1. This sample of breast cancer survivors averaged 53 years old. Most were married with children; employed full-time; received combined surgery, chemo-, and radiation therapy; and two-thirds of the respondents indicated that they have previously taken or are currently taking AET. The three study groups differed significantly on several characteristics, with those currently taking AET being younger, less likely to have children, more likely to have employer-based health insurance, and having a shorter time since diagnosis and duration of treatment compared to the other two groups.

The three most common physical concerns were cognitive dysfunction, fatigue, and sexual dysfunction (54 %, 52 %, and 46 %, respectively; Table 2). On average, survivors endorsed experiencing 3.1 post-cancer onset physical concerns within the last 6 months. The average number of physical concerns was significantly different among the three AET groups and tended to be higher among those who have previously taken and are currently taking AET compared to those who have never taken AET ($p < 0.01$). Thyroid dysfunction was reported more commonly among those who have previously taken AET compared with those who have never taken and are currently taking AET ($p < 0.01$). Fatigue, sexual dysfunction, and pain ($p < 0.01$) were less commonly reported among those who have never taken AET compared to those who previously have taken and are currently taking AET.

The three most common emotional concerns were fear of recurrence, emotional distress, and issues with identity or grief (67 %, 56 %, and 55 %, respectively; Table 3). On average, survivors endorsed having experienced, within

Table 1 Demographics, treatment and disease-related variables (all values are *n* (%) except where noted)[a]

	All *n* = 1,013	Never AET *n* = 387 (38)	Prior AET *n* = 105 (10)	Current AET *n* = 521 (51)	*p* value
Age: mean (SD)	53 (10)	54 (11)	54 (9)	51 (9)	<0.001[b]
Race: White vs. Other[c]	893 (88)	334 (86)	92 (88)	467 (90)	0.303[d]
Marital Status: Married/Domestic Partner vs. Other[e]	709 (71)	266 (69)	79 (75)	364 (71)	0.493[d]
Children: Yes	733 (72)	301 (78)	78 (74)	354 (68)	0.005[d]
Education: Bachelor's Degree or higher	555 (56)	198 (52)	61 (59)	296(57)	0.215[d]
Employment:					0.249[f]
Full-time	474 (47)	168 (44)	45 (43)	261 (50)	
Part-time/Self-employed	241 (24)	92 (24)	28 (27)	121 (23)	
Retired	139 (14)	62 (16)	18 (17)	59 (11)	
Unemployed/other	152 (15)	61 (16)	14 (13)	77 (15)	
Income:					0.461[d]
0–40,000	143 (14)	61 (16)	13 (12)	69 (13)	
41,000–60,000	128 (13)	54 (14)	12 (11)	62 (12)	
61,000–80,000	129 (13)	46 (12)	10 (10)	73 (14)	
81,000–100,000	112 (11)	42 (11)	17 (16)	53 (10)	
101,000 or more	238 (24)	80 (21)	24 (23)	134 (26)	
Prefer not to answer	247 (25)	96 (25)	29 (28)	122 (24)	
Health insurance:					0.002[d]
Employer only	617 (68)	222 (64)	54 (56)	341 (73)	
Private or Military only	94 (10)	34 (10)	20 (21)	40 (9)	
Government or None only	87 (10)	38 (11)	9 (9)	40 (9)	
Multiple or other	112 (12)	52 (15)	13 (14)	47 (10)	
Treatment facility:					0.245[d]
University or Cancer Center	231 (23)	76 (20)	31 (30)	124 (24)	
Hospital	351 (35)	136 (36)	36 (34)	179 (35)	
Community Center/Physician's Office/Other	422 (42)	171 (45)	38 (36)	213 (41)	
Time since diagnosis [years, mean (SD)]	5.4 (5.2)	7.3 (5.9)	9.0 (4.6)	3.4 (3.8)	<0.001[f]
Duration of primary treatment [years, mean (SD)]	1.6 (3.0)	1.8 (3.4)	2.6 (3.9)	1.3 (2.2)	<0.001[f]
Treatment Categories (Mutually Exclusive)					0.652[d]
No Chemotherapy	322 (32)	115 (30)	41 (39)	166 (32)	
Chemotherapy or Chemotherapy + either Surgery or Radiation	210 (21)	85 (22)	22 (21)	103 (20)	
Chemotherapy + Surgery + Radiation	481 (47)	187 (48)	42 (40)	252 (48)	

