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Endocrine therapy and urogenital outcomes among women with a breast cancer diagnosis

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Abstract

Purpose—Endocrine therapy for breast cancer can exacerbate menopausal symptoms. The association between endocrine therapy and common pelvic floor disorders including urinary incontinence has rarely been evaluated. We examined urogenital and sexual side effects among women with a breast cancer diagnosis, comparing endocrine therapy users to nonusers.

Methods—Urogenital and sexual symptoms were self-reported during the enrollment interview within the University of North Carolina Cancer Survivorship Cohort. Tumor characteristics and endocrine therapy use were collected from medical and prescription records. We calculated multivariable prevalence ratios (PR) and 95 % confidence intervals (CI) for the association of endocrine therapy (versus no endocrine therapy) and urinary incontinence, overall and by therapy type (tamoxifen or aromatase inhibitors). PROMIS Sexual Function and Satisfaction domain scores were compared across endocrine therapy groups.

Results—Among the 548 women with a breast cancer diagnosis, 49 % received endocrine therapy. Overall, 18 % of women reported urinary incontinence symptoms. We observed no association between urinary incontinence and endocrine therapy use overall (PR = 0.97; 95 % CI

0.67, 1.43), tamoxifen (PR = 1.20; 95 % CI 0.74, 1.96), or aromatase inhibitors (PR = 0.89; 95 % CI 0.55, 1.42), compared to no use. Approximately 55 % of women were sexually active. Sexual function scores did not vary according to endocrine therapy use, although urinary incontinence was associated with lower satisfaction scores ($p = 0.05$).

Conclusions—Our findings demonstrate a high prevalence of urinary incontinence after breast cancer diagnosis similar to the overall prevalence in older U.S. women, and this did not vary strongly according to use of endocrine therapy.

Background

Breast cancer is the most frequently diagnosed cancer in women in the USA, with an expected 231,840 new cases of invasive breast cancer to have been diagnosed in 2015 [1]. Long-term survival following a breast cancer diagnosis is nearly 90 % [2], making the health and well-being of the more than 3 million breast cancer survivors living in the USA a public health priority [3].

Adjuvant endocrine therapy is indicated for breast cancer patients with hormone receptor-positive invasive breast cancers, which comprise approximately 75 percent of cases overall [3]. Premenopausal women with hormonally responsive tumors are treated with tamoxifen in the adjuvant setting; postmenopausal women have the additional option of using aromatase inhibitors (AIs) for endocrine therapy [4]. Endocrine therapies have been associated with the onset or exacerbation of menopausal symptoms and can cause urogenital side effects including vaginal dryness, incontinence, and painful intercourse [5]. Evidence suggests that AIs may be more strongly associated with sexual function symptoms than tamoxifen due to their systemic anti-estrogenic effects. In contrast, tamoxifen can act both as a pro- or anti-estrogen, depending on the tissue [6–8].

Endocrine therapy may also impact the prevalence of common conditions such as urinary incontinence by altering the pelvic floor, but little research exists to address this possibility. In the USA, 15–20 % of women over 50 years old report experiencing urinary incontinence symptoms [9, 10]. Adult cancer survivors, including survivors of breast cancer, have been shown to be more likely to report urinary incontinence than those without a history of cancer [11]. Many breast cancer survivors may be faced with both age-related and potential endocrine therapy-related increases in pelvic floor disorders, including sexual dysfunction; however, limited data exist regarding these issues [12–15]. As the breast cancer survivor population continues to grow, addressing therapy side effects that contribute to health-related quality of life has become a key concern. To examine the association between endocrine therapy use and incident urinary incontinence and sexual dysfunction, we analyzed data from the University of North Carolina at Chapel Hill (UNC) Cancer Survivorship Cohort.

Methods

Study population

The UNC Cancer Survivorship Cohort is an ongoing registry of well-characterized cancer patients that integrates clinical, epidemiological, and interview data with correlated biologic specimens including DNA and tumor tissue. Patients included in this study were recruited through UNC Health Care oncology outpatient clinics from August 2010 to August 2015. Eligibility criteria for enrollment in the UNC Cancer Survivorship Cohort include: ages 18 years or older; a North Carolina mailing address; and English or Spanish proficiency. All participants provided informed consent in either English or Spanish. This project was reviewed and approved by the Human Research Protections Program (IRB Number: 09-0605) at UNC Chapel Hill.

