Late Effects in a High-Risk Population of Breast Cancer Survivors

Jennifer Y. Sheng (✉ jsheng7@jhmi.edu)

The Johns Hopkins University School of Medicine   https://orcid.org/0000-0002-4513-4235

Sarah J. Skuli

The Hospital of the University of Pennsylvania

Elissa D. Thorner

The Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center

Nelli Zafman

The Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center

Carol D. Riley

The Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center

Jessica M. Ruck

The Johns Hopkins University School of Medicine

Katherine C. Smith

The Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center

Claire Snyder

The Johns Hopkins University School of Medicine

Karen L. Smith

The Johns Hopkins University School of Medicine

Vered Stearns

The Johns Hopkins University School of Medicine

Antonio C. Wolff

The Johns Hopkins University School of Medicine

Abstract

Purpose: To better understand the impact of cancer and treatment on outcomes and guide program development, we evaluated breast cancer survivors at risk for long-term medical and psychosocial issues who participated in survivorship care visits (SVs) at Johns Hopkins Hospital.

Methods: We conducted a prospective survey study of women with stage I-III breast cancer who participated in SVs from 2010-2016. The same 56-item questionnaire administered at SV and follow-up included an assessment of symptoms, social factors, demographics, anxiety, depression, and comorbidities. We added the Godin Exercise questionnaire to the follow-up.

Results: In 2018, 74 participants were identified as disease-free and mailed a follow up survey; 52 (70.3%) completed the survey. At a median follow-up time of 3.1 years after diagnosis, participants were less likely to be employed (54% vs. 67%) than at the SV. About two thirds were sedentary, and this was associated with high body mass index (p=0.02). Sufficiently active participants (≥150 minutes per week of moderate intensity activity) were less likely to report pain (p=0.02) or fatigue (p=0.001). Although 20% had moderate/severe anxiety or depression at follow up, participants who reported employment satisfaction were less likely to be depressed (p=0.02).

Conclusions: Awareness of issues faced by survivors is critical for enhancing care and developing models to identify patients who might benefit most from targeted long term interventions.

Implications for Cancer Survivors: Interventions to address physical activity, persistent symptoms and mental health are critical for breast cancer survivors.

Introduction

There are over 3.5 million breast cancer survivors in the United States, and this growing population presents unique challenges and opportunities,[1] including care for treatment-related issues and coexisting medical conditions.[2] Several longer-term comorbidities observed in cancer survivors, such as weight gain, obesity, infertility, psychological distress, depression, sexual dysfunction, second cancers, bone loss, and body image issues can have lasting effects on quality of life.[3] In 2006, the Institute of Medicine proposed standardizing practices for survivorship care by improving patient education and facilitating communication between providers with a survivorship care plan (SCP).[4] While these treatment summaries and plans for follow-up care were intended to standardize communication among cancer and non-cancer providers as well as patients, implementation has encountered barriers including time, reimbursement, and, most important, evidence of effectiveness.[5,6]

The breast cancer survivorship program at Johns Hopkins Hospital (JHH) was established in 2008, and since 2010 has offered a one-time survivorship visit (SV) with a nurse practitioner following completion of local and systemic therapy for patients with early stage breast cancer.[7] At the SV, participants complete questionnaires to assess lingering side effects and to screen for depression and anxiety, and

receive a SCP. Our group previously reported on a cohort of JHH breast cancer patients, most of whom received adjuvant chemotherapy and were subsequently referred by their medical oncology providers for a single SV.[8] Compared to those in the breast cancer registry, SV participants were younger, more likely to be African American, and more likely to have a higher TNM stage, hormone receptor-negative disease, and HER2-positive disease. They were also more likely to have received chemotherapy and radiation therapy. In this new analysis, we report on their long-term follow up outcomes (employment, physical activity, symptoms, comorbidities and mental health) based on subsequent review of medical records and a follow-up survey.

