Original Article

Prevalence of Breast Cancer Treatment Sequelae Over 6 Years of Follow-Up

The Pulling Through Study*

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BACKGROUND: There is a need to better describe and understand the prevalence of breast cancer treatment-related adverse effects amenable to physical therapy and rehabilitative exercise. Prior studies have been limited to single issues and lacked long-term follow-up. The Pulling Through Study provides data on prevalence of adverse effects in breast cancer survivors followed over 6 years. **METHODS:** A population-based sample of Australian women (n = 287) diagnosed with invasive, unilateral breast cancer was followed for a median of 6.6 years and prospectively assessed for treatment-related complications at 6, 12, and 18 months and 6 years after diagnosis. Assessments included postsurgical complications, skin or tissue reaction to radiation therapy, upper-body symptoms, lymphedema, 10% weight gain, fatigue, and upper-quadrant function. The proportion of women with positive indication for each complication and 1 or more complication was estimated using all available data at each time point. Women were only considered to have a specific complication if they reported the highest 2 levels of the Likert scale for self-reported issues. **RESULTS:** At 6 years after diagnosis, more than 60% of women experienced 1 or more side effects amenable to rehabilitative intervention. The proportion of women experiencing 3 or more side effects decreased throughout follow-up, whereas the proportion experiencing no side effects remained stable around 40% from 12 months to 6 years. Weight gain was the only complication to increase in prevalence over time. **CONCLUSIONS:** These data support the development of a multidisciplinary prospective surveillance approach for the purposes of managing and treating adverse effects in breast cancer survivors. ***Cancer*** **2012;118(8 suppl):2217–25.** © *2012 American Cancer Society.*

KEYWORDS: breast neoplasms, side effects, survivors, surveillance, rehabilitation.

Advances in diagnostic and treatment approaches over the past few decades have resulted in a new reality in which survival after a diagnosis of breast cancer is favorable. It is estimated here are 2.5 million breast cancer survivors alive in the United States,[1] and millions more worldwide.[2] The curative care for breast cancer includes surgery, radiation treatment, chemotherapy, hormonal therapy, and other targeted therapies. The physical impairments associated with these treatments include those noted in the prospective surveillance model described elsewhere in this supplement.[3] The incidence and prevalence of these persistent adverse effects and the extent to which women's lives remain affected by breast cancer treatment is poorly understood. Further, the question as to whether evidence that functional changes of arms and shoulders, or other breast cancer treatment complications, occur with high enough frequency to necessitate formal surveillance efforts has not been answered. For decades, formal prospective surveillance programs have demonstrated effectiveness at determining true incidence proportions and rates, ability to detect early and optimal intervention periods for a variety of illnesses,[4-6] and health-related conditions or behaviors.[7-9] These include surgical site infection,[4] venous thrombosis,[5] melanoma,[6] and adverse drug reactions,[7] as well as behaviors related to diabetes, exercise,[8] and human immunodeficiency virus testing.[9] It is reasoned that breast cancer treatment adverse effects would be amenable to prospective surveillance as well. Therefore, it is of interest to pursue the proposed prospective surveillance model, highlighted in this supplement, in order to determine how often breast cancer survivors experience any of the 9 issues reviewed in this supplement.

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The articles in this supplement were commissioned based on presentations and deliberations at a *Roundtable Meeting on a Prospective Model of Care for Breast Cancer Rehabilitation*, held February 24-25, 2011, at the American Cancer Society National Home Office, in Atlanta, Georgia.

**A Prospective Surveillance Model for Rehabilitation for Women with Breast Cancer, Supplement to Cancer*

DOI: 10.1002/cncr.27474, **Received:** October 19, 2011; **Revised:** October 18, 2011; **Accepted:** November 7, 2011, **Published online** April 6, 2012 in Wiley Online Library (wileyonlinelibrary.com)

