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Impact of Survivorship Care Planning of Oncology Care at the End of Treatment for Breast Cancer: A Randomized Controlled Trial

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ABSTRACT

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Background: In 2006, the Institute of Medicine (IOM) issued a report recommending that all cancer survivors receive a customized survivorship care plan (SCP) to increase survivors' understanding of diagnoses, long-term treatment effects, and ideas for improving overall health. Therefore, the purpose of this study was to compare a tailored SCP program (POST) to treatment as usual (TAU) on patient ratings of quality and content of discussion with providers at the end of their breast cancer treatment.

Methods: Two hundred participants were randomized to receive either the POST treatment (n=100) or TAU (n=100) at their last treatment visit. Women were presented with a checklist of 29 survivorship topics and indicated whether their healthcare provider discussed it at their last visit. They were also asked to rate overall quality of discussion (QOD) with their providers and across several QOD subscales.

Results: Analyses indicated that on average, POST women endorsed 20 out of the 29 topics compared to 14 topics endorsed by TAU. Additionally, POST women reported a better QOD overall and across all subscales.

Conclusion: POST women remembered discussing more survivorship topics and reported better discussions with their providers. As a practical implication, cancer survivors should receive an individualized SCP to ensure that patients feel well informed of their road to survivorship.

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INTRODUCTION

Cancer is the second leading cause of death in the United States with nearly 1.9 million new cancer cases

expected to be diagnosed in 2021.¹ Because the mortality rate for all combined cancers has been decreasing for the past few decades, in 2006, the Institute of Medicine (IOM) recommended that all cancer survivors receive a survivorship care plan (SCP) as part of standard care.¹ Both the IOM and the American Society of Clinical Oncology (ASCO) recommend that all SCPs contain information including, but not limited to, the prevention of new cancers, surveillance for recurrence, psychosocial and medical late

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effects, referrals to specialists, coordination between their primary care physicians (PCPs) and oncologists, financial issues, and diet/nutrition needs.²

Survivorship care planning content

Previous studies have demonstrated a need for such structured approaches, such as care planning, to help patients feel better informed when ending treatment for cancer.³⁻⁵ For example, Nicolaije *et al.* studied a group of women who were ending treatment for endometrial cancer and asked them to report ratings of satisfaction with 'information' received at the end of treatment.⁶ Although most patients reported receiving a large amount of information about their cancer and test results, most survivors reported feeling 'not informed' (54%), or feeling 'little informed' (24%), about the causes of their disease. Many also reported feeling 'not informed' (36%) or 'little informed' (27%) about the potential side effects of treatment. The researchers found that information about social and sexual life, rehabilitation, psychological assistance, and additional help was insufficient and that 15% of survivors indicated the need for more information. Nicolaije *et al.* recommended SCPs as a potential solution for patients feeling ill-informed as they enter survivorship. In addition, healthcare stakeholders (medical professionals and nurses) have expressed great support for the basic structure and general content of SCPs.⁷

Although there is a wide range of literature examining the impact of SCPs on health outcomes, there have been limited investigations of the *content* among SCPs. Specifically, there have been few studies that have examined patients' perceptions of care, and even fewer studies have examined exactly what kind of information patients receive from their oncologists at the end of treatment.^{3,5} Burg *et al.*³ analyzed the quality of care among breast cancer patients and found that although survivors received a great amount of survivorship-related information (i.e., types and frequencies of follow up care, self-care, diet/nutrition, prevention, and surveillance of secondary cancer), most of the survivors still wished that they had more knowledge, specifically regarding late effects (i.e., information regarding hair loss, sleep apnea, lymphedema, memory loss, etc.). The researchers recommended the use of SCPs in order to offer a comprehensive guideline of survivorship.

After establishing the apparent need for SCPs, Marbach and Griffie addressed the gap in the literature pertaining to survivors' preferences for content, delivery, and method of discussing SCPs.⁵ Forty cancer survivors participated in four focus groups to discuss their initial treatment plan, what was included, what they wished to be included, and their preferred format for an SCP. Some survivors reported that their oncologists gave verbal information regarding follow-

up care and possible long-term side effects. However, most survivors expressed anger and confusion as many of them were unaware of the roles of the cancer staff, how to reach their oncologist, essential treatment information, and, most importantly, who to call if they could not find the answers themselves. In addition, most participants reported that they wished they had received a written document with detailed information including diagnosis, surveillance for recurrence, types of treatment, and support services.