For this analysis, patients were further restricted to women with a pathologically confirmed diagnosis of stage 0–3 breast cancer who were diagnosed or treated in the UNC Health Care system and who completed a baseline questionnaire. We further excluded participants who did not have timing information on the start of their endocrine therapy ($n = 7$) and women whose baseline questionnaire was recorded prior to their diagnosis date ($n = 3$). When analyzing urinary incontinence outcomes, we further excluded women who reported having urinary incontinence prior to breast cancer diagnosis ($n = 80$) to exclude prevalent cases. After these exclusions, 468 women contributed data to our urinary incontinence analysis and 548 women contributed to the analysis of sexual function (Fig. 1).

Data collection

Self-reported demographics including age, race/ethnicity, employment, education and marital status were obtained at enrollment. The baseline interview was completed by trained staff using a computer-assisted telephone interview software tool. The interview took approximately 1 h, during which participants responded to both general (45 min) and cancer-specific (15 min) survey questions, including the patient's health history, lifestyle, health care, and health-related quality of life indicators.

Exposure assessment

Endocrine therapy drugs were obtained from one of two electronic medical record databases: the UNC Health Care pharmacy prescription database and the patient's self-reported medication list. When the pharmacy prescription database and the patient's self-reported medication list were not concordant (22 %), medical records were manually abstracted by a blinded certified tumor registrar to correctly classify patients' endocrine therapy status. Endocrine therapy was classified in this analysis as use versus nonuse prior to the baseline questionnaire and further classified as use of tamoxifen, AIs, or multiple drugs. For the urinary incontinence analysis, women who reported the onset of incontinence symptoms after breast cancer diagnosis but prior to endocrine therapy initiation were analyzed as nonusers.

Outcome assessment

Urinary incontinence was defined by participant interview responses to the question "How often do you leak urine?" Possible responses were never, about once a week or less, two or three times a week, about once a day, several times a day, or all the time. We defined never versus any self-reported leakage to indicate urinary incontinence. Stress incontinence was defined as leakage with coughing or sneezing or physical activity/exercise. Urgency incontinence was defined as leakage before reaching the toilet or when sleeping. Participants were also asked "In what month and year did you first start to leak urine? (MM/YYYY)," and these responses were used to estimate the timing of urinary incontinence.

The PROMIS Sexual Function and Satisfaction Measures Brief Profile (SexFS) provides scores on seven different subdomains of sexual function, including interest in sexual activity, vaginal discomfort, lubrication, orgasm, and global satisfaction with sex life. Responses to this questionnaire were used to create a raw summed score for each question in a given subdomain and then translated to a standardized T-score. For the subdomains of global satisfaction with sex life, interest in sexual activity and lubrication, higher scores indicate better sexual health outcomes. The vaginal discomfort subdomain is scored so that higher scores indicate more negative sexual health outcomes (i.e., more discomfort) [16, 17]. Minimally important differences in domain scores were defined as half the standard deviation of domain score means [18]. This questionnaire has been validated in cancer populations [16].

Statistical analysis

Frequencies and proportions of demographic and clinical characteristics were generated by endocrine therapy status (yes/no) and type (tamoxifen or AI). Few participants ($n = 20$, 4.3 %) switched between tamoxifen and AIs and were excluded from analyses. Continuous variables such as age, time since diagnosis, and body mass index (BMI) were categorized into clinically meaningful groupings. Domain scores from the SexFS questionnaire were summarized by estimating means and standard deviations.

Prevalence ratios (PR) and 95 % confidence intervals (CI) estimates were calculated using a Poisson distribution with robust standard errors to approximate the binomial distribution [19]. Covariates were selected based on expert opinion and the scientific literature on endocrine therapy use, urinary incontinence, and sexual function and included for age, time since diagnosis, race, parity, smoking status, hysterectomy history, and BMI.

To analyze the PROMIS sexual function measures, we estimated adjusted means using generalized linear models for continuous dependent variables. Each domain score (satisfaction, interest, vaginal discomfort, and lubrication) was evaluated as a continuous outcome in models adjusting for age at study entry and time from diagnosis to baseline questionnaire. All analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC).