Thus far, most research on the incidence and prevalence of adverse effects of breast cancer treatment potentially amenable to rehabilitation have focused on the likelihood that any 1 of the myriad problems occurs. Estimates for incidence of chemotherapy-induced peripheral neuropathy vary widely according to timing, chemotherapy dosage, agent used, and severity, but it seems to occur in up to 83% of patients who are treated with taxanes, with reports that this adverse effect may or may not dissipate by itself over time.[10] Bone health challenges are also common, in part due to hormonal therapies used to improve disease-free survival. Breast cancer survivors are 5-fold more likely than age-matched women with no cancer history to have vertebral fractures.[11] Arthralgia and joint pain have been reported to occur in 36% of breast cancer survivors taking aromatase inhibitors.[12] Lymphedema incidence ranges from 6% to 70%, according to length of follow-up, method of detection, and population studied.[13] Fatigue occurs in up to 94% of breast cancer patients at some point after diagnosis.[14] Upper-body problems are estimated to occur in 20% to 44% of patients, depending on method of assessment, severity, and length of follow-up.[15] Evidence that women have functional limitations after breast cancer include the results from 3 large population-based studies,[16-18] all of which indicate that self-reported functional status is likely to be worse in breast cancer survivors than in age-matched peers, with prevalence of functional limitations in cancer survivors ranging from 18% to 54% across the 3 studies. The variability in reported occurrence of these adverse treatment effects is likely due to differences across studies with regard to methods of diagnosis, length of follow-up, differences in the cohorts examined, and presentation of data.

Although we have the estimates reported above, defined and collected per individual impairments of interest, an area of research with limited evidence is the proportion of breast cancer survivors who avoid *all* of these problems, and what proportion of survivors still have these issues over multiple years of survival. Cancer treatment is aggregate in nature, and its impact on morbidity could be assumed to be likewise. It seems exceptionally unlikely that women who experience a single physical impairment would never develop additional impairments or functional limitations; in fact, it is most likely that physical impairments occur simultaneously.

Two prior cross-sectional studies have been identified that have examined the likelihood of experiencing any 1 of multiple possible impairments.[19,20] In 1 of these prior studies, 66% of 202 consecutively enrolled cancer patients who were undergoing outpatient cancer treatment reported 1 or more functional problems, with nearly 23% reporting a problem with ambulation.[19] Review of electronic medical records revealed only 2 referrals for rehabilitation in the entire study population. The other study, also cross-sectional, assessed 163 community-dwelling women with metastatic cancer at a single time point during chemotherapy treatment. Of these, 92% reported 1 or more physical impairments.[20] Although 88% of these women were determined to need rehabilitation upon examination, only 21% were sent to physical therapy services. Both studies involved patients actively undergoing treatment and conducted assessments at a single time point. To our knowledge, no study has followed breast cancer survivors over a period of years after the end of treatment and reported on the persistence of prevalent physical impairments related to cancer treatment.

Determining the proportion of breast cancer survivors who have 1 or more of the physical impairments noted in the proposed prospective surveillance model is important to establishing the need for multidisciplinary coordinated care that includes rehabilitation and exercise for breast cancer survivors. Data from the Pulling Through Study (PTS) can address this gap in the literature. This longitudinal observational cohort study originally recruited 287 breast cancer survivors 3 to 4 months after diagnosis, who were shown to be generally representative of the wider breast cancer population.[20] Study participants were followed for more than 6 years, allowing for the estimation of the prevalence of specific treatment complications after breast cancer over time. The primary aim of this analysis was to examine the number of breast cancer survivors who experienced any 1 of the issues addressed in the surveillance model, to the extent that they were measured at multiple time points over 6 years of follow-up.

MATERIALS AND METHODS

Patient Population

The PTS was a longitudinal investigation designed to assess the physical and psychosocial recovery of women after breast cancer treatment.[21-24] Women diagnosed with unilateral breast cancer between January and December 2002, who were aged 75 years or younger, and residing within a 100-km radius of Brisbane, Queensland, Australia, were randomly selected from the Queensland Cancer Registry to participate (n = 511). Younger women (aged <50 years) were oversampled to ensure adequate numbers were available for specific age group analyses. A unilateral diagnosis allowed for the untreated side to serve

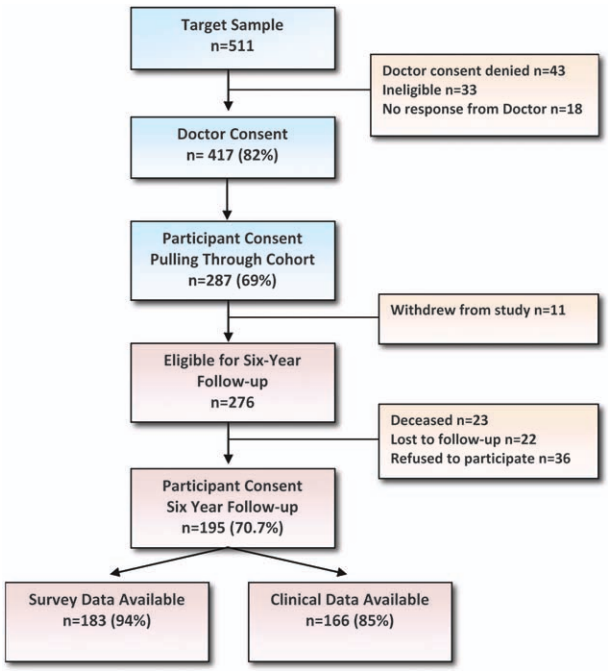

Figure 1. The figure depicts a flow chart of study participation.