[a] Percentages were calculated based on non-missing data

[b] ANOVA

[c] American Indian or Alaskan Native, Asian, Black or African American Native Hawaiian or Other Pacific Islander, Hispanic or Latino, other, prefer not to answer

[d] Chi-square

[e] Single, separated, divorced, widowed, prefer not to answer

[f] Kruskal–Wallis test

the 6 months prior to survey participation, 3.1 emotional concerns. The average number of emotional concerns was significantly different between the three AET groups: those who currently are taking AET reported a higher number compared to those who have never or previously taken AET ($p < 0.02$). The incidence of specific emotional concerns differed among AET groups, as those who are currently taking AET more commonly reported fear of recurrence, emotional distress, and concern about their appearance than those who have previously and never taken AET ($p < 0.01$). However, women who had previously taken and are currently taking AET reported more stigma concerns than those who have never used AET ($p < 0.001$).

Table 2 Physical concerns[a,b]

	All $n=1,013$	Never AET $n=387$ (38)	Prior AET $n=105$ (10)	Current AET $n=521$ (51)	p value
Physical concern					
Cognitive	545 (54)	195 (51)	54 (51)	296 (57)	0.149[c]
Fatigue	520 (52)	168 (44)	55 (53)	297 (57)	<0.001[c]
Sexual dysfunction	456 (46)	144 (38)	49 (48)	263 (51)	<0.001[c]
Neuropathy	351 (35)	124 (32)	37 (35)	190 (36)	0.409[c]
Pain	337 (33)	106 (28)	37 (36)	194 (37)	0.007[c]
Lymphedema	278 (28)	101 (26)	27 (26)	150 (29)	0.600[c]
Incontinence	143 (14)	51 (13)	14 (13)	78 (15)	0.724[c]
Oral	109 (11)	40 (10)	10 (10)	59 (11)	0.827[c]
Vision	103 (10)	34 (9)	12 (12)	57 (11)	0.500[c]
Lung	94 (9)	35 (9)	10 (10)	49 (9)	0.977[c]
Thyroid	56 (6)	27 (7)	11 (11)	18 (4)	0.005[c]
Heart	49 (5)	24 (6)	4 (4)	21 (4)	0.293[c]
Hearing	46 (5)	19 (5)	6 (6)	21 (4)	0.689[c]
Feeding	45 (4)	21 (5)	6 (6)	18 (4)	0.289[c]
Any physical concern	854 (84)	306 (79)	91 (87)	457 (89)	0.002[c]
Number of physical concerns: mean (SD)	3.1 (2.4)	2.8 (2.5)	3.2 (2.4)	3.3 (2.3)	0.001[d]

[a] Percentages were calculated based on non-missing data

[b] All values are n (%) except where noted

[c] Chi-square test

[d] Kruskal–Wallis test

Independent associations of AET and other characteristics with a higher versus lower burden of physical and emotional concerns

Logistic regression analysis (Table 4) showed that relative to women who have never received AET, women who have previously taken or are currently taking AET reported a statistically significant higher number of physical concerns, even after controlling for other demographic and medical factors ($p=0.003$). Additional independent correlates of reporting a higher number of physical concerns were having children, a shorter time since cancer diagnosis, a longer duration of primary treatment, and receipt of chemotherapy ($p \leq 0.01$).

Logistic regression analysis (Table 5) revealed no statistically significant relationship between the number of emotional concerns and AET. However, a higher number of emotional concerns were reported among those who were younger, were closer to their time of diagnosis, had longer primary treatment durations, and had received chemotherapy ($p \leq 0.01$).