Methods

In February 2018, we mailed a 56-item survey to a cohort of patients who participated in a SV between 2012 and 2016 and who were disease-free. This study was approved by the Johns Hopkins Institutional Review Board (IRB Number: NA_00079523) with informed consent obtained from each participant or each participant's guardian. The same 56-item questionnaire was administered at both the SV and follow up including: a locally developed patient symptom questionnaire, reassessment of behavioral factors (e.g. alcohol, smoking, employment) and demographic characteristics, the General Anxiety Disorder-7 (GAD-7) and Patient Health Questionnaire-9 (PHQ-9), and comorbidity assessment[9]. For the symptom questionnaire, used a 4-item Likert scale ranging from none to severe to rate their concerns in the following areas: musculoskeletal pain, mobility, neuropathy, fatigue, sleep difficulty, memory decline, hot flashes, menstrual cycle pattern, sexuality, vaginal dryness, fertility, weight changes, inability/difficulty working, and difficulty with family/relationships. To evaluate employment, we assessed domains including being laid off, discrimination after diagnosis and current job satisfaction at follow-up but not at baseline. Lymphedema data was not collected. We added the 3-item Godin Exercise questionnaire that was not included in the clinical SV to the mailed survey.[10]

In order to ensure maximum mailed survey response, we implemented mailed survey best practices as described by Dillman et al.[11], including a survey format that is easy to read and understand, a plan for up to five contacts, inclusion of a stamped and addressed return envelope, and personalization of all correspondence. All eligible subjects were mailed a pre-notice letter informing them of the upcoming survey mailing (contact #1) to enhance participation rates.[12] One week later, all eligible subjects were mailed a packet including 1) cover letter on institutional stationary explaining the study and the purpose of the study, 2) two copies of the informed consent document, 3) survey instructions for survey completion, 4) survey packet, 5) a stamped self-addressed return envelope, and 6) an opt-out form (contact #2). Disease status was confirmed prior to contact of subjects. The opt-out form included a request for reason for disinterest and was to be returned if a subject did not wish to participate in the study or receive additional study-related mailings. One week later, a thank you letter was sent to all eligible subjects expressing appreciation for those who completed the survey; this also served as a reminder for those who had not yet returned the survey (contact #3). Those who responded to the survey also had a $10 honorarium mailed with the thank you letter. For those who had not responded after the

initial three contacts, a second survey packet was sent (contact #4) three weeks later.[13] One week after that, a telephone call was be placed to non-responders to request survey completion (contact #5).

We also performed a retrospective chart review to assess data from the most recent follow-up. These data supplemented an existing database on JHH Survivorship Visit that has previously been described.[8] Participant characteristics at diagnosis (e.g. age, race and ethnicity, insurance, marital status, employment status, menopausal status, parity, BMI, family history, comorbidities and genetic testing), cancer characteristics (stage and tumor phenotype) and treatment (surgery, radiation and systemic therapy) had already been collected.[8] We supplemented these with updated information on BMI, comorbidities and survival data (e.g. vital status, cancer status), time from diagnosis to survivorship visit, and time from diagnosis to most recent recorded follow-up. We calculated ' Charlson Comorbidity Index (CCI)[14] at time of diagnosis and at most recent follow-up. For alive at the end of the follow-up period, survival data were administratively censored on February 1, 2018.

Data were described using descriptive statistics. Fisher's exact testing was utilized to make a conservative estimate of association (e.g. endocrine therapy, employment, employment satisfaction, activity, anxiety, and depression) due to limited sample size. Univariate associations were explored between survey elements (e.g. employment, activity) and abstracted data from the medical record (e.g. obesity, Charlson Comorbidity Index) using univariate logistic regression, while changes in continuous variable measurements between time points were assessed using the paired t-test. Adjusting for age and race, multivariate logistic regression was used to compare symptoms at SV to those at most recent follow-up. All statistical tests were two-tailed. P-values were considered significant if less than 0.05. All analyses were performed using Stata 14.1/MP for Windows (College Station, Texas).

