

Urinary Symptoms in Breast Cancer

A Systematic Review

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A large body of research has documented the prevalence and severity of menopausal symptoms, especially vasomotor symptoms, in breast cancer survivors and their impact on quality of life. However, urinary symptoms as part of the constellation of menopausal symptoms have received relatively little attention. Thus, less is known about the prevalence and severity of urinary symptoms in breast cancer survivors. The authors of this report conducted a systematic review of studies published between 1990 and 2010 to describe the prevalence and severity of urinary symptoms in breast cancer survivors. In total, 16 eligible studies that involved >2500 women were identified. The studies varied with respect to purpose, design, and nature of the samples included; the majority used the same definition and assessment approach for urinary symptoms. Prevalence rates for symptoms ranged from 12% of women reporting burning or pain on micturition to 58% reporting difficulty with bladder control. Although, in many studies, the largest percentage of women rated symptoms as mild, 23% reported severe symptoms. Symptoms appeared to adversely affect women's quality of life. The authors concluded that there is a need for additional research assessing the natural history of urinary symptoms using consensus definitions and validated measures in diverse populations. Nevertheless, this review suggested that clinicians should screen for urinary symptoms in breast cancer survivors and should offer treatment recommendations or make referrals as appropriate. *Cancer* 2012;118:582-93. © 2011 American Cancer Society.

KEYWORDS: breast cancer, menopause, urogenital system, survivorship.

INTRODUCTION

Women with a history of breast cancer currently account for approximately 22% of cancer survivors in the United States, making them the largest group of cancer survivors today.¹ With ongoing advances in early detection and treatment, this trend is likely to continue. Nearly 90% of women who are diagnosed with invasive breast cancer are expected to survive >5 years after diagnosis.^{2,3} Consequently, interest has shifted increasingly to include the prevention and treatment of long-term and late effects of breast cancer and its treatment. In addition, national cancer research goals include a focus on survivorship issues to improve health-related outcomes and to enhance quality of life in survivorship.⁴ Consistent with this, the loss of menses because of chemotherapy and the menopausal transition have received considerable attention in breast cancer survivorship research.

Symptoms of menopause in women with breast cancer are typically the result of ovarian suppression and failure secondary to chemotherapy in premenopausal women and the use of endocrine therapy in both premenopausal and postmenopausal women.^{5,6} These symptoms often are more severe than those experienced with natural menopause.⁷⁻⁹ To date, a relatively large body of research has documented the prevalence and severity in breast cancer survivors of menopausal symptoms, especially vasomotor symptoms, such as hot flashes and night sweats, and genital symptoms, such as vaginal dryness, and their impact on quality of life in survivorship. Urinary symptoms also are commonly associated with menopause⁹⁻¹² and include urgency, urgency incontinence, stress incontinence, dysuria or burning, pelvic pressure and frequency, and recurrent urinary tract infections and dryness.⁶ Estrogen receptors have been identified in the structures of the lower urinary and genital tracts, including the uterus, vagina, ovaries, bladder, urethra, external genitalia, and pelvic

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floor muscles. Thus, researchers have postulated that the development of urinary symptoms in menopause may be the result of lower urinary tract atrophy secondary to estrogen deficiency.^{10,12-15} Urinary symptoms may occur after other menopausal symptoms, such as vasomotor symptoms, have abated.⁶ And, unlike menopausal vasomotor symptoms, if left untreated, urinary symptoms continue throughout life and may even worsen over time.^{16,17}

Research on women in the general population consistently has demonstrated that urinary symptoms adversely affect women's quality of life¹⁸⁻²⁰ and that the impact of these symptoms is determined by type and severity of symptoms.^{21,22} Treatment options for urinary symptoms associated with menopause depend on the symptom and its severity.¹⁷ There are several noninvasive, behavioral interventions available to treat mild-to-moderate symptoms.^{17,23-26} Many women with urinary symptoms, however, do not seek treatment because of embarrassment, a misconception that symptoms are a normal part of aging, uncertainty about available treatment options, or the belief that they can cope on their own.^{19,27-30}

Despite the attention to menopausal symptoms in breast cancer survivors, urinary symptoms as part of the constellation of menopausal symptoms appear to have received little attention. Consequently, less is known about the prevalence and severity of urinary symptoms and their impact on quality of life in breast cancer survivors. We conducted a systematic literature review to identify studies that assessed urinary symptoms as part of the constellation of menopausal symptoms in women with a diagnosis of breast cancer. The objectives of this report were to review and characterize the available scientific literature with respect to urinary symptoms and breast cancer and to describe the prevalence and severity of urinary symptoms in breast cancer survivors.

MATERIALS AND METHODS

Search and Selection Strategy

The identification of relevant studies began with electronic searches of English language journal articles in the Medline, PsycINFO, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases from 1990 through June 2010. The Medical Subject Heading search terms used were "breast neoplasms" and "menopause." The first 2 authors (K.A.D. and A.R.B.) separately screened study abstracts based on 2 eligibility criteria: 1)

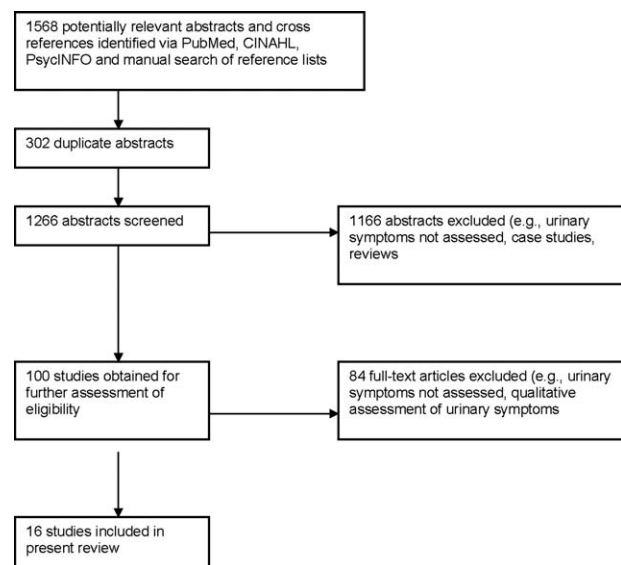


Figure 1. This chart illustrates the process of article identification for the current review.

each study must have been published in a peer-reviewed, English-language journal; and 2) each study had to report on the quantitative assessment of any urinary symptom in the context of menopausal symptoms and breast cancer. Articles that reported menopausal symptoms but that did not include urinary symptoms as part of the constellation of symptoms were excluded. Similarly, articles involving qualitative assessments of menopausal symptoms in women with breast cancer and reviews of existing research that summarized results from published studies on menopause in women with breast cancer were excluded. Reference lists from studies retrieved also were reviewed to ensure all possible studies were identified.