Results

Among the 548 breast cancer survivors in our study, 270 (49.3 %) received endocrine therapy prior to study entry. The average age at enrollment was 58.1 years, with most ages at

diagnosis and study enrollment falling between 51 and 60 years (Table 1). Average age at diagnosis was 55.6 years. Among women with ER+ breast cancer who had not used endocrine therapy at the time of symptom assessment, 69.5 % initiated endocrine therapy after enrollment ($n = 107$) and 17.5 % had stage 0 disease, where endocrine therapy is less common due to variability in treatment strategies. Women with ER− breast cancer who had received endocrine therapy either had stage 0 (in situ) disease or PR+ tumors. The average time from breast cancer diagnosis to study entry was 2.6 years (SD = 3.3 years; range <1 to 21).

Among the 468 women in the urinary incontinence analysis (Fig. 1), 86 (18.4 %) reported urinary incontinence symptoms. We observed no association between endocrine therapy and urinary incontinence overall (PR = 0.97; 95 % CI: 0.67, 1.43), or specific to use of tamoxifen (PR = 1.20; 95 % CI: 0.74, 1.96) or AIs (PR = 0.89; 95 % CI 0.55, 1.42), adjusting for age, time since diagnosis, race, parity, smoking status, hysterectomy history, and BMI (Table 2). In a sensitivity analysis restricting the study population to women with ER+ breast cancer, age-adjusted and multivariable prevalence ratios were similar to the overall estimates (data not shown). We also considered a more stringent definition of urinary incontinence that required leaking urine at least 2–3 times per week. With this definition, there were 54 cases of incontinence and the multivariable-adjusted PR for the association with endocrine therapy was 0.95 (95 % CI 0.57, 1.57). The majority of women who reported urinary incontinence had symptoms characteristic of both stress and urgency incontinence, also known as mixed incontinence ($n = 44/86$, 51.2 %). Therefore, sample sizes were insufficient to analyze stress or urgency incontinence alone. The prevalence ratios for urinary incontinence overall, any stress, or any urgency incontinence were suggestive of increased risk among tamoxifen users in age-adjusted models (PR = 1.37–1.82) but were attenuated after multivariable adjustment (PR = 1.20–1.67) and were not statistically significant. PRs for incontinence among AI users were generally closer to or below the null across incontinence definitions.

In our study population of women with a breast cancer diagnosis, 40–47 % reported no sexual activity in the last 30 days across domains of the SexFS questionnaire. Among those who were sexually active, there were no statistically significant differences according to endocrine therapy use across the domains of satisfaction, interest, vaginal discomfort, or lubrication. Mean scores showed slightly higher interest in sexual activity (45.4 vs. 44.0, $p = 0.08$) and greater vaginal discomfort (44.8 vs. 42.8, $p = 0.07$) among women who used endocrine therapy compared to nonusers. However, differences were not large enough to exceed the minimally important difference for each domain (Table 3).

We further explored the relation between urinary incontinence and sexual function among women in our study. In age-adjusted models, urinary incontinence was significantly associated with lower scores in the satisfaction with sex life subdomain ($p = 0.05$), but not other sexual function domains. The proportion of women reporting no sexual activity was similar between women who did and did not experience urinary incontinence (43–44 %).

Discussion

In our sample of women with early-stage breast cancer treated in the UNC Health Care system, we observed no overall difference in the prevalence of urinary incontinence or sexual dysfunction according to endocrine therapy use. The estrogenic response in pelvic floor tissues may vary between tamoxifen and AIs; however, no significant differences were observed for either type of endocrine therapy in our study population. These results provide reassuring evidence for women and providers that endocrine therapy may not substantially increase risk of urinary incontinence or sexual dysfunction after accounting for other factors including age, race, parity, or prior hysterectomy.

Our findings are consistent with a study conducted in postmenopausal breast cancer patients in Sweden, which detected no significant differences in urinary incontinence between endocrine therapy users and control subjects without treatment [19]. The Swedish study reported increased prevalence of sexual dysfunction symptoms associated with endocrine therapy, including vaginal dryness and pain with sexual intercourse. However, the comparison group consisted of women without breast cancer, [19] whereas our study compared endocrine therapy users to other women with breast cancer who did not use endocrine therapy.