Results

Participants who primarily received adjuvant chemotherapy and were subsequently referred by their medical oncology providers for a single SV were included in this follow up survey study. Of 87 participants in the initial SV analysis, 74 were alive with no evidence of disease in February 2018. The surveys were mailed to these 74 individuals with a return rate of 70% (54 of 74). In total, there were 52 returned completed surveys, two opt outs, and 18 without a return (**Figure 1**). Forty participants had the same questionnaires completed at SV visit and 12 did not have these accessible in the medical record.

Participant demographics and cancer characteristics and treatment

This analysis includes the 52 women with early-stage breast cancer (stages I-III) who participated in a SV between January 2012 and December 2016 and returned the follow up survey (**Table 1**). Median age at follow up was 54.5 (interquartile range [IQR] 43, 65.5) years old. Most were Caucasian (71%), married (61%), and had private insurance (73%). Overall, the median time from diagnosis to most recent follow-up in survey responders was 3.1 years.

Employment

Compared to the time of diagnosis, the proportion of participants who reported they were currently employed decreased from 67% to 54% (**Table 2**). Three participants did report that they felt discriminated against at work following their breast cancer diagnosis. While job satisfaction was not assessed with the baseline survey at the SV, specific questions were added to the follow up survey. Among those who completed the recent survey, 46% and 29% reported they were very satisfied and somewhat satisfied with their current employment, respectively, while 25% were not too satisfied or not at all satisfied.

Physical activity

At both diagnosis and median follow up of 3.1 (2.4, 4.2) years, the mean body mass index (BMI) were similar (28.5 and 28.9 kg/m^2, respectively), and less than one third had a normal BMI (29% v 31%). However, there were more participants in the obese category (46% v 38%) and fewer in the overweight category (23% v 31%) at follow up compared to diagnosis. The only factor associated with normal BMI was sufficient physical activity (≥150 minutes per week of moderate intensity physical activity per guidelines[15]) (p=0.02), while endocrine therapy, employment, anxiety, and depression were not. Level of daily activity was sufficient in 21% and insufficient (10-149 minutes per week) in 19%, while 60% were sedentary or inactive (<10 minutes per week) (**Table 2**).

Participant symptoms

Forty of 52 participants had symptom data available at both the SV and most recent follow-up. Commonly reported symptoms at most recent follow-up included: insomnia (33%), weight change (33%), myalgias (28%), paresthesias (28%), hot flashes (23%), weakness (21%), fatigue (21%), and pain (18%) (**Table 3**). Among the 40 participants with questionnaires at both SV and follow up, after adjusting for age and race, both pain (p=0.02, OR 0.15 [CI 0.02-0.77]) and fatigue (p=0.001, OR 0.03 [CI 0.004-0.22]) were associated with less activity at follow up. After adjusting for age and race, paresthesias were significantly associated with unemployment (p=0.03, OR 0.12 (CI 0.02-0.81). At most recent follow-up, there was an association with more pain among those who were obese compared to those who have normal BMI (p=0.003). There were no significant associations of other symptoms (myalgias, weakness, paresthesias, fatigue, insomnia, or hot flashes) with employment, mental health, BMI or activity at follow up.

Comorbidities and mental health

Comorbidity data were similar between diagnosis and the most recent follow-up (**Table 4**). Median Charlson Comorbidity Index (CCI) at both diagnosis and most recent follow-up was 0 (IQR 0, 1). There was a 12% incidence of deep vein thrombosis at follow up; none of these participants with DVT were on tamoxifen. Among the same 40 participants who completed the generalized anxiety disorder 7-item scale (GAD-7) and the depression module of patient health questionnaire (PHQ-9) at both the SV visit and follow up, the median GAD-7 score for anxiety was 0 ("none") with an IQR of 1 ("none") to 7 ("mild"), and the median PHQ-9 score for depression was 1 ("minimal") with an IQR of 1 ("minimal") to 6 ("mild"). A higher proportion of participants reported moderate or severe anxiety (17% vs. 12%) and depression (18%