as a control for certain outcomes, such as lymphedema, whereas the residence criterion facilitated the logistics of data collection for objective outcomes. Women 75 years and older were excluded to minimize the potential impact of age-related comorbidities.

The ethical approval process required doctor consent prior to contacting eligible participants and was obtained for 417 women (82%). Potential participants were mailed an invitation letter and study information package and were followed-up via the telephone to ascertain study interest. Informed consent was obtained for 69% (n = 287). Participation in the PTS involved a clinical assessment and/or completion of a self-administered questionnaire every 3 months from 6 to 18 months after diagnosis. Some participants consented to participate on a "questionnaire-only" basis (26%), restricting the data available on clinically assessed outcomes to 74% (n = 218). Following completion of the PTS, ethical approval was sought and granted to recontact participants at approximately 6 years after surgery (PTS-FU). Of the 287 original baseline participants, 11 withdrew from the original study and were therefore not recontacted. The records of the remaining 276 women were cross-referenced with the mortality database at the Queensland Cancer Registry in August 2008 and April 2009 to determine vital status, including date and cause of death. Residing address was confirmed through a search of the electronic White Pages, and a change of address search was carried out through Australia Post. Of the 276 potential participants, 22 (8.0%) were lost to follow-up, 36 (13.0%) refused to participate, 23 (8.3%) were deceased, and the remaining 195 (70.7%) women provided consent. Of these, 94% (n = 183) returned the questionnaires and 85% (n = 166) had clinical measures of lymphedema taken. Four women died (2 participants and 2 previously lost-to-follow-up) between time of the 6-year follow-up assessment and the final death search, yielding a total of 27 deaths from the original baseline cohort of 287. Metastatic breast cancer was the recorded cause of death for 23 of the women; 1 death was due to cancer at a site other than the breast, and 3 women died due to noncancer causes. Figure 1 presents recruitment and participant flow into the original PTS and follow-up (PTS-FU) study.

Data Collection

Tumor characteristics were abstracted from histopathology reports at the Queensland Cancer Registry. Personal characteristics including age and body mass index, and treatment characteristics (type of surgery, radiation, chemotherapy, hormone therapy, number of lymph nodes removed) were collected by participant-administered questionnaires. Also collected via the questionnaire were the following outcomes of interest: the self-report Functional Assessment of Cancer Therapy, Breast+4 (FACT-B+4) survey,[25] self-report upper-body function (Disability of the Arm, Shoulder, and Hand [DASH] Scale),[26,27] weight and height, and posttreatment complications experienced. Lymphedema, height, and weight were assessed with objective measures. Individual items of the self-report FACT-B+4 survey and the self-report DASH scale were combined to create the following 3 unique variables: "upper-body symptoms," "upper-body function," and "fatigue." We describe below the specifics of how the aforementioned measurement elements were used to create an analytic data set that could address the question of prevalence of any 1 of multiple physical impairments at 6, 12, and 18 months and 6 years after diagnosis.

The variable "postsurgical adverse effects" was created using self-reported wound infection, other infection, seroma or hematoma, or axillary web syndrome. Women self-reported these concerns as yes/no/don't know (categorized as "no"). The 6-, 12-, and 18-month time points cover the occurrence of these symptoms in the previous 6 months, whereas the 6-year time point asks women to recall these concerns in the previous 12 months.

The variable "skin or tissue reaction to radiation therapy" was created using self-report of this concern in

the same manner as described above for the "postsurgical adverse effects" variable.