Limited existing data suggest that the impact of estrogen on urinary incontinence varies based on whether estrogens are administered systemically (oral estrogens) or locally (vaginal estrogens) [13, 20, 21]. Oral menopausal hormone therapy with estrogen or estrogen plus progestin increased incidence of urinary incontinence after one year of treatment among participants in the Women's Health Initiative trials (estrogen plus progestin trial RR 1.39, 95 % CI 1.27, 1.52; estrogen alone trial 1.53, 95 % CI 1.37, 1.71) [13], suggesting that increasing systemic estrogen levels may be associated with urinary incontinence. However, topical estrogens used locally have been associated with a reduction in incontinence for postmenopausal women [20]. Although not statistically significant, our estimates for AIs, which work by blocking estrogen synthesis, were in the direction of a decreased risk of urinary incontinence (PR 0.89, 95 % CI 0.55, 1.42). Additionally, the Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial showed a reduced incidence of urinary incontinence associated with anastrozole, an AI, as compared with tamoxifen (2 % versus 4 %) [22]. Our study population had a lower prevalence of urinary incontinence (18 %) than other similar studies of women with breast cancer, with estimates ranging from 36 to 73 % [5, 19]; however, our population was also slightly younger (58.1 versus 62.7), not limited to postmenopausal women, and excluded preexisting urinary incontinence prior breast cancer diagnosis.

Our findings are consistent with a previous study that reported a minimal impact of endocrine therapy on sexual function [23]. Researchers evaluated sexual function before and after six months of endocrine therapy in a population of 66 postmenopausal women who had completed primary breast cancer therapy. Sexual function, as defined by lubrication, pain during intercourse, and sexual desire, arousal or satisfaction remained stable after endocrine therapy [23]. In an investigation of quality of life indicators during the first two years of the ATAC trial, tamoxifen users reported greater incidence of vaginal irritation, bleeding, or

spotting than AI users; however, AI users were more likely to report pain or discomfort with intercourse (AI 17.8 %, tamoxifen 7.5 %) and loss of interest in sex (AI 15.8 %, tamoxifen 8.5 %) [7]. Though our results were not statistically significant, we observed differences in SexFS subdomain scores that suggest endocrine therapy users may have more trouble with vaginal discomfort and lubrication than nonusers, which is consistent with study results suggesting that both tamoxifen and AIs are associated with these effects [8, 19]. Vasomotor symptoms such as vaginal dryness appeared to be associated with both tamoxifen and AI use in our study and previous work [19].

Strengths of our analysis include a larger sample size to address these questions compared to prior reports [19, 23]. Extensive self-reported information was augmented by tumor and treatment information from medical records and prescription databases to obtain accurate information on endocrine therapy use and timing. Additionally, the PROMIS SexFS questionnaire has been previously validated in cancer patient populations to measure sexual function [16]. While the urinary incontinence assessment has not been previously validated, the prevalence of urinary incontinence in our sample was consistent with national averages for women over 50 in the general population [10].

Limitations of our analysis should also be considered. We did not have detailed information on the duration of endocrine therapy use or adherence to treatment. Additionally, women who were exposed to endocrine therapy were more likely to be further from diagnosis than those who were not (average time since diagnosis = 3.4 vs. 1.8 years, respectively). However, adjustment for years since diagnosis had minimal impact on multivariable model estimates. The majority of participants in our study were diagnosed with breast cancer within three years of study enrollment. Nearly half of our population reported no sexual activity in the last 30 days and, therefore, did not contribute to three of the four domain scores. This impacted our ability to look closely at the differences between tamoxifen and AI users. Sample sizes were also insufficient for stratified analyses of stress and urgency incontinence alone.

Urinary incontinence is a highly prevalent condition (15 %) among U.S. women over 50. In our study, the prevalence among women with a breast cancer diagnosis was similar and was associated with lower satisfaction scores on validated sexual function scales for women with a cancer diagnosis. Providers should be attentive to these symptoms whether or not endocrine therapy is recommended as part of the treatment plan.