Review and Data Extraction

The first 2 authors (K.A.D. and A.R.B.) separately reviewed the retrieved studies and extracted data from all studies that met eligibility criteria using a standardized form. Data extracted included basic descriptive information from each study about participants, including demographic and clinical characteristics; the purpose and design of the study; and the manner in which menopausal symptoms, including urinary symptoms, were assessed. Extraction of results focused on published findings that provided information about urinary symptoms in women with a diagnosis of breast cancer. Any discrepancies in study eligibility criteria and data extraction were discussed, and a consensus was reached. Bias was reduced by conducting a comprehensive search of published studies

Table 1. Characteristics of Studies Included in the Systematic Review

Study	Study Design	Sample Size	Age: Mean±SD (Range), y	Race/ Ethnicity, %	Disease Characteristics, %	Treatment Characteristics, %	Menopausal Status, %	Position in Disease/ Treatment Trajectory, %	Time Since Diagnosis/ Treatment: Mean±SD (Range)
Alfano et al 2006 ⁴²	Longitudinal	803	56±10 (29-86)	White, 60.4; black, 24.8; Hispanic, 11.8	Localized, 56.4; regional, 21.4; in situ, 22.2	Surgery only, 32.3; surgery/radiotherapy, 36.9; surgery/chemotherapy, 9.2; surgery/radiation/chemotherapy, 21.7	At 24-mo assessment: premenopausal, 18.3; postmenopausal, 75.9; unclassifiable, 5.8; taking tamoxifen, 45	Post-treatment when checklist administered	40.5±6.5 mo
Avis et al 2004 ³⁶	Cross-sectional	204	43.5±6.2	Caucasian, 96; African American, 2; other, 2	Stage I, II, or III	No mastectomy, 56.5; mastectomy without reconstruction, 20; mastectomy with reconstruction, 23.5; initial chemotherapy, 74.9; initial radiation, 69.3	NR	Initial treatment ended, no current treatment, 70.3; initial treatment ongoing, 11.88; initial treatment ended, currently undergoing treatment 17.82	23.32±9.8 mo (4-42 mo)
Avis et al 2005 ⁴⁰	Cross-sectional	202	43.5±6.2	White, 96	Stage I, II, III, or recurrent disease	No mastectomy, 56.6; mastectomy without reconstruction, 19.7; mastectomy with reconstruction, 23.7; initial chemotherapy, 75.1; initial radiation, 69.6	NR	Initial treatment ended, no current treatment, 70.5; initial treatment ongoing, 12; initial treatment ended, currently undergoing treatment 17.5	23.32±9.8 mo (4-42 mo)
Chin et al 2009 ⁴⁶	Cross-sectional	251	60.5±10.79 (32-91)	NR	Early stage, 84; metastatic 16	Endocrine therapy for early stage, 84; being treated for metastatic disease, 16; on tamoxifen, 31; on aromatase inhibitor, 69	Postmenopausal, 100	NR	NR/mean duration of endocrine treatment, 23 mo (1-84 mo)
Couzi et al 1995 ³¹	Cross-sectional	190	54.9±6.1 (41-65)	White, 83; black, 14; other, 3	In situ BC, 15; invasive locoregional, 85	Surgery only with or without radiation, 37; adjuvant therapy in form of chemotherapy, tamoxifen, or both, 63; tamoxifen at time of survey, 35; ERT at some time before diagnosis, 29	Postmenopausal	Post-treatment: taking tamoxifen, 35	NR/NR
Ganz et al 2000 ³²	Randomized controlled trial	72	54.5±5.9	Asian, 1.4 [1]; black, 7 Hispanic, 1.4; white 90	7 Stage I or II	Lumpectomy, 67; mastectomy, 33; tamoxifen, 56; prior radiation, 69; prior chemotherapy, 47	Mean, 6.9±7.3 y postmenopausal	Between 8 mo and 5 y after diagnosis; completed treatment ≥4 mo prior	2.5±1.3 y
Ganz et al 2002 ³⁴	Longitudinal	763	Initial survey, 55.6; at follow-up, 58.5	White, 83.5; black, 8.9; other, 7.6	Stage I or II	Lumpectomy, 52.6; mastectomy, 28.5; mastectomy with reconstruction, 18.9; received chemotherapy, 42.2; on tamoxifen, 48.4	NR	Between 1 y and 5 y postdiagnosis at first assessment; between 5 y and 10 y post-diagnosis at follow-up	6.3 y (5.0-9.5 y)

(Continued)

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Study	Study Design	Sample Size	Age: Mean±SD (Range), y	Race/Ethnicity, %	Disease Characteristics, %	Treatment Characteristics, %	Menopausal Status, %	Position in Disease/Treatment Trajectory, %	Time Since Diagnosis/Treatment: Mean±SD (Range)
Ganz et al 2003 ³⁵	Cross-sectional	577	49.5 (30-61.6)	White, 70.2; African American, 11.6; Hispanic, 7.3; Asian, 8.5; other, 2.4	Stage 0, I, or II	Lumpectomy, 55.8; mastectomy, 44.2; reconstruction, 23.3; received adjuvant therapy, 62; ever used tamoxifen, 37.4; current tamoxifen, 18; adjuvant therapy: none, 27.5; tamoxifen only, 10.4; chemotherapy only, 35; tamoxifen and chemotherapy, 27	Premenopausal, 16; perimenopausal, 13; postmenopausal, 60; unclassifiable, 11	Disease free between 2 y and 10 y without recurrence/post-treatment	2 5.9±1.5 y
Greendale et al 2001 ³³	Cross-sectional	61	54.5 (43.1-70.3)	White, 92; nonwhite, 8	Stage I-II	Mastectomy, 38; lumpectomy, 62; current tamoxifen, 61; past chemotherapy, 46	Postmenopausal	At least 8 mo but not more than 5 y postdiagnosis; completed chemotherapy or radiotherapy ≥4 mo before enrollment	2.4 y (0.8-5.6 y)
Gupta et al 2006 ⁴³	Cross-sectional	200	53.9±8.21 (29-65)	Caucasian, 95.2; Afro-Caribbean, 1.1; Asian, 3.7	NR	Chemotherapy, 42; radiotherapy to lower abdomen or pelvis, 2.5; bilateral oophorectomy, 2.5; GnRH analog, 3.; tamoxifen, 56; anastrozole, 7.5	Premenopausal, 6.1; perimenopausal, 9.1; postmenopausal, 65.5; hysterectomy, 19.3	Received treatment within last 5 y	>5 y, 8%; 3-5 y, 20%; 1-3 y, 56%; <1 y, 16%
Land et al 2004 ³⁷	Longitudinal	160	≤49, 50.6%; 50-59, 32.5%; ≥60, 16.9	White, 74.4; black, 18.8; other, 3.7; unknown, 3.1	Axillary lymph node negative, ER negative	Surgery: lumpectomy and ALND, 58.1; modified radical mastectomy, 41.9; receiving AC or CMF	NR	NR	NR
Leining et al 2006 ⁴⁴	Cross-sectional	371	36.2	Caucasian, 89; African American, 2; other, 9; missing, 1	Stage 0-III	Radiation, 65; mastectomy, 58; no systemic treatment, 6; chemotherapy, 89; tamoxifen, 49; ovarian suppression, 15; aromatase inhibitors, 4%; at time of survey: Tamoxifen only, 36; ovarian suppression, 9; aromatase inhibitors only, 3	NR	At least 1 y postdiagnosis	1-2 y, 53%; 3-5 y, 33%; ≥6 y, 14%
Morales et al 2004 ³⁸	Longitudinal	164	62	NR	NR	Adjuvant hormone treatment, 80; palliative treatments, 20%	Mean, 10 y postmenopausal	Scheduled to start endocrine treatment	NR
Oleske et al 2004 ³⁹	Cross-sectional	123	58.3±4.0	White, 93	NR	NR	NR	At least 1 y from therapy	3.6±2.6 y