The variable "upper body symptoms" was created using items in the FACT-B+4 and DASH questionnaires. From the FACT-B+4, items within the arm subscale ask women to rate the severity of pain, range of movement, numbness, stiffness, and swelling on the treated side during the past 7 days, by reporting how "true" on a 5-point Likert scale of "not at all" through to "very much," are statements regarding each symptom (eg, "one or both of my arms are swollen or tender," and "I have poor range of arm movement on this [treated] side"). Items from the DASH questionnaire were also used to capture the presence and severity of 2 symptoms: tingling and weakness. The DASH asks women to rate the presence and severity of these symptoms during the past 7 days using a 5-point Likert scale of "not at all" through to "extreme." Women were considered to have a positive indication for any of the above upper-body symptoms when reporting "quite a bit" to "very much" (4 or 5 on a 5-point Likert scale) for FACTB+4 items or "severe" to "extreme" (4 or 5 on a 5-point Likert scale) for DASH items. The proportion of women reporting at least 1 of these symptoms at each time point was then estimated.

The variable "lymphedema" was assessed using 2 possible measures: bioelectrical impedance (BIS) or circumferences. A woman was considered to have lymphedema if she met the threshold for either of the 2 objective measures used at a given measurement time point. Multifrequency BIS measurements were performed (SEAC SFB3; Impedimed), and the impedance of the extracellular fluid for each arm was estimated. The ratio of the impedance for the treated and untreated sides was then estimated, and values outside normal range (ie, more than 3 standard deviations from the normative mean, with side of dominance accounted for) were considered diagnostic for lymphedema.[28] Circumferences were measured at the hand (at the 1st and 5th metacarpal), wrist (the distal edge of the styloid process), and then every 10 cm along each arm up to 40 cm. The sum of these 6 circumferences was estimated, and the difference between arms was assessed (treated minus untreated side). When the difference of sums was >5 cm, women were classified as having lymphedema. The definition for this technique was chosen as it is commonly used within clinical practice and research settings.[29]

The DASH questionnaire is a validated self-reported measure of "upper-body function." The questionnaire asks participants to rate how difficult certain daily and recreational tasks are to perform and the extent to which any upper-body problem interferes with normal activities, and also collects information regarding severity of arm symptoms. The final score of the 30-item instrument ranges from 0 to 100, whereby 0 reflects no disability (good function) and 100 represents extensive disability (poor function). Scores of >20 were deemed to reflect poor upper-body function, based on review of the literature on the use of DASH in the posttreatment breast cancer patient population.[30-32] The median score in the present study population at 6 months after diagnosis was 11.[33]

Weight was assessed objectively at 6, 12, and 18 months and 6 years. Change in weight was determined by comparing self-reported weight 6 months prior to diagnosis (baseline) with follow-up objective weight measures. Increases of >10% of baseline values were considered gains.

The presence of fatigue was determined by responses to the FACT-B+4 item, "I have lack of energy." Those who reported "quite a bit" to "very much" (4 or 5 on a 5-point Likert scale) were classified as having fatigue.

The presence of "one or more" of the measured physical impairments was estimated, as was the total sum of impairments present. A participant was categorized as having 1 or more impairment(s) if she had a positive indication for any of the aforementioned treatment-related impairments. The number of impairments present was estimated by summing all positive indications. The maximum total number of impairments was 6.

Statistical Analysis

Baseline personal and treatment characteristics of the original PTS cohort and participants who consented for the 6-year follow-up period (PTS-FU) are described, using means and standard deviation for normally distributed continuous outcomes, medians and ranges for nonparametric continuous data, and proportions for categorical data. Proportions of women reporting the presence of breast cancer concerns including postsurgical complications, skin or tissue reaction to radiation therapy, upper-body symptoms, lymphedema, weight gain, fatigue, and upper-quadrant function at 6, 12, and 18 months and 6 years after diagnosis were estimated, using all available data at each time point.

RESULTS

As specified earlier, the original cohort was shown to be generally representative of the wider Queensland population of those with breast cancer. Also, demographic and treatment-related characteristics were similar for women in the original cohort and those in the target sample

Table 1. Characteristics of the Target Sample and Pulling Through Cohort at Baseline and 6 Years