vs. 7%) at most recent follow-up than at SV. While employment status was not associated with depression, employment satisfaction was associated with lower likelihood of depression (p=0.02). Moderate or severe depression at most recent follow-up was associated with higher likelihood of myalgias (p=0.006), pain (p<0.001), weakness (p=0.007), fatigue (p<0.001), insomnia (p<0.001), and hot flashes (p=0.007). There were no observed differences in levels of depression or anxiety based on use of endocrine therapy, obesity, activity level, and paresthesias.

Discussion

As advances in the management of early-stage breast cancer reduce the risk of cancer recurrence and death, recognition of issues faced by survivors are essential for optimizing survivorship care and future research. A growing body of data show that adverse effects of breast cancer treatment can negatively affect survivors' ability to work and to remain physically activity.[16,17] Excess body weight is one of the strongest determinants of reduced life expectancy and morbidity.[18–20] Therefore, it is important to identify subsets of patients who might be at greater risk for adverse events long term and who could potentially benefit from more targeted interventions early on.[21,22]

In this long-term follow-up study, we surveyed a cohort of patients (including minorities) who were initially referred by their medical oncology providers for a SV after locoregional and initial systemic therapy. We observed a large proportion of participants who were dissatisfied at work or who dropped out of the work force, along with a significant association with presence of symptoms like paresthesias. Over two thirds of our breast cancer survivors were sedentary and had excess weight (BMI $\geq$ 25 kg/m^2) at diagnosis and at the SV, which is higher than expected when compared to cancer survivors at large.[23] Use of endocrine therapy, employment, anxiety, and depression were not associated with BMI, while the only factor associated with BMI was activity. Activity was also associated with lower odds of pain or fatigue, though there were no significant changes in comorbidities between diagnosis and most recent follow up. Moderate or severe depression was observed in 19% of participants, which is increased from 6% at SV and higher than the reported prevalence of depression in the general cancer survivor population. [24] Moreover, for those with moderate or severe depression at most recent follow up, there was an association with myalgias, pain, weakness, fatigue, insomnia, and hot flashes. Moderate or severe anxiety was observed in 17% of participants, which is increased from 12% at and comparable to observed estimates in general cancer survivors.

Our data suggest that certain breast cancer survivors, such as those who have received systemic chemotherapy, may face heightened issues after completing initial treatments. Additionally, given the association between depression and employment satisfaction, detection and treatment of underlying depression and sequela of therapy, like paresthesias, could favorably impact their ability to work. Adult physical activity guidelines recommend moderate intensity aerobic physical activity for 150–300 minutes per week and muscle strengthening exercise 2–3 times a week.[15] Increasing physical activity could also help improve BMI and possibly symptoms such as pain and fatigue. Thus, helping patients return to work

and increase physical activity may improve the quality of their survivorship. Further studies examining work discrimination and work satisfaction after diagnosis may better inform us of the long term challenges that patients experience.

Our study has limitations. First, our study population is small, has incomplete data at SV, may underestimate comorbidities, and is insufficiently powered to test many associations of interest. While all participants who received SVs completed an initial survey, these were not scanned into the medical record at intake and not accessible upon chart review. The SVs were not designed to assess their effectiveness, but instead to better understand the individual impact of cancer diagnosis and treatment, as well as to guide program development. Additionally, not all patients were systematically offered to participate in them, resulting in a potential referral bias with clinicians identifying patients felt to be at greater risk or challenges after treatment and late effects. Despite these limitations, the major strengths of the study include high survey participation rate and a broad assessment of domains with long-term follow up.