(Continued)

Table 1. (Continued)

Study	Study Design	Sample Size	Age: Mean±SD (Range), y	Race/Ethnicity, %	Disease Characteristics, %	Treatment Characteristics, %	Menopausal Status, %	Position in Disease/Treatment Trajectory, %	Time Since Diagnosis/Treatment: Mean±SD (Range)
Schover et al 2006 ⁴⁵	Randomized controlled trial	48	49.29±8.3 (30-77)	African American, 100	Stage 0-IIIa	Mastectomy without reconstruction, 33; mastectomy with reconstruction, 19; breast conservation, 48; past chemotherapy, 74; tamoxifen only in past, 17; tamoxifen currently, 25; currently taking other hormone therapy, 4	Currently having menstrual cycles 19 [9]	At least 1 y from diagnosis; had completed treatment except hormone therapy, not undergoing breast reconstruction	4.52±3.8 y
Stanton et al 2005 ⁴¹	Cross-sectional	Sample 1, 863; Sample 2, 577; Sample 3, 560; Sample 4, 208	Sample 1, 56±11.5 (31-88); Sample 2, 50±5.6 (30-62); Sample 3, 57±11.4 (27-87); Sample 4, 47±7.3 (20-66)	Sample 1, 77% white, 14% black, 9% other; Sample 2, 70% white, 12% black, 16% other; Sample 3, 86% white, 7% black, 7% other; Sample 4, 96% white, 3% black, 1% other	Sample 1, stage 0-II; Sample 2, stage 0-II; Sample 3, stage I-II; Sample 4, high risk	Chemotherapy: Sample 1, 38; Sample 2, 62; Sample 3, 50; Sample 4: NA; surgery (lumpectomy): Sample 1, 51; Sample 2, 56; Sample 3, 67; Sample 4, NA; tamoxifen (current): Sample 1, 47; Sample 2, 18; Sample 3, 54; Sample 4, 0	NR	Sample 1, diagnosed 5 y earlier; Sample 2, disease free for 2-10 y; Sample 3, recently completed treatment; Sample 4, NA	Sample 1, 36 mo (10-78 mo); Sample 2, 71 mo (18-140 mo); Sample 3, 7 mo (1-19 mo); Sample 4, NA

Abbreviations: AC, doxorubicin and cyclophosphamide; ALND, axillary lymph node dissection; BC, breast cancer; CMF, cyclophosphamide, methotrexate, and 5-fluorouracil; ER, estrogen receptor; ERT, external-beam radiotherapy; GnRH, gonadotropin-releasing hormone; NA, not available; NR, not reported; QOL, quality of life; SD, standard deviation.

in several electronic databases and searching reference lists of published reviews.

RESULTS

Search Results and Nature of Selected Studies

Of 1266 abstracts that were screened, 1166 did not meet eligibility criteria (Fig. 1). The complete texts of 100 published studies were retrieved, and an additional 84 studies were excluded based on eligibility criteria. Consequently, 16 publications³¹⁻⁴⁶ were included in this review (Table 1). Thirteen of the identified studies were conducted in the United States, and the remaining 3 studies were conducted in Belgium,³⁸ Canada,⁴⁶ and the United Kingdom.⁴³ The nature and purpose of each study varied widely. Five studies focused specifically on the prevalence and severity of menopausal symptoms in women with breast cancer.^{31,32,43-45} Two of those 5 studies tested an intervention that was focused at least in part on relieving menopausal symptoms.^{32,45} Four studies focused on treatments for breast cancer and their relation to menopausal symptoms.^{35,37,38,46} Two studies^{41,42} evaluated the psychometric properties of a modified version of the Breast Cancer Prevention Trial (BCPT) Symptom Checklist, a 43-item checklist from the National Surgical Adjuvant Breast and Bowel Project, a multicenter chemoprevention trial evaluating the efficacy of tamoxifen.⁴⁷ Another study used an early version of the BCPT Symptom Checklist to identify particular "problem areas" women experienced after breast cancer.³⁶ Three studies described quality of life,^{33,34,40} including sexual function, after breast cancer and included the assessment of menopausal symptoms in their assessment battery. Finally, 1 study assessed factors associated with hospitalization after breast cancer.³⁹ With respect to study design, the 16 studies identified included 10 cross-sectional studies, 4 longitudinal studies, and 2 randomized controlled intervention trials.

Demographic and Clinical Characteristics of Study Participants

All but 1 of the studies reported the mean age of the sample, which ranged from 36 years to 62 years. Eight of the studies also reported age range, and the women ranged in age from 27 years^{35,36,40,41,46} to 91 years. Three studies included only women who were aged ≤ 50 years at diagnosis, and 1 study⁴⁴ included only women who were aged ≤ 40 years at diagnosis. Fourteen studies provided race

and/or ethnicity information for participants. Across these studies, a mean of 84% of women were classified as white (range, 60%-96%), and a mean of 17% were classified as black or African American (range, 1%-100%).