Characteristic	Target Sample	Entire Cohort	Follow-Up Cohort at 6 y
	n = 511	n = 287	n = 188
Age, y, mean (SD)[a]	54.8 (10.1)	55.3 (10.0)	55.1 (9.5)
	n (%)[a]	n (%)[a]	n (%)[a]
Body mass index	–		
Underweight (<18.5 kg/m^2)		4 (1.2)	2 (1.0)
Healthy weight (18.5-24.9 kg/m^2)		129 (44.1)	81 (42.2)
Overweight (25-29.9 kg/m^2)		73 (25.7)	52 (27.8)
Obese (30+ kg/m^2)		48 (16.9)	30 (16.1)
Missing	33 (12.1)	23 (12.8)	
Children	–		
Yes		247 (86.1)	158 (86.3)
No		40 (13.9)	25 (13.7)
Current smoker	–		
Yes		30 (10.2)	18 (9.3)
No		255 (89.1)	164 (90.2)
Missing		2 (0.6)	1 (0.5)
Education Level	–		
Year 10 or less		126 (45.2)	70 (39.8)
High school		32 (11.3)	27 (14.9)
Trade/diploma		67 (22.4)	46 (24.0)
Undergraduate or postgraduate degree		60 (20.3)	39 (20.7)
Missing		2 (0.8)	1 (0.6)
Physical activity[b]	–		
Sedentary		49 (16.8)	22 (11.9)
<150 min/wk		67 (23.3)	35 (18.8)
≥150 min/wk		171 (59.8)	142 (69.3)
Cancer Stage			
Stage 1	271 (53.8)	160 (56.6)	104 (56.7)
Stage 2	227 (43.6)	117 (39.8)	80 (41.2)
Stage 3+	10 (1.9)	8 (2.8)	3 (1.6)
Missing	3 (0.6)	2 (0.8)	1 (0.6)
Lymph node dissection			
No nodes removed	70 (13.7)	38 (13.1)	24 (12.9)
1-4 nodes removed	43 (8.7)	27 (9.7)	14 (7.8)
5+ nodes removed	398 (77.6)	222 (77.2)	150 (79.3)
Number of positive lymph nodes			
None removed	70 (13.7)	38 (13.1)	24 (12.9)
None positive	266 (52.8)	158 (55.9)	108 (58.5)
1-3 positive	122 (23.3)	59 (20.1)	42 (21.7)
4+ positive	51 (9.7)	29 (9.8)	13 (6.4)
Missing	2 (0.4)	3 (1.1)	1 (0.6)
Surgery type			
Mastectomy (partial/full)	195 (37.8)	102 (35.1)	65 (33.7)
Lumpectomy	316 (62.2)	185 (64.9)	123 (66.3)
Chemotherapy[c] (% yes)	–	122 (41.0)	80 (40.6)
Radiation[c] (% yes)	–	215 (75.0)	138 (73.7)
Hormonal therapy[c] (% yes)	–	165 (57.9)	109 (58.5)

SD indicates standard deviation.
[a] Results have been appropriately weighted (<50 years, 1.0; ≥50 years, 1.3) for oversampling of younger women.
[b] Physical activity included total weekly moderate and vigorous activity.
[c] Data represents ever receiving chemotherapy, radiation, or hormonal therapy over the study period up to 18 months after diagnosis.

(Table 1). In brief, the average age of participants was 55 years (standard deviation = 10 years). At baseline, 44% were of healthy weight, 26% were overweight, and nearly 17% of study participants were obese. One-third had a partial or full mastectomy, whereas two-thirds had a lumpectomy. The majority had at least 1 lymph node excised (77%) with more than three-quarters having 5 or more nodes removed. Radiation was a common adjuvant

Table 2. Trends in Prevalence of Symptoms Over Time

Characteristic	6 mo		12 mo		18 mo		6 y	
	n	%	n	%	n	%	n	%
Postsurgical issues[a]	115/287	40.1	63/281	22.4	42/276	15.2	16/183	8.7
Skin/tissue reaction to radiotherapy	154/287	53.7	97/281	34.5	33/276	12.0	15/183	8.2
Upper-body symptoms[b]	65/287	22.6	51/277	18.4	40/272	14.7	25/183	13.7
Lymphedema (circumference)[c]	23/207	11.1	19/182	10.4	23/190	12.1	–	–
Lymphedema (BIS)[d]	22/211	10.4	13/173	7.5	27/103	14.7	10/160	6.3
Weight gain of 10% or more[e]	35/195	17.9	38/174	21.8	42/179	23.5	37/152	24.3
Fatigue[f]	74/283	26.1	43/275	15.6	32/272	11.8	29/182	15.9
Upper-body function[g]	66/258	25.6	43/254	16.9	52/246	21.1	38/180	21.1
One or more adverse treatment effects[h]	157	89.7	101	68.7	104	64.6	86	61.9
Number of above adverse treatment effects[h]								
0	18	10.3	46	31.3	57	35.4	53	38.1
1	49	28.0	43	29.3	47	29.2	48	34.5
2	49	28.0	32	21.8	32	19.9	28	20.1
3	35	20.0	14	9.5	17	10.6	8	5.8
4	18	10.3	11	7.5	5	3.1	2	1.4
5	4	2.3	1	0.7	3	1.9		
6	2	1.1						
7								
Total	175	100.0	147	100.0	161	100.0	139	100.0