Perceptions of Quality of Patient Provider Interactions

In addition to increasing knowledge, researchers have speculated that care planning may improve patient-provider relationships and patient satisfaction with care.^{2,3,8-12} For example, several studies have found that women who were given an SCP reported higher quality of care/satisfaction compared to survivors who either received standard care,⁹ or those whose receipt of an SCP was delayed.¹⁰ In addition to these RCTs, another study administered SCPs to all cancer survivor participants and found that most (79%) were highly satisfied with the care plan.¹¹ However, it was found that although these women were highly satisfied, many reported that after receiving the care plan, they were still unsure of the role of their primary care provider and oncology nurse in terms of their follow-up care.¹¹

Further, relatively few studies have asked patients to rate the overall quality of their final care planning discussion.^{3,4,12} Although several studies have indicated that survivors believe that receiving an SCP may result in feeling better prepared for the struggles of survivorship,^{4,5,12,13} it is unclear whether receiving an SCP actually impacts the perceived quality of patient-provider interactions or if the content of the plans being delivered is adherent to IOM and ASCO content suggestions.

Theoretical Framework

The Polaris Oncology Survivorship Transition (POST) system is a web-based program that combines information from electronic health records (EHRs) and from the oncology care providers to generate an individualized survivorship care plan that abides by the IOM and ASCO survivorship planning guidelines.¹³ Therefore, the present study utilizes Tucker and Kelley's (2000) patient satisfaction theory as its theoretical framework.¹⁴ Developed from Linder-Peltz's expectancy-value theory, along with the work of several other studies, patient satisfaction theory posits that satisfaction is determined by the perception of access, communication, quality of care, and outcomes. Because the POST SCP is tailored to each patient, we expected that women who received this care plan



would have a positive perception of communication and knowledge with their providers and would receive more information on survivorship topics. Therefore, we predicted that POST women would report a better quality of discussion with their providers compared to those receiving standard care.

Purpose of Present Study and Hypotheses

As part of a larger, ongoing RCT investigating the impact of the POST SCP on quality of life ratings (the larger RCT is in press at the *Journal of Psychosocial Oncology*,¹⁵), the purpose of the present study was to do a secondary analysis to examine perceptions of content received at the end of survivorship care planning using IOM and ASCO content guidelines as benchmarks for the content that should be included in care plans. We examined patient perceptions of care planning content covered by their oncology providers as well as quality of discussion with their providers at the end of care planning sessions. We hypothesized that the women who received the POST intervention would report discussing significantly more cancer-related topics with their providers at the end of active treatment and would rate the quality of discussions significantly better than women receiving TAU.

METHODS

The present POST Phase 2 study is an RCT designed to investigate the impact of SCPs on patient and provider outcomes. Women were deemed eligible to participate if they were 18 years or older, had a confirmed non-metastatic breast cancer diagnosis (stages 0 to III), had a scheduled active treatment plan with the study's affiliated hospital, were alert and oriented, could read and comprehend English at a 6th grade level, volunteered to participate in the study, and were available for follow-up assessments. Participants were excluded from the study if they had visual problems that prevented them from reading the reports and assessments, had an altered mental state (e.g., delirium, psychosis, dementia), had a serious/severe illness that prevented communication with the research team, could not read or comprehend English at a 6th grade level, were not available for follow-up assessments, and/or had already received an SCP as part of their cancer care prior to being identified for the present study.

Several assessments were administered throughout the study that examined physical and emotional health symptoms, as well as perceptions of quality of oncology care related to breast cancer survivorship care planning. For the purposes of the present paper, we highlight the assessment tools that are directly relevant to the current analyses. Additionally, it is worthy to note that several of the assessments used

were created from a grant funded by the National Cancer Institute (NCI) and, therefore, were not validated measures.

Researchers administered an 8-item measure at enrollment to collect demographic and cancer-related information. Patients self-reported information such as race, ethnicity, age, marital status, education level, diagnosis, and date of diagnosis. The research staff included information from the patients' health records concerning their end of active treatment, status of survivorship care planning, and ongoing therapies, to ensure the accuracy of the self-reported information.