With respect to disease characteristics, 13 studies provided information about disease stage. Across studies, the majority of patients had stage I through III disease, some patients had stage 0 disease, and some had recurrent disease. Ten studies reported the mean time since diagnosis, which ranged from 7 months to 6.3 years. Five of the studies also reported the range of time since diagnosis: the shortest time since diagnosis was 1 month,⁴¹ and the longest was 11.7 years.⁴¹ With respect to position in the treatment trajectory, 1 study³⁷ included only women who were in active treatment. Twelve studies included only women who had completed adjuvant therapy. Of these, 10 studies specified whether the women were receiving endocrine therapy after having completed adjuvant therapy. Two studies were exclusive to women who were receiving endocrine therapy for early stage or advanced breast cancer.^{38,46} Finally, 2 studies,^{36,40} which were drawn from the same sample of women, included both women who were post-treatment and women who were in active treatment.

Thirteen studies provided details about adjuvant therapies received by study participants. Each of these studies included women who had received some combination of surgery and chemotherapy; most studies also included women who had received radiotherapy. No samples were comprised exclusively of women who had undergone surgical resection and received chemotherapy with or without radiotherapy. For example, in the study by Alfano et al,⁴² 32.3% of patients had undergone surgery only, 36.9% had undergone surgery and received radiotherapy, 9.2% underwent surgery and received chemotherapy, 21.7% underwent surgery and received both radiotherapy and chemotherapy; and 45% were receiving tamoxifen. One study,³⁷ as noted above, involved women who were active treatment with doxorubicin and cyclophosphamide (AC) or with standard cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) and tamoxifen or placebo after surgical resection. In addition, as also noted above, most studies included information about whether the women were currently receiving endocrine therapy. Of those studies that provided no detail about adjuvant therapy with surgery, chemotherapy, or radiotherapy, 2 studies^{38,46} limited participation to those women who were currently receiving endocrine therapy.

Assessment of Menopausal Symptoms

The assessment of menopausal symptoms varied minimally across studies (Table 2).³¹⁻⁴⁶ Twelve studies used a modified version of the 43-item BCPT Symptom Checklist, which is a measure of common physical and psychological symptoms as well as symptoms associated with menopause and tamoxifen use. Respondents are asked to rate how bothered they were by each symptom during the past 4 weeks using a 5-point Likert scale ranging from 0 to 4, with 0 indicating not bothered at all; 1, slightly bothered; 2, moderately bothered; 3, bothered quite a bit; and 4, extremely bothered. The versions used in the 12 studies included an early 50-item version that was later modified for use in the BCPT,³⁹ 42-item versions,³⁵ 16-item versions,^{42,44} 15-item versions,^{36,40} and an “abbreviated” version with the number of items not specified.³⁴ One study³⁷ used a symptom checklist constructed from existing instruments, including the BCPT Symptom Checklist. Four studies used the 7-item Menopausal Symptom Scale adapted from the 43-item BCPT Symptom Checklist.^{32,33,41,45} The study by Stanton et al⁴¹ used both the 42-item version of the BCPT Symptom Checklist and the 7-item Menopausal Symptom Scale. Among the 4 studies that did not use the BCPT Symptom Checklist, the approach to assessing menopausal symptoms included a study-specific, 66-item survey that included vasomotor and gynecologic symptoms³¹; the Functional Assessment of Cancer Therapy-Endocrine Symptoms scale supplemented by study-specific questions about urinary symptoms⁴⁶; the 10-item Menopause Rating Scale⁴³; and the 20-item Leuven menopause form.³⁸

Assessment of Urinary Symptoms

All of the studies assessed urinary symptoms as part of a constellation of menopausal or hormone-related symptoms. Twelve studies used some version of the BCPT Symptom Checklist to assess the relevant symptoms, as noted above. In 10 of those 12 studies, urinary symptoms were assessed with 2 items: “difficulty with bladder control when laughing or crying” and “difficulty with bladder control at other times.” Respondents were asked to rate how bothered they were by each symptom during the past 4 weeks using the 5-point Likert scale described above. The 4-week time frame was used in each of the 10 studies with 1 exception: the study by Alfano et al⁴² used the past year as the time period of interest. The 2 (of 12) remaining studies that used some version of the BCPT Symptom Checklist apparently did not include both bladder-control items but reportedly used “difficulty in bladder control”³⁹

and “bladder problems”³⁷ to assess urinary symptoms, although this is not completely clear. Difficulty in bladder control was rated on a 4-point Likert scale ranging from 0 (not present) to 3 (serious problem)³⁹ in the past 7 days, whereas “bladder problems” were rated with respect to bother associated with the symptom on a 5-point Likert scale ranging from 0 (not at all) to 4 (very much) in the past 7 days and since the beginning of the last chemotherapy cycle.³⁷

Urinary symptoms were assessed in various ways in the remaining studies. For example, Morales et al³⁸ defined “urinary problems” as “frequent urination (even at night) and urgency, urine loss when coughing, sneezing, and laughing,” and then asked respondents in a single question to rate the degree of inconvenience associated with these urinary problems during the past 7 days. Chin et al⁴⁶ used 4 questions specific to dysuria, urinary incontinence, urgency, and increased frequency of urinary tract infections in which respondents rated how true a statement about each of these symptoms had been for them in the past 7 days on a 5-point Likert scale.

Prevalence and Severity of Urinary Symptoms

Ten of the 16 studies reported data related to the prevalence of urinary symptoms. In general, the rate of women reporting any type of urinary symptom ranged from a low of 12% reporting burning or pain on micturition in a study of women who were receiving endocrine therapy for early stage or metastatic breast cancer⁴⁶ to a high of 58% reporting difficulty with bladder control at other times in a study of the psychometric properties of a BCPT-derived checklist for measuring hormone-related symptoms in breast cancer survivors.⁴² Across those studies that assessed bladder-control using items from the BCPT Symptom Checklist,^{31,32,36,39,40,42,44} a mean of 37% reported difficulty with bladder control either in general, when laughing or crying, or at other times. In 2 studies,^{38,43} a mean of 34% reported “urinary problems.”