[a] Postsurgical issues include; wound infection, other infection, seroma/hematoma, axillary web, cording. Counts include women who reported at least 1 issue.
[b] Upper-body symptoms from DASH (Disability of the Arm, Shoulder, and Hand) include tingling and weakness (rated severe to extreme), and items from FACT-B+4 (Functional Assessment of Cancer Therapy, Breast+4) symptom specific concerns include pain, stiffness, range of motion, swelling, and numbness (rated quite a bit to very much). Counts include women who reported at least 1 symptom.
[c] Lymphedema measured via sum of arm circumferences: lymphedema = when treated side was $\geq$5 cm than untreated side.
[d] Lymphedema as measured via bioimpedance spectroscopy (BIS): lymphedema = when ratio is >3 standard deviations of normative values.
[e] Weight gain was assessed by comparing measured values at 6, 12, 18 months and 6 years after diagnosis, and comparing these values to self-reported weight 6 months prior to diagnosis. Increases of >10% over these self-reported weights from 6 months prior to diagnosis were considered gains.
[f] Fatigue "I have a lack of energy" from FACT-B+4 Physical Well-being domain rated as quite a bit to very much.
[g] Function as assessed by the DASH (range 0-100): scores >20 categorized as poor function.
[h] One or more and Number of above complications includes; postsurgical issues, skin/tissue reaction to radiotherapy, upper-body symptoms, lymphedema (via sum of circumference or BIS), clinical weight gain, fatigue and function. Only women with data available for all outcomes in each time point were included in this analysis.

therapy, received by approximately 75% of women, whereas just more than 40% received chemotherapy. Of note, women included in the 6-year follow-up did not differ significantly from participants in the first study assessment (eg, "baseline") with regard to any personal or treatment-related characteristics (data previously published[33]; data not shown).

The trends in the prevalence of symptoms over time are shown in Table 2. At 6 years after diagnosis, more than 60% of women were experiencing 1 or more adverse treatment effects. About 20% of women reported experiencing 2 or more physical impairments 6 years after diagnosis. The proportion of women experiencing 3 or more physical impairments decreased throughout follow-up, whereas the proportion experiencing none remained stable from 12 months to 6 years.

The prevalence of most physical impairments decreased throughout the 6 years of follow-up, with the exception of lymphedema and weight gain. Lymphedema remained relatively stable, near 10% at each measurement time point, regardless of measurement technique. At baseline, 18% of participants had gained 10% body weight, which increased to 24% of participants at 6 years. Weight gain was also the most prevalent adverse treatment effect at the 18-month and 6-year time point. Without weight gain in Table 2, the prevalence of 1 or more adverse treatment effects becomes 87.4%, 61.9%, 56.5%, and 50.4% at the 4 time points, respectively.

When only data from the 80 women who had complete data at all 4 time points were included (data not shown), the results did not differ. More than 63% of women have 1 or more complications at 6 years after diagnosis. The proportion of women who experience no side effects after the 6-month measurement is just under 40% throughout follow-up.

DISCUSSION

The majority of breast cancer survivors who participated in the PTS report at least 1 of a myriad of adverse effects of breast cancer treatment over the course of 6 years of

follow-up. As noted in the introduction, there is evidence of a sizeable gap between the need versus referral to rehabilitation services during active treatment.[19,20] In prior cross-sectional studies, the likelihood of referral to physical therapy was lower among minority and socioeconomically disadvantaged patients. Taken together, this evidence lends support for the hypothesis that the proposed prospective surveillance model may particularly benefit those with the fewest resources, and may address this potential health disparity among cancer survivors.