Discussion

More than half of the breast cancer survivors in this sample reported still experiencing certain post-cancer onset physical

Table 3 Emotional concerns[a,b]

	All $n=1,013$	Never AET $n=387$ (38)	Prior AET $n=105$ (10)	Current AET $n=521$ (51)	p value
Emotional concern					
Fear of recurrence	673 (67)	232 (60)	68 (65)	373 (72)	<0.001[c]
Distress	570 (56)	191 (49)	55 (52)	324 (62)	<0.001[c]
Identity/Grief	562 (55)	201 (52)	58 (55)	303 (58)	0.176[c]
Risk to family	451 (45)	187 (49)	43 (41)	221 (43)	0.114[c]
Appearance	405 (40)	135 (35)	34 (33)	236 (45)	0.002[c]
Relationships	240 (24)	77 (20)	24 (23)	139 (27)	0.062[c]
Stigma	193 (25)	69 (18)	43 (41)	101 (33)	<0.001[c]
Faith	87 (9)	31 (8)	6 (6)	50 (10)	0.351[c]
Any emotional concern	905 (89)	332 (86)	94 (90)	479 (92)	0.012[c]
Number of emotional concerns: mean (SD)	3.1 (1.9)	2.9 (2.0)	3.0 (1.8)	3.4 (1.9)	0.001[d]

[a] Percentages were calculated based on non-missing data

[b] All values are n (%) except where noted

[c] Chi-square test

[d] Kruskal–Wallis test

Table 4 Multiple logistic regression model for high versus low number[a] of physical concerns[b]

	Odds ratio (95 % CI)	*p* value
AET		0.003
Never	REF	
Prior	1.51 (0.88–2.57)	
Current	1.85 (1.30–2.65)	
Age	0.99 (0.97–1.01)	0.468
Race: White[c]	1.25 (0.76–2.07)	0.387
Marital status: Marital/Domestic Partner[d]	1.09 (0.74–1.61)	0.649
Children: Yes	1.71 (1.19–2.45)	0.004
Education: Bachelor's Degree or higher	0.81 (0.59– 1.13)	0.214
Employment:		0.151
Full-time	REF	
Part-time/Self-employed	1.17 (0.78–1.75)	
Retired	0.62 (0.35–1.09)	
Unemployed/other	0.209 (0.51–1.33)	
Income:		0.048
0–40,000	REF	
410,000–600,000	1.17 (0.63–2.18)	
610,000–800,000	1.43 (0.74–2.77)	
810,000–1000,000	1.46 (0.71–3.00)	
1010,000 or more	0.69 (0.37–1.31)	
Prefer not to answer	0.88 (0.47–1.62)	
Health insurance:		0.839
Employer only	REF	
Private or Military only	1.20 (0.69–2.06)	
Government or None only	1.26 (0.67–2.38)	
Multiple or other	1.01 (0.59–1.71)	
Type of treatment facility:		0.050
University or Cancer Center	REF	
Hospital	0.66 (0.43–1.00)	
Community Center/Doctor's Office/Other	0.62 (0.41–0.92)	
Time since diagnosis (years)	0.94 (0.90–0.99)	0.010
Duration of treatment (years)	1.09 (1.02–1.15)	0.007
Mutually exclusive treatment cat:		<0.001
No Chemo	REF	
Only Chemo or Chemo + either Surgery or Radiation	4.58 (2.93–7.16)	
Chemo + Surgery + Radiation	4.01 (2.75–5.83)	

[a] Low burden: <3 and high burden ≥3 concerns

[b] All predictors were fit in one model

[c] Referent group: American Indian or Alaskan Native, Asian, Black or African American Native Hawaiian or Other Pacific Islander, Hispanic or Latino, other, prefer not to answer

[d] Single, separated, divorced, widowed, prefer not to answer

Table 5 Multiple logistic regression model for high versus low number[a] of emotional concerns[b]