Nine studies reported data related to the perceived severity of urinary symptoms. The method of reporting these data and, thus, the information provided with respect to symptom severity was quite variable. In 3 of these 9 studies,^{41,42,45} data were reported as mean scores on the BCPT 5-point Likert scale of bother associated with symptoms. For example, in the study by Alfano et al,⁴² which was designed to evaluate the psychometric properties of a 16-item version of the BCPT Symptom Checklist, the mean ($\pm$ standard deviation) severity score for women reporting difficulty with bladder control while

Table 2. Assessment of Menopausal and Urinary Symptoms by Studies Included in the Systematic Review

Study	Assessment of Menopausal Symptoms	Assessment of Urinary Symptoms	Prevalence/Severity of Urinary Symptoms
Alfano et al 2006 ⁴²	16 Items from BCPT Symptom Checklist	In past y, difficulty with bladder control when laughing or crying and difficulty with bladder control at other times; Bother rated from 0 (<i>not at all</i>) to 4 (<i>extremely</i>)	Difficulty with bladder control when laughing or crying, 46% (mean±SD severity, 1.8±0.9); difficulty with bladder control at other times, 58.2% (mean±SD severity, 1.8±1.0)
Avis et al 2004 ³⁶	15 Items from BCPT Symptom Checklist	In past 4 wk, how bothered have you been by difficulty with bladder control when laughing or crying/at other times: From 1 (<i>not at all</i>) to 5 (<i>very much</i>)	Bladder control/laughing: Not at all, 74.8%; a little, 9.9%; somewhat, 8.9%; quite a bit, 4%; very much, 2.5%; bladder control/other: Not at all, 73.9%; a little, 14.3%; somewhat, 6.4%; quite a bit, 3.5; very much, 2%; difficulty with bladder control was reported as bothersome by <30%
Avis et al 2005 ⁴⁰	15 Items from BCPT Symptom Checklist	In past 4 wk, how bothered have you been by difficulty with bladder control when laughing or crying/at other times: From 1 (<i>not at all</i>) to 5 (<i>very much</i>)	Difficulty with bladder control by age category: 25-34 y, 25 patients (16%); 35-39 y, 41 patients (22%); 40-44 y, 54 patients (30.2%); 45-50 y, 82 patients (51.2%); total, 202 patients (35.3%); $P = .0007$; problems increased with age
Chin et al 2009 ⁴⁶	FACT-ES	In past 7 d, 4 questions about urinary tract symptoms since endocrine therapy; asked to indicate how true a statement was for them from 0 (<i>not at all</i>) to 4 (<i>very much</i>)	Dysuria: None, 87%; mild (score 1-2), 10%; moderate/severe (score 3-4), 2%; urinary incontinence: None, 63%; mild (score 1-2), 30%; moderate/severe (score 3-4), 3%; urinary urgency: None, 57%; mild (score 1-2), 27%; moderate/severe (score 3-4), 14%; increased urinary tract infections: None, 88%; mild (score 1-2), 8; moderate/severe (score 3-4), 4%
Couzi et al 1995 ³¹	Investigator-developed questionnaire	In last 4 wk, difficulty with bladder control	Reported symptom, 36% ($n = 66/183$); 55% of those reported symptom severity as mild, 22% as moderate, 23% as severe
Ganz et al 2000 ³²	7 Items adapted from BCPT Symptom Checklist	In past 4 wk, how bothered have you been by difficulty with bladder control when laughing or crying/at other times: From 0 (<i>not at all</i>) to 4 (<i>extremely</i>)	Reported "stress urinary incontinence" at baseline, 51%; 1 reported urinary incontinence only; 8 reported urinary incontinence and hot flashes; 27 reported urinary incontinence, hot flashes, and vaginal dryness; 1 reported urinary incontinence and vaginal dryness; at baseline, urinary scale score for all women, 0.59±0.82; effect of intervention on urinary incontinence not reported separately from menopausal symptoms
Ganz et al 2002 ³⁴	Items from BCPT Symptom Checklist	In past 4 wk, how bothered have you been by difficulty with bladder control when laughing or crying/at other times: From 0 (<i>not at all</i>) to 4 (<i>extremely</i>)	Frequency of bladder problems when laughing or crying ($P = .003$) and at other times ($P = .007$) increased significantly over time
Ganz et al 2003 ³⁵	42 Items from BCPT Symptom Checklist	In past 4 wk, how bothered have you been by difficulty with bladder control when laughing or crying / at other times: From 0 (<i>not at all</i>) to 4 (<i>extremely</i>)	Age approximations from graph: 25-34 y, 21%; 35-39 y, 20%; 40-44 y, 35%; 45-51 y, 38%
Greendale et al 2001 ³³	Items from BCPT Symptom Checklist	In past 4 wk, difficulty with bladder control when laughing or crying, difficulty with bladder control at other times: Bother rated from 0 (<i>not at all</i>) to 4 (<i>extremely</i>)	Urinary incontinence score mean±SD, 14.8±20.2; range, 0-100
Gupta et al 2006 ⁴³	Menopausal Rating Scale with 2-wk recall	Urinary problems (difficulty urinating, increased need to urinate, bladder incontinence); Severity rated from 0 (<i>mild</i>) to 4 (<i>severe</i>)	Reported urinary problems, 55%; reported moderate-to-severe symptoms, 39%

(Continued)

Table 2. (Continued)

Study	Assessment of Menopausal Symptoms	Assessment of Urinary Symptoms	Prevalence/Severity of Urinary Symptoms
Land et al 2004 ³⁷	17 Items from existing instruments, including the BCPT Symptom Checklist	In past 7 d, bladder problems	CMF versus AC: Ratio of the odds of reporting being at least a <i>little bit bothered</i> by bladder problems, 4.2; 99.8% CI, 1.262-13.767; <i>P</i> = .0002
Leining et al 2006 ⁴⁴	16 Items from BCPT Symptom Checklist	In past 4 wk, how bothered have you been by difficulty with bladder control when laughing or crying/at other times: From 0 (<i>not at all</i>) to 4 (<i>extremely</i>)	Reported loss of bladder control <i>slightly bothersome or more severe symptoms</i> : Laughter, 26%; other, 25%
Morales et al 2004 ³⁸	Leuven Menopause Form	In past 7 d, did you have frequent urination (even at night) and urgency, urine loss when coughing, sneezing and laughing: Rated <i>not at all</i> ; yes, with <i>minor inconvenience</i> ; yes, with <i>moderate inconvenience</i> ; yes, with <i>severe inconvenience</i> ; yes, <i>intolerable</i>	Endocrine therapy-naïve patients (<i>n</i> = 144): prevalence of urinary problems at baseline, 28% (<i>n</i> = 41); urinary problems at baseline (<i>n</i> = 164): tamoxifen first-line patients, 23% mild to moderate; randomized trial of tamoxifen or letrozole patients, 23% mild to moderate; NSAI first-line patients, 39% mild to moderate; (NSAI) previous tamoxifen patients, 25% mild to moderate; urinary problems at 1 mo (<i>n</i> = 163): tamoxifen first-line patients, 35% mild to moderate; randomized trial of tamoxifen or letrozole patients, 28% mild to moderate; NSAI first-line patients, 43% mild to moderate; (NSAI) previous tamoxifen patients, 37% mild to moderate; urinary problems at 3 mo (<i>n</i> = 162): tamoxifen first-line patients, 36% mild to moderate; randomized trial of tamoxifen or letrozole patients, 32% mild to moderate; NSAI first-line patients, 35% mild to moderate; (NSAI) previous tamoxifen patients, 15% mild to moderate ^a
Oleske et al 2004 ³⁹	Symptom Rating Scale (later modified for use in the National Surgical Adjuvant Breast and Bowel Project)	In past 7 d, difficulty in bladder control	Reported symptoms, 39%: Mild, 25%; moderate, 16%; severe, 4%
Schover et al 2006 ⁴⁵	7 Items adapted from BCPT Symptom Checklist	In past 4 wk, how bothered have you been by difficulty with bladder control when laughing or crying/at other times: From 0 (<i>not at all</i>) to 4 (<i>extremely</i>)	Mean±SD score, 0.67±1.2 at baseline
Stanton et al 2005 ⁴¹	42 Item from BCPT Symptom Checklist	In past 4 wk, difficulty with bladder control (when laughing or crying); difficulty with bladder control (at other times); presence/absence (1/0) and bother rated from 0 (<i>not at all</i>) to 4 (<i>extremely</i>)	Sample 1, 0.52 (range, 0.47-0.58); Sample 2, 0.38 (range, 0.33-0.43); Sample 3, 0.32 (range, 0.28-0.38); Sample 4, 0.40 (range, 0.31-0.50)