Acknowledgments

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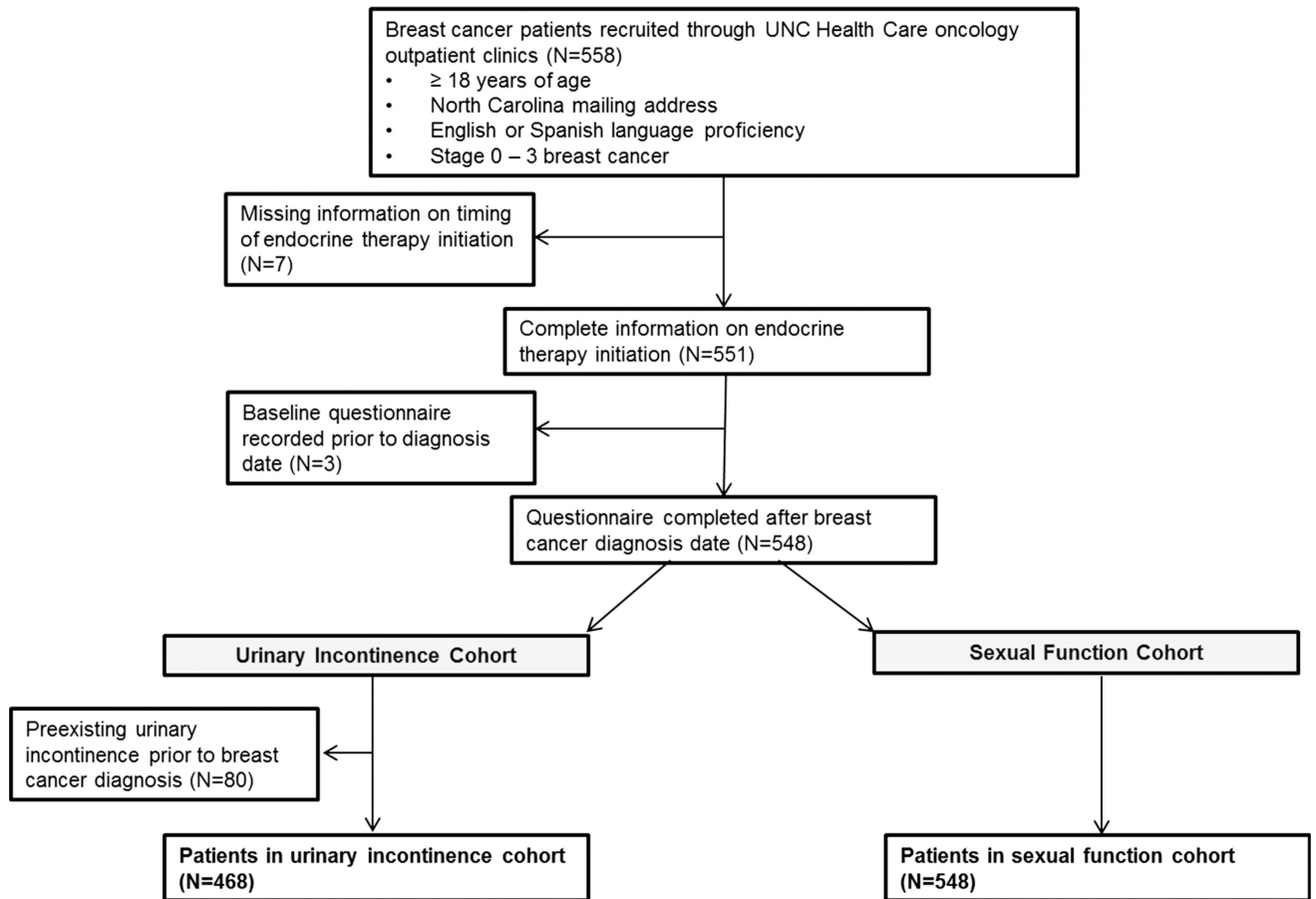**Fig. 1.**
Study flow chart for cohort selection for participants selected from the UNC Health
Registry, August 2010–August 2015

Table 1

Cohort characteristics, by endocrine therapy status and type of therapy ($n = 548$)