	Odds ratio (95 % CI)	*p* value
AET		0.897
Never	REF	
Prior	1.10 (0.65–1.85)	
Current	1.07 (0.75–1.52)	
Age	0.97 (0.95–0.99)	<0.001
Race: White[c]	1.78 (1.09–2.89)	0.021
Marital Status: Marital/Domestic Partner[d]	0.92 (0.63–1.35)	0.668
Children: Yes	1.38 (0.97–1.97)	0.072
Education: Bachelor's Degree or higher	1.14 (0.83–1.56)	0.430
Employment:		0.525
Full-time	REF	
Part-time/Self-employed	1.28 (0.86–1.90)	
Retired	1.02 (0.59–1.77)	
Unemployed/other	1.30 (0.81–2.09)	
Income:		0.021
0–40,000	REF	
41,000–60,000	0.87 (0.48–1.60)	
61,000–80,000	1.06 (0.55–2.01)	
81,000–100,000	1.32 (0.64–2.69)	
101,000 or more	0.87 (0.46–1.63)	
Prefer not to answer	0.54 (0.29–0.99)	
Health Insurance:		0.563
Employer only	REF	
Private or Military only	0.76 (0.45–1.28)	
Government or None only	0.75 (0.41–1.40)	
Multiple or other	1.07 (0.64–1.80)	
Type of treatment facility:		0.634
University or Cancer Center	REF	
Hospital	0.88 (0.58–1.33)	
Community Center/Doctor's Office/Other	0.83 (0.56–1.22)	
Time since diagnosis (years)	0.93 (0.89–0.97)	<0.001
Duration of Treatment (years)	1.08 (1.02–1.15)	0.008
Mutually exclusive treatment cat:		0.002
No Chemo	REF	
Only Chemo or Chemo + either Surgery or Radiation	2.01 (1.31–3.09)	
Chemo + Surgery + Radiation	1.75 (1.22–2.51)	

[a] Low burden: <3 and high burden ≥3 concerns

[b] All predictors were fit in one model

[c] Referent group: American Indian or Alaskan Native, Asian, Black or African American Native Hawaiian or Other Pacific Islander, Hispanic or Latino, other, prefer not to answer

[d] Single, separated, divorced, widowed, prefer not to answer

and emotional concerns within the 6 months prior to survey participation (i.e., cognitive dysfunction, fatigue, fear of recurrence, emotional distress, and identity/grief issues). Logistic regression analysis showed a statistically significant relationship between a higher number of post-diagnosis physical concerns and current or prior receipt of AET.

Regarding specific concerns, those who have previously received AET reported more thyroid concerns than those who are currently taking or have never taken AET. Other studies have also reported on the association between thyroid disease and breast cancer, raising thoughts about a possible endocrine commonality (possibly iodine mediated) or an immunological interaction (possible immune response to the thyroid triggered by the cancer) [24–26]. The role of AET exposure in thyroid dysfunction among breast cancer survivors deserves further exploration as we currently lack insight into its frequency and cause.

Overall, in bivariate analyses, those who are currently taking (and, to a lesser degree, those who have previously taken) AET reported a higher number of physical and emotional concerns compared to those who have never taken AET. However, multiple logistic regression analyses indicated that current or prior AET usage was associated with statistically significant higher odds of reporting a high number of physical concerns, though AET status was not associated with odds of high emotional concern burden. In contrast, Fan et al. [27] found that AET did not have an additional effect on fatigue, menopausal symptoms, and cognitive dysfunction above and beyond primary therapy when compared to matched healthy women. However, Fan et al. enrolled early breast cancer survivors who were different from those in our sample; they were younger, within their first 2 years of diagnosis, had all received adjuvant chemotherapy, and AET was mostly limited to tamoxifen. It is possible that the physical and emotional concerns queried in the LIVESTRONG Survey — particularly those that were associated with current or prior AET exposure — are late effects or side effects that may have become more noticeable over time as the effects of other completed cancer treatments (i.e., surgery, chemotherapy, and/or radiation) remit. Lastly, some concerns queried in the LIVESTRONG Survey are mainly related to surgery and/or chemotherapy and are less specific to known side effects of AET (e.g., joint pain), which may explain why we observed no differences among AET groups for some concerns such as lymphedema and neuropathy.