Abbreviations: AC, doxorubicin and cyclophosphamide; BC, breast cancer;

BCPT, Breast Cancer Prevention Trial Symptom Checklist from the National Surgical Adjuvant Breast and Bowel Project; CI, confidence interval; CMF, cyclophosphamide, methotrexate, and 5-fluorouracil; FACT-ES, Functional Assessment of Cancer Therapy-Endocrine Symptoms; MCS, Mental Component Summary Score; (NSAI, nonsteroidal and steroidal aromatase inhibitors; NSAI, nonsteroidal aromatase inhibitors; PCS, Physical Component Summary Score; QOL, quality of life.

^aData also are presented for no symptoms and for severe-to-intolerable symptoms.

laughing or crying was 1.8 ± 0.9 . This score corresponds most closely to “somewhat” bothersome on the BCPT 5-point Likert scale of bother. In a study to identify particular problem areas for women with breast cancer, Avis et al³⁶ reported the percentage of women in every category of bother on the 5-point Likert scales for each bladder control question; 15.4% rated difficulty with bladder control while laughing or crying as at least somewhat bothersome, whereas 11.9% rated difficulty with bladder control at other times as at least somewhat bothersome. In 5 studies,^{31,38,39,43,46} perceived severity was reported as the percentage of patients reporting some combination of no symptoms, mild symptoms, moderate symptoms, and severe symptoms. For example, in the study by Chin et al⁴⁶ to assess the prevalence and severity of symptoms of urogenital atrophy, 57% reported no urinary urgency, 27% reported mild urinary urgency, and 14% reported moderate/severe symptoms. In a similar study by Couzi et al,³¹ among those who reported difficulty with bladder control, 55% reported mild symptom severity, 22% reported moderate symptom severity, and 23% reported severe symptoms.

Relation of Urinary Symptoms to Treatment and Quality of Life

Two studies examined the effects of adjuvant therapy with surgery, chemotherapy, and/or radiotherapy on urinary symptoms. In the study by Land et al,³⁷ women who received CMF were approximately 4 times more likely to be bothered by bladder problems during and immediately after treatment than women who received AC. Conversely, Alfano et al⁴² reported that neither receipt of chemotherapy nor type of surgery were predictive of bladder control problems in the post-treatment period. The primary objective of 2 studies^{38,46} was to examine the effects of endocrine therapy for breast cancer, as noted above. In a longitudinal study of women with breast cancer who were about to start endocrine therapy, Morales et al³⁸ observed no significant changes in urinary problems from baseline to 1 month and 3 months of therapy with first-line tamoxifen or nonsteroidal aromatase inhibitors. The Chin et al⁴⁶ study likewise included only women who were currently on endocrine therapy; thus, no comparisons with a control group were possible, and no comparisons were made between types of endocrine therapy used. Four other studies⁴¹⁻⁴⁴ included an examination of the effect of endocrine treatment on urinary symptoms in their analyses with mixed results. In the study by Stanton et al,⁴¹ women currently receiving tamoxifen reported significantly more bladder-control problems than nonusers

of tamoxifen. Conversely, 3 studies⁴²⁻⁴⁴ identified no difference in urinary symptoms between current tamoxifen users and nonusers. Taken together, these results suggest that the effects of endocrine therapy on urinary symptoms are not yet known.

Finally, 4 studies^{32,33,41,43} examined the relation between urinary symptoms and quality of life, including sexuality,^{33,43} after a breast cancer diagnosis. Less vitality, worse physical quality of life,^{41,43} worse social life,⁴³ and worse overall quality of life⁴³ were significantly associated with more urinary symptoms in the post-treatment period. With respect to sexuality, more urinary incontinence³³ and worse urinary problems⁴³ were significantly associated with adverse effects on sexuality in the post-treatment period.

DISCUSSION

We identified 16 studies published between 1990 and June 2010 that examined urinary symptoms as part of the constellation of menopausal symptoms in women with breast cancer. The studies varied widely with respect to study purpose, design, and the nature and size of the samples included. There was less variation in terms of how urinary symptoms were defined and assessed. In general, this reflects the state of the science related to urinary symptom research among women in the general population, in which such variability makes evaluating existing findings and estimating prevalence more difficult.^{48,49} Nevertheless, most (but not all) of the studies we identified reported data on the prevalence of urinary symptoms. A high of 58% of women reported difficulty with bladder control. On average, using items from the BCPT Symptom Checklist,⁴⁷ a mean of 37% reported difficulty with bladder control when laughing or crying or other times. Similarly, 34% reported “urinary problems.” More than half of the studies reported data related to severity. All points along a continuum of mild, moderate, and severe were represented. Although in many studies the largest percentage of women rated their symptoms as mild, as many as 23% of women rated their symptoms as severe. Treatments commonly associated with menopausal symptoms in women with breast cancer include chemotherapy and endocrine therapy. In our review, relatively few studies examined the relation of specific cancer treatments to urinary symptoms. Among these studies, the results were mixed. The relation of urinary symptoms to quality of life was relatively clearer, with the results suggesting that such symptoms adversely affect quality of life in women with a diagnosis of breast cancer.