Finally, increasing efforts in wellness promotion are vital for cancer survivors. Our current care models lack emphasis on assessment and cultivation of interpersonal relationships, review of employment, reinforcement of lifestyle interventions, and conversations about mental health. A better understanding of long-term issues affecting cancer survivors have informed our breast cancer survivorship program, and influenced the build and design of various targeted intervention studies. For example, we have examined the impact of mindfulness meditation and survivorship education on behavioral health, including depressive symptoms, fatigue, sleep disturbance and vasomotor symptoms for long term survivors as far as 5 years post end of treatment. Our previous weight management studies have tested the efficacy of remote behavioral interventions with weight loss[25], and our recent studies have examined the effective of a sleep intervention prior to a behavioral weight loss strategy (NCT03542604). Our current weight management studies are determining the effects of pharmacotherapy and remote behavioral weight loss intervention, and the impact of weight loss on serum biomarkers and gut microbiome (NCT04499950). Future studies should focus on clear selection criteria for higher risk patients for targeted interventions. Moving forward, we will be testing a recently developed behavioral battery, which assesses demographics, social determinants of health, mental health, medication adherence, lifestyle factors, and symptoms. Risk models incorporating a behavioral battery may help health systems deploy meaningful interventions for those at greatest risk for worse outcomes, address their needs as cancer survivors, more effectively use health care resources, and ultimately improve their overall health-related quality of life.

Declarations

Abbvie. VS receives funding (to the institution) from Pfizer, Novartis, Puma Biotechnology, Biocept, and AbbVie, and as a Member, Data Safety Monitoring Board, Immunomedics, Inc.

References

1. Shapiro CL (2018) Cancer Survivorship. N Engl J Med 379(25):2438–2450
2. Jacobs LA, Shulman LN (2017) Follow-up care of cancer survivors: challenges and solutions. Lancet Oncol 18(1):e19–e29
3. Sheng JY, Visvanathan K, Thorner E, Wolff AC (2019) Breast cancer survivorship care beyond local and systemic therapy. Breast Edinb Scotl 48(Suppl 1):S103–S109
4. National Research Council and Institute of Medicine. From Cancer Patient to Cancer Survivor: Lost in Transition [Internet]. 2005 [cited 2018 Sep 25]. Available from: https://www.nap.edu/catalog/11468/from-cancer-patient-to-cancer-survivor-lost-in-transition
5. Ganz PA (2009) Quality of Care and Cancer Survivorship: The Challenge of Implementing the Institute of Medicine Recommendations. J Oncol Pract 5(3):101–105
6. Coyle D, Grunfeld E, Coyle K, Pond G, Julian JA, Levine MN (2014) Cost Effectiveness of a Survivorship Care Plan for Breast Cancer Survivors. J Oncol Pract 10(2):e86–e92
7. Peairs KS, Wolff AC, Olsen SJ et al (2011) Coordination of care in breast cancer survivors: an overview. J Support Oncol 9(6):210–215
8. Skuli SJ, Sheng JY, Bantug ET et al (2019) Survivorship care visits in a high-risk population of breast cancer survivors. Breast Cancer Res Treat 173(3):701–708

9. Kroenke K, Spitzer RL, Williams JBW (2001) The PHQ-9. J Gen Intern Med 16(9):606–613

10. Amireault S, Godin G, Lacombe J, Sabiston CM (2015) The use of the Godin-Shephard Leisure-Time Physical Activity Questionnaire in oncology research: a systematic review. BMC Med Res Methodol 15(1):60

11. Dillman DA (2006) Mail and Internet Surveys: The Tailored Design Method – 2007 Update with New Internet, Visual, and Mixed-Mode Guide. Wiley

12. Mindell JS, Giampaoli S, Goesswald A et al (2015) Sample selection, recruitment and participation rates in health examination surveys in Europe – experience from seven national surveys. BMC Med Res Methodol 15(1):78

13. Claycomb C, Porter SS, Martín CL. Riding the Wave: Response Rates and the Effects of Time Intervals between Successive Mail Survey Follow-up Efforts. 2000

14. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40(5):373–383

15. U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans, 2nd edition. Wash DC 2018;118

16. Dumas A, Vaz Luis I, Bovagnet T et al (2019) Impact of Breast Cancer Treatment on Employment: Results of a Multicenter Prospective Cohort Study (CANTO). J Clin Oncol 38(7):734–743

17. Ekenga CC, Pérez M, Margenthaler JA, Jeffe DB. Early-stage breast cancer and employment participation after 2 years of follow-up: A comparison with age-matched controls. Cancer 2018

18. Wu H-S, Davis JE, Chen L. Impact of Comorbidity on Symptoms and Quality of Life Among Patients Being Treated for Breast Cancer. Cancer Nurs 2018

19. Cho WK, Choi DH, Park W et al. Effect of Body Mass Index on Survival in Breast Cancer Patients According to Subtype, Metabolic Syndrome, and Treatment. Clin Breast Cancer 2018

20. Sung H, Siegel RL, Torre LA et al. Global patterns in excess body weight and the associated cancer burden. CA Cancer J Clin [Internet] 2018 [cited 2018 Dec 25];0(0). Available from: http://onlinelibrary.wiley.com/doi/abs/10.3322/caac.21499

21. Palmer SC, Stricker CT, Panzer SL et al (2015) Outcomes and Satisfaction After Delivery of a Breast Cancer Survivorship Care Plan: Results of a Multicenter Trial. J Oncol Pract 11(2):e222–e229

22. Bulloch KJ, Irwin ML, Chagpar AB et al (2015) Systematic Approach to Providing Breast Cancer Survivors With Survivorship Care Plans: A Feasibility Study. J Oncol Pract 11(2):e170–e176

23. Underwood JM, Townsend JS, Stewart SL et al. Surveillance of demographic characteristics and health behaviors among adult cancer survivors–Behavioral Risk Factor Surveillance System, United States, 2009. Morb Mortal Wkly Rep Surveill Summ Wash DC 2002 2012;61(1):1–23

24. Mitchell AJ, Ferguson DW, Gill J, Paul J, Symonds P (2013) Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: a systematic review and meta-analysis. Lancet Oncol 14(8):721–732

25. Santa-Maria CA, Coughlin JW, Sharma D et al (2020) The Effects of a Remote-based Weight Loss Program on Adipocytokines, Metabolic Markers, and Telomere Length in Breast Cancer Survivors: the POWER-Remote Trial. Clin Cancer Res 26(12):3024–3034

Tables

Table 1. Participant Demographics, Cancer Characteristics and Treatment at most recent follow up

Characteristic (N=52)		Frequency
Age at diagnosis (years), median (IQR)		54.5 (43, 65.5)
Current age, median (IQR)		59 (47, 71.5)
Race	Caucasian	71%
	African American	27%
	Other	2%
Ethnicity	Hispanic	2%
	Non-Hispanic	98%
Education	Less than high school	4%
	High school/GED	17%
	Vocational and Associates	21%
	Undergraduate degree BA/BS	25%
	Graduate degree MS/MBA/JD/PhD/MD	33%
Insurance status	Private	73%
	Medicare	27%
Marital status*	Single	12%
	Married/Partnered	61%
	Separated/Divorced	17%
	Widowed	10%
Menopausal at diagnosis	Yes	62%
	No	38%
Mutation present in those with genetic testing (n=25)	BRCA1 (n=4)	16%
	BRCA2 (n=1)	4%
	PALB2 (n=1)	4%
Stage	1	31%
	2	52%
	3	17%
Node status	Positive	54%