Additional data are needed to confirm whether the findings of the PTS can be replicated in other breast cancer populations. These data would be helpful to answering the question of whether there is a "mountain" of underserved issues among long-term breast cancer survivors or whether the issue of needing prospective surveillance and rehabilitation is a "molehill." There is a growing body of evidence to support the hypothesis that available rehabilitative and exercise interventions result in better outcomes when adverse treatment effects are identified and treated sooner.[35-40] Yet, there is merit to conducting additional trials that address multiple treatment-related adverse events to provide a more definitive basis for the value of the prospective surveillance model proposed in another article within this issue.[3] In addition, the cost/risk benefit of such programs will also need to be established.

The observed prevalence estimate of 60% of survivors who experience at least 1 adverse treatment effect may well be an underestimate, given that several common treatment sequelae were not measured in the current study (eg, cardiotoxicity, bone health, arthralgias, chemotherapy-induced peripheral neuropathy). In addition, relying on patients to recall subjective reports of physical impairments has limitations, with both under- and overestimation.[41] On the other hand, for some adverse effects included in the prevalence estimates, it is not possible to discern whether the issue is truly the result of breast cancer treatment. Consideration must be given to the impact of other comorbid conditions as well as the natural course of aging, which may affect the overall health and functional status of women, regardless of breast cancer treatment. For example, upper-body functional impairments may arise among older women independent of cancer history. Furthermore, the causes of weight gain extend far beyond adverse cancer treatment effects; however, when weight gain was removed from the list of adverse treatment effects, the prevalence of 1 or more complication remained more than 50% at all time points. Regardless of the cause, if the impairments are observable and common in the population of breast cancer survivors, there is merit to surveillance if early treatment can be shown to reduce morbidity and be cost-effective compared to the current system of less frequent referral to rehabilitation and exercise.[19,20]

Trends in the prevalence of adverse treatment effects reported in this study were limited to those effects with established and accepted clinical definitions,[29,42] and those that had an impact on the top of the Likert scale used (eg, a 4 or 5 on a scale of 1 to 5, where 5 was most severe). This approach was used to enhance a focus on clinically meaningful issues that affected function and were not likely to be self-limiting, in order to avoid overestimating adverse treatment effects. Creating the infrastructure for surveillance and rehabilitation of mild, self-limiting adverse treatment effects could lead to increased anxiety on the part of survivors and possibly contribute to the impression that there may be reason to avoid exercise for safety reasons. This is certainly a matter of concern, given the ample evidence of the safety of exercise training in this population.[43] It is broadly agreed that any additional barriers to starting and maintaining an exercise program should be avoided.

The PTS allowed an initial examination of the longitudinal prevalence of persistent adverse treatment effects, given the length of follow-up and variety of measures and survey instruments used. However, these data were analyzed as a subset of a larger study, which was not specifically designed to examine aggregate impairments. Limitations of the measures used include the fatigue measure, which was based on a single question from the FACT-B+4 survey and lack of data on multiple adverse treatment effects included in the proposed prospective surveillance model.[3] Additional measurement time points, inclusion of more objective measures, and a larger cohort would serve to improve our ability to draw conclusions regarding the trends in prevalence of persistent adverse effects of breast cancer treatment. Generalizability of the current findings is limited to caucasian women 75 years of age and younger and to those treated for breast cancer per the practices and policies common to Australia. The cohort was generally representative of the wider breast cancer population and was representative of the target sample (women diagnosed in urban Queensland) in terms of age and cancer history at baseline and at 6 years. However, 77% of the sample had 5 or more lymph nodes removed. The PTS recruitment occurred prior to when sentinel lymph node biopsy was widely used in Australia. This makes the current findings most applicable to women with more extensive axillary surgery than those who underwent a sentinel lymph node biopsy.

In conclusion, it is striking that the proportion of survivors who maintained 1 or more adverse treatment effects remains stable over 6 years of follow-up. Although additional research is needed to confirm these initial findings, the stability of the prevalence over 6 years lends merit to the proposal of prospective surveillance for adverse treatment effects in breast cancer survivors.

FUNDING SOURCES

Support for this meeting and supplement were provided by the American Cancer Society through The Longaberger Company®, a direct selling company offering home products including handcrafted baskets made in Ohio, and the Longaberger Horizon of Hope® Campaign, which provided a grant to the American Cancer Society for breast cancer research and education.
The Pulling Through Study was funded by the National Breast Cancer Foundation, whereas the 6-year follow-up component was funded by the National Health and Medical Research Council and Cancer Australia. The National Breast Cancer Foundation also supports the research positions of S.A. Rye, T. DiSipio, and S.C. Hayes.

CONFLICT OF INTEREST DISCLOSURE

The authors made no disclosure.

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