Limitations of Existing Research

Several limitations of the existing literature should be acknowledged. Relatively few studies, as noted above, have explored the relation of various treatments for breast cancer to urinary symptoms as part of the constellation of menopausal symptoms. To our knowledge, no studies have made comparisons with a healthy, noncancer control group of women; thus, it is not known whether urinary symptoms are more closely associated with breast cancer treatment. Furthermore, only 2 studies explored whether urinary symptoms may be associated more strongly with other factors, such as age, obesity, and race or ethnicity, in women with breast cancer. Ganz et al³⁵ reported that, among breast cancer survivors, urine loss with sneezing or coughing increased in frequency with age. Morales et al³⁸ observed that, among women who were receiving endocrine therapy for early stage or advanced breast cancer, those with a higher body mass index were more likely to report urinary problems. To our knowledge, no studies have included a pretreatment assessment of menopausal symptoms, so it is not possible to know whether reported urinary symptoms predate a breast cancer diagnosis. There are limited data available about the course of symptoms and whether symptoms resolve or worsen over time. Only 2 studies^{34,42} of the 16 studies we identified were longitudinal in design, and the results were mixed. Studies have been limited by either a single focus on a symptom of stress urinary incontinence or a lack of specificity. To date, no study that we know of has examined the full range of urinary symptoms, including urgency, urgency incontinence, stress incontinence, dysuria or burning, pelvic pressure and frequency, and recurrent urinary tract infections and dryness. This is particularly significant because the appropriate course of treatment for urinary symptoms is determined by the type and severity of symptoms.^{21,22} The vast majority of studies used 2 questions related to bladder control from the BCPT Symptom Checklist⁴⁷ to assess the prevalence and severity of urinary symptoms. In the remaining studies, either individual questions about select urinary symptoms were used, or women were asked to reflect on a short list of urinary symptoms and respond to a single question related to severity or inconvenience. To date, no studies have used validated measures specifically designed to assess urinary symptoms or urologic condition-specific quality of life measures as recommended by the International Consultation on Incontinence.⁵⁰ Finally, although research among women in the general population consistently has demonstrated that urinary symptoms adversely affect women's quality of life,¹⁸⁻²⁰

there are limited data available about the effect of urinary symptoms on quality of life after breast cancer; however, existing data suggest that symptoms do have a negative effect on women's quality of life after breast cancer.

In conclusion, our systematic review of the literature suggests that urinary symptoms are prevalent among women who are diagnosed and treated for breast cancer and that these symptoms tend to be mild to moderate in severity. Among women in the general population, conservative first-line treatment of mild to moderate urinary symptoms includes behavioral strategies, such as self-monitoring, lifestyle changes,^{24,51} and pelvic floor muscle exercises.⁵² Such treatment typically results in significant improvement and minimal adverse outcomes. More severe symptoms may require more invasive interventions and pharmacologic management. Our findings support the notion that clinicians should screen for urinary symptoms in women with breast cancer and offer treatment recommendations or make referrals as appropriate. Our review also highlights the need for additional research assessing the natural history of urinary symptoms using consensus definitions,⁵³ their relation to breast cancer treatments, and their impact on women's quality of life using validated, recommended assessment approaches in diverse populations. Results from such studies would serve to inform the development of interventions to ameliorate the effects of urinary symptoms in survivorship.

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REFERENCES

- Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System Survey Questionnaire. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2007.
- American Cancer Society. Breast Cancer Facts & Figures 2007-2008. Atlanta, GA: American Cancer Society; 2007.
- American Cancer Society. Cancer Facts & Figures 2008. Atlanta, GA: American Cancer Society; 2008.
- Institute of Medicine and National Research. From Cancer Patient to Cancer Survivor: Lost in Transition. Washington, DC: National Academy of Sciences; 2006.
- Ganz PA. Menopause and breast cancer: symptoms, late effects, and their management. *Semin in Oncol*. 2001;28: 274-283.
- Lester JL, Bernhard LA. Urogenital atrophy in breast cancer survivors. *Oncol Nurs Forum*. 2009;36:693-698.
- Harris PF, Remington PL, Trentham-Dietz A, Allen CI, Newcomb PA. Prevalence and treatment of menopausal symptoms among breast cancer survivors. *J Pain Symptom Manage*. 2002;23:501-509.