	Negative	46%
Hormone receptor status	Positive	56%
	Negative	44%
HER-2 receptor status	Positive	42%
	Negative	58%
Surgery	Lumpectomy	44%
	Bilateral mastectomy	31%
	Bilateral nipple sparing mastectomy	8%
	Bilateral skin-sparing mastectomy	6%
	UL mastectomy	11%
Lymph node assessment	Sentinel lymph node (SLN) biopsy	73%
	Axillary lymph node dissection (ALND)	19%
Chemotherapy	Yes	94%
	No	6%
Endocrine Therapy	Overall	56%
	Among HR-positive	97%
	Tamoxifen	31%
	Aromatase inhibitor 20	69%
Anti-HER2 therapy	Yes	42%
	No	58%
Radiation	Breast	56%
	Chest	44%
	Boost	18%
	LN	59%
Months from diagnosis to SV (years), median (IQR)		0.9 (0.7, 1.3)
Months from diagnosis to most recent follow-up (years), median (IQR)		3.1 (2.4, 4.2)

*At SV, 13% were single, 66% were married/partnered, 9% were separated/divorced, and 11% were widowed.

Table 2. Employment, Body Mass and Physical Activity

Characteristic (N=52)	Frequency at present
Employment status	
Employed	54%
Homemaker	36%
Retired	6%
Unemployed	4%
Current employment type	
Regular	86%
Independent contractor	7%
On call	4%
Agency	3%
Employment length	
<6 months	3%
6-12 months	11%
>12 months	86%
Employment years, median (IQR)	9.5 (5.8, 12)
Employment satisfaction	
Very	46%
Somewhat	29%
Not too	14%
Not at all	11%
BMI, mean (IQR)	28.9 (24.5, 32.7)
BMI class	
<18.5 (Underweight)	0%
18.5-24.9 (Normal)	31%
25-29.9 (Overweight)	23%
>30 (Obese)	46%
Exercise	
Sedentary or inactive	60%

Insufficiently active	19%	
Sufficiently active	21%	

*At diagnosis[8]: 67% were employed, 29% retired, 4% homemaker and 0% unemployed. Mean BMI (IQR) was 28.5 (24.3, 31.6). BMI classes include 2% underweight, 29% normal BMI, 31% overweight, and 38% obese.

BMI Body Mass Index.

Table 3. Symptom questionnaire among those with paired data (at both SV and follow up)

Symptom	Frequency of moderate or severe symptom at SV (n=40)	Frequency of moderate or severe symptom at follow-up (n=40)
Insomnia	31%	33%
Weight change	36%	33%
Myalgias	28%	28%
Paresthesias	25%	28%
Hot flashes	18%	23%
Weakness	10%	21%
Fatigue	28%	21%
Pain	21%	18%
Sexuality	17%	15%
Memory	13%	13%
Menstrual changes	7%	13%
Vaginal dryness	21%	13%
Difficulty at work	10%	11%
Difficulty with relationships	11%	8%
Fertility	3%	3%
% weight change, median (IQR)	1.8% (-3.6%, 6.0%)	n/a
Significant weight gain (>10%)	15%	n/a

Patients used a 4-item Likert scale ranging from none to severe to rate their concerns. For analysis, scores of none and mild, as well as moderate and severe were grouped together.

Table 4. Comorbidity and Mental Health

Comorbidity	Frequency at follow-up (N=52)
HTN	42%
Thyroid issues	15%
DVT	12%
Pulmonary issues	10%
Diabetes without damage	6%
MI	6%
PVD	4%
Diabetes with damage	2%
Liver disease, mild	2%
CKD	2%
Stroke	2%
Hemiplegia	2%
CT	2%
Charlson comorbidity score, median (IQR)*	0 (0, 1)
Mental health	**At recent survey (N=40)**
Anxiety score, median (IQR)	0 (0,1)
None/Mild	83%
Moderate/Severe	17%
Depression score, median (IQR)	1 (1,2)
None/Mild	81%
Moderate/Severe	19%

*Charlson comorbidity score includes moderate/severe liver disease, metastatic cancer, AIDS, CHF, dementia, PUD, and leukemia/lymphoma/local cancer (all of which were 0% for participants).