Characteristics	No endocrine therapy[a] (n = 278)	Endocrine therapy (n = 270)	Tamoxifen (n = 107)	Aromatase inhibitors (n = 131)
Age at enrollment				
18–40	18 (6.5)	6 (2.2)	5 (4.7)	0 (0.0)
41–50	67 (24.1)	44 (16.3)	33 (30.8)	5 (3.8)
51–60	89 (32.1)	81 (30.0)	44 (41.1)	28 (21.4)
61–70	77 (27.7)	98 (36.3)	16 (15.0)	71 (54.2)
70–88	27 (9.7)	41 (15.2)	9 (8.4)	27 (20.6)
Age at diagnosis				
18–40	28 (10.1)	15 (5.6)	11 (10.3)	0 (0.0)
41–50	71 (25.5)	61 (22.6)	45 (42.1)	7 (5.3)
51–60	93 (33.1)	87 (32.2)	35 (32.7)	43 (32.8)
61–70	66 (23.7)	77 (28.5)	11 (10.3)	60 (45.8)
70–85	21 (7.6)	30 (11.1)	5 (4.7)	21 (16.0)
Time since diagnosis				
0 to 1 year	181 (65.1)	61 (22.6)	22 (20.6)	36 (27.5)
>1 to 2 years	28 (10.1)	65 (24.1)	24 (22.4)	38 (29.0)
>2 to 3 years	18 (6.5)	36 (13.3)	16 (15.0)	18 (13.7)
>3 to 21 years	51 (18.4)	108 (40.0)	45 (42.1)	39 (29.8)
Race				
White	196 (70.5)	220 (81.5)	83 (77.6)	110 (84.0)
Black	68 (24.5)	35 (13.0)	18 (16.8)	16 (12.2)
Other	14 (5.0)	15 (5.6)	6 (5.6)	5 (3.8)
Stage				
0	43 (15.5)	28 (10.4)	18 (16.8)	8 (6.1)
1	104 (37.4)	122 (45.2)	34 (31.8)	75 (57.3)
2	101 (36.3)	87 (32.2)	42 (39.3)	35 (26.7)
3	30 (10.8)	33 (12.2)	13 (12.2)	13 (9.9)
Estrogen receptor test status				
Positive	154 (55.4)	259 (95.9)	100 (93.5)	128 (97.7)
Negative	117 (42.1)	4 (1.5)	2 (1.9)	2 (1.5)
Unknown	7 (2.5)	7 (2.6)	5 (4.7)	1 (0.8)
Received chemotherapy				
Yes	170 (64.4)	127 (47.0)	54 (49.5)	54 (41.2)
No	99 (35.6)	143 (53.0)	53 (49.5)	77 (58.8)
Parity				
0	48 (17.3)	40 (14.8)	13 (9.9)	21 (19.6)
1 or 2	152 (54.7)	154 (57.0)	75 (57.3)	64 (59.8)
3–8	76 (27.3)	73 (27.0)	43 (32.8)	19 (17.8)
Missing	2 (0.7)	3 (1.1)	0 (0.0)	3 (2.8)

Characteristics	No endocrine therapy[a] (n = 278)	Endocrine therapy (n = 270)	Tamoxifen (n = 107)	Aromatase inhibitors (n = 131)
Smoking status				
Never	152 (54.7)	166 (61.5)	64 (59.8)	81 (61.8)
Former	95 (34.2)	87 (32.2)	36 (33.6)	42 (32.1)
Current	22 (7.9)	9 (3.3)	3 (2.8)	5 (3.8)
Missing/do not know	9 (3.2)	8 (3.0)	4 (3.7)	3 (2.3)
Hysterectomy				
Yes	85 (30.6)	87 (32.2)	28 (26.2)	47 (35.9)
No	193 (69.4)	183 (67.8)	79 (73.8)	84 (64.1)
Body mass index (kg/m^2)				
<18.5	3 (1.1)	2 (0.7)	1 (0.9)	1 (0.8)
18.5–24.9	90 (32.4)	88 (32.6)	40 (37.4)	35 (26.7)
25.0–29.9	79 (28.4)	87 (32.2)	32 (29.9)	45 (34.4)
>30.0	102 (36.7)	91 (33.7)	34 (31.8)	48 (36.6)
Missing	4 (1.4)	2 (0.7)	0 (0.0)	2 (1.5)

[a] Endocrine therapy is defined as receiving endocrine therapy prior to study entry. Women in the "no endocrine therapy" group may have later received endocrine therapy after completing the baseline questionnaire

Table 2

Age-adjusted and multivariable prevalence ratios for the association of endocrine therapy and self-reported urinary incontinence