Cluze et al. [28] demonstrated that AET-related concerns are clinically relevant, as they are related to AET adherence throughout the entire 5-year course of AET therapy. Our results indicate that some physical concerns may persist for years beyond AET discontinuation; prior AET recipients, who were farther out from diagnosis than those who have never used AET, reported more concerns than never-recipients. Unfortunately, our inability to differentiate among those who have previously taken between those who had completed their recommended course of therapy or had to stop prematurely (for reasons such as intolerance) may have resulted in an underestimation of the difference between the reported current concerns among prior and current recipients.

The higher number of post-cancer onset physical and emotional concerns associated with some factors that are not easily modifiable (i.e., number of children, receipt of chemotherapy, age, time since cancer diagnosis, duration of treatment) is similar to reports of concerns among survivors previously treated with radiation and/or chemotherapy [27, 29]. Some of these characteristics (in particular younger age and receipt of chemotherapy) as well as treatment-emergent concerns have also been shown to be predictors of premature AET discontinuation [6], indicating that sociodemographic and medical factors that threaten AET adherence may overlap with some factors that relate to a higher number of post-treatment concerns. In this way, supportive care efforts might be targeted towards those survivors whose sociodemographic and/or medical characteristics place them at high risk for both AET non-adherence and increased post-treatment concerns.

Limitations

The strengths of our study relate to the utilization of the LIVESTRONG 2010 survey data. This data set includes a large sample of breast cancer survivors at different stages in their cancer survivorship trajectories, which enables comparison of multiple physical and emotional concerns between those who have previously taken, are currently taking, or have never taken AET. However, there are several important limitations worth noting. First, the survey was designed to probe general concerns relevant to cancer survivors, and as such does not provide insight into some adverse effects of AET such as vasomotor symptoms and arthralgias. The survey relied on self-report assessments of cancer treatment history and AET exposure. Therefore, we do not have specific agent or dosing information about chemotherapy, radiation, and endocrine treatment histories. Additionally, the data does not specify whether respondents who have previously taken AET were able to complete their entire course, or if they prematurely discontinued the medication due to intolerance. Furthermore, the number of concerns rather than the severity of concerns was assessed; hence, the impact of severity of concerns on global functioning cannot be determined. Second, there is a potential selection bias given that the survey respondents consisted of those who volunteered to complete an online questionnaire; the women in this sample are likely not representative of the entire population of breast cancer survivors. Finally, the cross-sectional nature of the data makes it impossible to determine whether AET exposure caused the differences in reported physical and emotional concerns observed in the data. More longitudinal research that measures physical and emotional concerns before AET exposure and over time during the course of treatment is needed to fully understand the role of AET in physical and emotional functioning among breast cancer survivors. While these results cannot confirm the hypothesis that AET exposure causes more

physical and emotional concerns in the post-treatment period, the data presented here do lend support to continued research on this important topic, and can be valuable in generating hypotheses concerning ways in which supportive care might help women adhere to AET regimens.

In conclusion, breast cancer survivors who are currently taking or have previously taken AET in this nationwide sample were more likely to experience an increased number of physical concerns in the post-treatment period. Further research is needed to help design individualized, yet cost-efficient management approaches that target the unique needs of not only current, but also prior AET recipients. These data also suggest the need for innovative care models that allow: (1) monitoring of survivors' patient-reported outcomes over time and (2) responding in a timely, pro-active manner that meets the dynamic needs of these cancer survivors (e.g., interval provision of mailed, online, phone, or even face-to-face support depending on the nature and severity of survivors' needs).

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Conflict of interest The authors declare that they have no conflict of interest.

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