**At SV, 12% had moderate/severe anxiety and 7% had moderate/severe depression (n=52).

Figures

Enrollment

Patients from initial analysis who are disease free on follow up (n= 74)

Opted out (n= 2)

Survey not returned (n=18)

Returned completed survey (n=52)
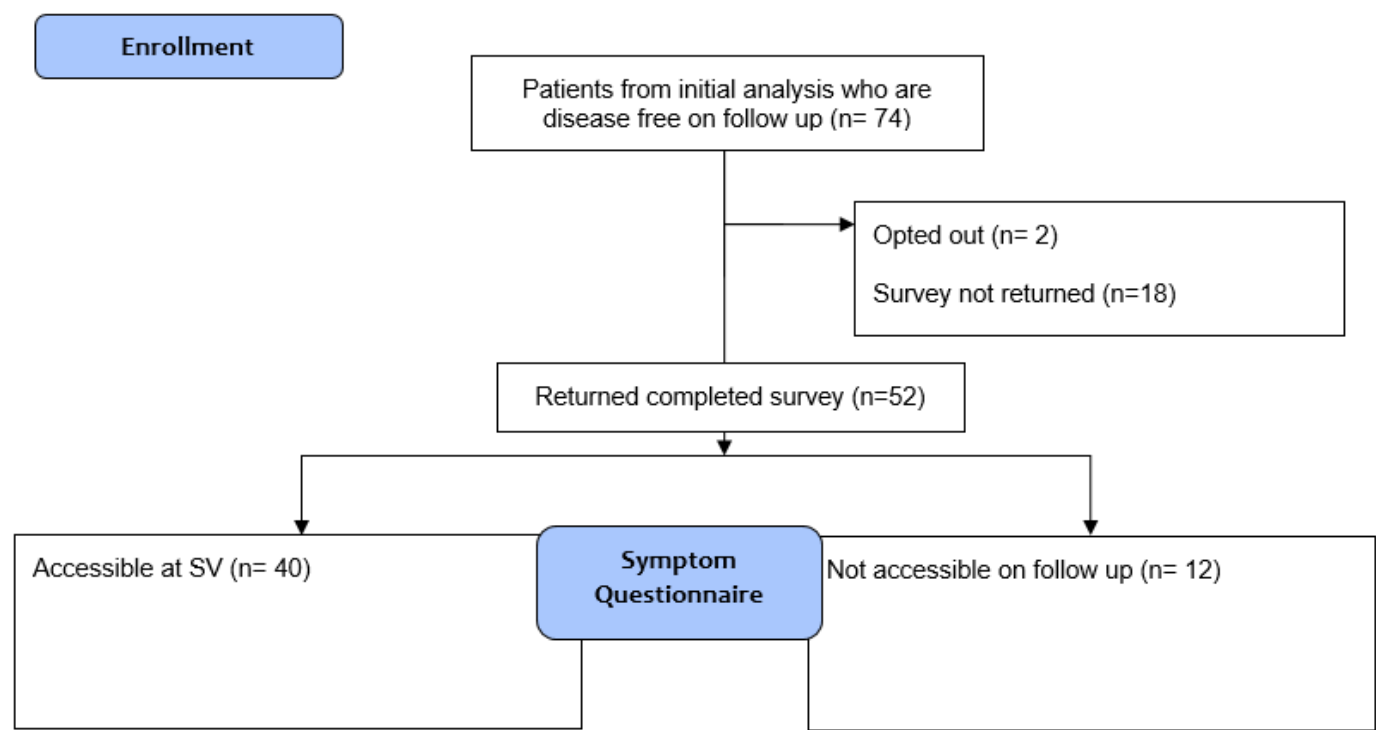
Accessible at SV (n= 40)

Symptom Questionnaire

Not accessible on follow up (n= 12)

Figure 1

CONSORT Flow Diagram