	Urinary Incontinence	No urinary Incontinence	Age-adjusted[a]		Multivariable-adjusted[b]	
	$n = 86$	$n = 382$	PR	95 % CI	PR	95 % CI
No endocrine therapy	40 (46.5)	204 (53.4)	1.00	Ref	1.00	Ref
Endocrine therapy	46 (53.5)	178 (46.6)	1.11	0.75, 1.62	0.97	0.67, 1.43
Tamoxifen	19 (22.1)	73 (19.1)	1.37	0.86, 2.19	1.20	0.74, 1.96
Aromatase inhibitors	22 (25.6)	84 (22.0)	0.94	0.59, 1.51	0.89	0.55, 1.42
	Any stress incontinence	No urinary incontinence	Age-adjusted[a]		Multivariable-adjusted[b]	
	$n = 64$	$n = 382$	PR	95 % CI	PR	95 % CI
No endocrine therapy	26 (40.6)	204 (53.4)	1.00	Ref	1.00	Ref
Endocrine therapy	38 (59.4)	178 (46.6)	1.37	0.86, 2.18	1.26	0.78, 1.98
Tamoxifen	16 (25.0)	73 (19.1)	1.82	1.04, 3.18	1.67	0.96, 2.92
Aromatase inhibitors	19 (29.7)	84 (22.0)	1.24	0.72, 2.17	1.13	0.64, 1.98
	Any urge incontinence	No urinary incontinence	Age-adjusted[a]		Multivariable-adjusted[b]	
	$n = 62$	$n = 382$	PR	95 % CI	PR	95 % CI
No endocrine therapy	30 (48.4)	204 (53.4)	1.00	Ref	1.00	Ref
Endocrine therapy	32 (51.6)	178 (46.6)	1.03	0.65, 1.62	0.92	0.58, 1.46
Tamoxifen	15 (24.2)	73 (19.1)	1.50	0.88, 2.56	1.29	0.72, 2.33
Aromatase inhibitors	15 (24.2)	84 (22.0)	0.85	0.48, 1.49	0.77	0.44, 1.35

[a] Adjusted for age at baseline questionnaire

[b] Adjusted for age at baseline questionnaire, time from diagnosis to study entry, race, parity, smoking status, hysterectomy history, and BMI categories

Table 3

Association of endocrine therapy with PROMIS sexual function and satisfaction measures domain scores[a]

Domain	n (%)	Mean (SD)	p value	Minimally important difference[b]
Satisfaction: higher scores indicate more satisfaction with sex life				
Endocrine therapy	119 (44.1 %)[c]	54.5 (0.8)	0.90	4.2
No endocrine therapy	111 (37.9 %)[c]	54.3 (0.8)		
Interest: higher scores indicate more interest in sexual activity.				
Endocrine therapy	238 (88.1 %)[d]	45.4 (0.6)	0.08	4.5
No endocrine therapy	233 (83.8 %)[d]	44.0 (0.6)		
Vaginal discomfort: Higher scores indicate more discomfort.				
Endocrine therapy	114 (42.2 %)[e]	44.8 (0.8)	0.07	4.0
No endocrine therapy	105 (37.8 %)[e]	42.8 (0.8)		
Lubrication: higher scores indicate more lubrication.				
Endocrine therapy	115 (42.6 %)[f]	53.4 (0.8)	0.38	4.5
No endocrine therapy	105 (37.9 %)[f]	54.5 (0.8)		

[a] Adjusted for age at baseline and time from breast cancer diagnosis to study entry

[b] Estimated as $0.5 \times$ SD of the overall domain score means [18]

[c] 121 (40.0 %) endocrine therapy users and 122 (44.8 %) nonusers reported no sexual activity in the last 30 days. 30 (11.1 %) endocrine therapy users and 45 (16.2 %) nonusers did not respond to questions comprising the satisfaction domain

[d] 32 (11.9 %) of endocrine therapy users and 45 (16.2 %) nonusers did not respond to questions comprising the interest domain. There were no non-applicable response options for this domain

[e] 127 (47.0 %) endocrine therapy users and 126 (45.3 %) nonusers reported no sexual activity in the last 30 days. 29 (10.7 %) endocrine therapy users and 46 (16.5 %) nonusers did not respond to questions comprising the vaginal discomfort domain

[f] 124 (45.9 %) endocrine therapy users and 127 (45.7 %) nonusers reported no sexual activity in the last 30 days. 31 (11.5 %) endocrine therapy users and 46 (16.5 %) nonusers did not respond to questions comprising the vaginal discomfort domain