8. Smith IE, Dosett M. Aromatase inhibitors in breast cancer. *N Engl J Med*. 2003;348:2431-2442.
9. Trinkaus M, Chin A, Wolfman W, Simmons C, Clemons M. Should urogenital atrophy in breast cancer survivors be treated with topical estrogens? *Oncologist*. 2008;13:222-231.
10. Iosif CS, Bekassy Z. Prevalence of genito-urinary symptoms in the late menopause. *Acta Obstet Gynecol Scand*. 1984;63: 257-260.
11. Schaffer J, Fantl JA. Urogenital effects of the menopause. *Baillieres Clin Obstet Gynaecol*. 1996;10:401-417.
12. Van Voorhis BJ. Genitourinary symptoms in the menopausal transition. *Am J Med* 2005;118(suppl 12B):47-53.
13. Iosif CS, Batra S, Edk A, Astedt B. Estrogen receptors in the human female lower urinary tract. *Am J Obstet Gynecol*. 1981;141:817-820.
14. Saez S, Martin PM. Evidence of estrogen receptors in the trigone area of human urinary bladder. *J Steroid Biochem*. 1981;15:317-320.
15. Batra SC, Iosif CS. Progesterone receptors in the female lower urinary tract. *J Urol*. 1984;138:1301-1304.
16. Dew JE, Wren BG, Eden JA. A cohort study of topical vaginal estrogen therapy in women previously treated for breast cancer. *Climacteric*. 2003;6:45-52.
17. Holroyd-Leduc JM, Tannenbaum C, Thorpe KE, Straus SE. What type of urinary incontinence does this woman have? *JAMA*. 2008;299:1446-1456.
18. Wyman JF, Harkins SW, Choi SC, Taylor JR, Fantl JA. Psychosocial impact of urinary incontinence in women. *Obstet Gynecol*. 1987;70:378-382.
19. Margalith I, Gillon G, Gordon D. Urinary incontinence in women under 65: quality of life, stress related to incontinence and patterns of seeking health care. *Qual Life Res*. 2004;13:1381-1390.
20. Ragins AL, Shan J, Thom DH, Subak LL, Brown JS, Van Den Eeden SK. Effects of urinary incontinence, comorbidity and race on quality of life outcomes in women. *J Urol*. 2008;179:651-655.
21. van der Vaart CH, de Leeuw JRJ, Roovers JWR, Heintz APM. Measuring health-related quality of life in women with urogenital dysfunction: the Urogenital Distress Inventory and Incontinence Impact Questionnaire revisited. *Neurourol Urodyn*. 2003;22:97-104.
22. Paick J, Kim SW, Oh S, Ku JH. A generic health-related quality of life instrument, the Medical Outcomes Study Short Form-36, in women with urinary incontinence. *Eur J Obstet Gynecol*. 2007;130:18-24.
23. Dougherty MC, Dwyer JW, Pendergast JF, et al. A randomized trial of behavioral management for continence with older rural women. *Res Nurs Health*. 2002;25:3-13.
24. Wyman JF. Treatment of urinary incontinence in men and older women: the evidence shows the efficacy of a variety of techniques. *Am J Nurs*. 2003;suppl:26-35.
25. Boyington AR, Dougherty MC, Phetrasuwan S. Effectiveness of a computer-based system to deliver a continence health promotion intervention. *J Wound Ostomy Continence Nurs*. 2005;32:246-254.
26. Shamliyan TA, Kane RL, Wyman J, Wilt TJ. Systematic review: randomized, controlled trials of nonsurgical treatments for urinary incontinence in women. *Ann Intern Med*. 2008;148:459-473.
27. Dugan E, Roberts C, Cohen S, et al. Why older community-dwelling adults do not discuss urinary incontinence with their primary care physicians. *Am Geriatr Soc*. 2001; 49:462-465.
28. Hagglund D, Walker-Engstrom ML, Larsson G, Leppert J. Quality of life and seeking help in women with urinary incontinence. *Acta Obstet Gynecol Scand*. 2001;80:1051-1055.
29. Koch LH. Help-seeking behaviors of women with urinary incontinence: an integrative literature review [serial online]. *J Midwifery Womens Health*. 2006;51:e39-e44.
30. Melville JL, Wagner LE, Fan M, Katon WJ, Newton KM. Women's perceptions about the etiology of urinary incontinence. *J Womens Health*. 2008;17:1093-1098.
31. Couzi RJ, Helzlsouer KJ, Fetting JH. Prevalence of menopausal symptoms among women with a history of breast cancer and attitudes toward estrogen replacement therapy. *J Clin Oncol*. 1995;13:2737-2744.
32. Ganz PA, Greendale GA, Petersen L, Zibecchi L, Kahn B, Belin TR. Managing menopausal symptoms in breast cancer survivors: results of a randomized controlled trial. *J Natl Cancer Inst*. 2000;92:1054-1064.
33. Greendale GA, Petersen L, Zibecchi L, Ganz PA. Factors related to sexual function in postmenopausal women with a history of breast cancer. *Menopause*. 2001;8:111-119.
34. Ganz PA, Desmond KA, Leedham B, Rowland JH, Meyerowitz BE, Belin TR. Quality of life in long-term, disease-free survivors of breast cancer: a follow-up study. *J Natl Cancer Inst*. 2002;94:39-49.
35. Ganz PA, Greendale GA, Petersen L, Kahn B, Bower JE. Breast cancer in younger women: reproductive and late health effects of treatment. *J Clin Oncol*. 2003;21:4184-4193.
36. Avis NE, Crawford S, Manuel J. Psychosocial problems among younger women with breast cancer. *Psychooncology*. 2004;13:295-308.
37. Land SR, Kopec JA, Yothers G, et al. Health-related quality of life in axillary node-negative, estrogen receptor-negative breast cancer patients undergoing AC versus CMF chemotherapy: findings from the National Surgical Adjuvant Breast and Bowel Project B-23. *Breast Cancer Res Treat*. 2004;86:153-164.
38. Morales L, Neven P, Timmerman D, et al. Acute effects of tamoxifen and third-generation aromatase inhibitors on menopausal symptoms of breast cancer patients. *Anticancer Drugs*. 2004;15:753-760.
39. Oleske DM, Cobleigh MA, Phillips M, Nachman KL. Determination of factors associated with hospitalization in breast cancer survivors. *Oncol Nurs Forum*. 2004;31:1081-1088.
40. Avis NE, Crawford S, Manuel J. Quality of life among younger women with breast cancer. *J Clin Oncol*. 2005; 23:3322-3330.
41. Stanton AL, Bernards CA, Ganz PA. The BCPT symptom scales: a measure of physical symptoms for women diagnosed with or at risk for breast cancer. *J Natl Cancer Inst*. 2005;97:448-456.
42. Alfano CM, McGregor BA, Kuniyuki A, et al. Psychometric properties of a tool for measuring hormone-related symptoms in breast cancer survivors. *Psychooncology*. 2006;15:985-1000.
43. Gupta P, Sturdee DW, Palin SL, et al. Menopausal symptoms in women treated for breast cancer: the prevalence and severity of symptoms and their perceived effects on quality of life. *Climacteric*. 2006;9:49-58.
44. Leining MG, Gelber S, Rosenberg R, Przypyszny M, Winer EP, Partridge AH. Menopausal-type symptoms in young breast cancer survivors. *Ann Oncol*. 2006;17:1777-1782.
45. Schover LR, Jenkins R, Sui D, Adams JH, Marion MS, Jackson KE. Randomized trial of peer counseling on reproductive health in African American breast cancer survivors. *J Clin Oncol*. 2006;24:1620-1626.
46. Chin SN, Trinkaus M, Simmons C, et al. Prevalence and severity of urogenital symptoms in postmenopausal women receiving endocrine therapy for breast cancer. *Clin Breast Cancer*. 2009;9:108-117.
47. Ganz PA, Day R, Wre JE Jr, Redmond C, Fisher B. Baseline quality of life assessment in the National Surgical Adjuvant Breast and Bowel Project Breast Cancer Prevention Trial. *J Natl Cancer Inst*. 1995;87:1372-1382.
48. Landefeld CS, Bowers BJ, Feld AD, et al. National Institutes of Health state-of-the-science conference statement: prevention of fecal and urinary incontinence in adults. *Ann Intern Med*. 2008;148:449-458.
49. Altman D, Lapitan MC, Nelson R, Sillen I, Thom D. Epidemiology of urinary (UI) and faecal (FI) incontinence and pelvic organ prolapse (POP). In: Abrams P, Cardozo L, Khoury S, Wein A, eds. Incontinence: Proceedings from the Fourth International Consultation on Incontinence (Paris, France). Plymouth, United Kingdom: Health Publication Ltd, 2009:35-111.
50. Staskin D, Kelleher C, Bosch R, et al. Patient-oriented assessment. In: Abrams P, Cardozo L, Khoury S, Wein A, eds. Incontinence: Proceedings from the Fourth International Consultation on Incontinence (Paris, France). Plymouth, United Kingdom: Health Publications Ltd.; 2009: 363-412.
51. Kincade JE, Dougherty MC, Carlson JR, Hunter GS, Busby-Whitehead J. Randomized clinical trial of efficacy of self-monitoring techniques to treat urinary incontinence in women. *Neurourol Urodyn*. 2007;26:507-511.
52. Dumoulin C, Hay-Smith J. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Cochrane Database Syst Rev*. 2010; (1):CD005654.
53. Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA/International Incontinence Society [ICS]) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn*. 2009; 29:4-20.