POST Patient Assessment

The POST Patient Assessment was created specifically for this trial using the study's grant and was administered to both groups during enrollment. All women completed the assessment which included 23 items measuring social support, distress, physical functioning, physical symptoms, alcohol use, and tobacco use. In addition, participants rated how well they had been able to manage day to day life on a scale from "Very poorly" to "Very well". POST women received a slightly more comprehensive version of the assessment which included items on barriers experienced, need for referrals, interest in the 33 SCP library topics, unanswered questions about their cancer care, and the desire to send a copy of the SCP to their PCP.

We also created the Survivorship Care Planning Content Checklist specifically for this study to examine the patient-reported quality and content of discussion with their oncology providers. At the research visit, the study staff administered this checklist to all participants, and they responded either 'Yes', 'No', or 'I don't know' as to whether they remembered discussing 29 cancer-related topics at their last patient-provider interaction. Participants were also asked to rate the quality of discussion of their medical history and future care plan, emotional health, physical health, social support/practical matters, and overall quality of discussion with their health care provider on a scale from 1 to 7, with '1' indicating poor quality and '7' indicating excellent quality. Note that a chart review was completed 6 months after the completion of this study for all participants. That data will be published in future studies but is not relevant for the current paper.

Procedure

Data was collected from participants at 5 different time points.

First, Recruitment and Enrollment: Potential subjects were identified in several ways: 1) via direct recommendation from the patient's cancer care team, 2) recommendation from radiation oncology nurses, 3) through research assistants (RAs) using the medical



oncology provider schedule, 4) identification by RAs at the breast cancer/tumor board conference, 5) other direct recommendation from the oncology staff. Once the potential subjects were identified, RAs gathered data relevant to the inclusion/exclusion criteria via RED Cap and tracked these potentially eligible patients until the end of their active treatment. Patients were then approached by the RAs and if interested, they completed the written informed consent process. After enrolling in the study, participants were randomized to either the POST intervention arm or the TAU arm and completed baseline assessments, which are described below. It should be noted that in the present study, end of active treatment was defined as the last regimen of care such as the completion of radiation, surgery, or adjuvant chemotherapy. Drug maintenance therapies (i.e., Anastrozole, Herceptin, etc.) were not considered to be active treatment.

Second, Research Intervention Visit: One month after enrollment, women were invited back to a research intervention visit (second contact point). Here, the POST and TAU women received different protocols.

Third, at the research visit, the POST women received an individualized SCP which was created by the *Blinded for Review* RAs and the study nurse using both the patients' health records and their responses to the POST assessment (A sample POST SCP is attached in the appendix of this paper). A portion of the information from the patients' EHRs was prepopulated into the patients' SCP (e.g., demographics, care team, diagnosis, etc.). To ensure accuracy, the study nurse and research staff reviewed all pre-populated and manually entered information before completing the SCP. The final SCP consisted of 10 patient-centered topics: 1) demographic information, 2) cancer care team, 3) diagnosis, 4) surgery and therapy details, 5) dates of recent tests and exams, 6) side and late effects, 7) current medications, 8) upcoming appointments, 9) barriers, and 10) libraries of information and references. Every plan contained sections that included information on follow-ups, general recommendations for breast cancer survivors, possible late and long term effects, screening and surveillance tips, etc.

Fourth, the study nurse reviewed all the sections with the patients and allotted time specifically for questions and concerns. On average, it took about 30 to 45 minutes for the study nurse to review the SCP with the POST women. Further, all women received a hard copy of the SCP along with an electronic copy that was uploaded to their EHRs and for those women who consented, an additional electronic copy was sent to their PCP. In addition, it should be noted that only the

women in the POST intervention were given the opportunity to directly request a referral using the POST patient assessment. However, all patient responses were reviewed to determine if there was a reason to suggest a referral for TAU women (e.g., high levels of depression, anxiety, distress). Lastly, after receiving the SCP, women completed final baseline assessments.

Finally, at the research visit, the TAU women received the affiliated hospital's standard care planning procedure. Analyses later indicated that only 70% of TAU women received an SCP. For these women, the nurse spent approximately 20 to 30 minutes reviewing the care plan with them. Like the POST protocol, TAU women also completed final baseline assessments at this visit.

Although the data is not presented in this paper, all women completed follow-ups either via phone or email at 1, 3, and 6 months post-baseline that measured psychological, physical, and emotional outcomes. All subjects had the opportunity to earn \$80 for their participation; they were given a \$20 gift card after the completion of the baseline assessments at the research visit, and each of the follow-up surveys.

Statistical Analyses

Percentages were reported for discrete variables while means and standard deviations were given for continuous variables. In order to test for differences between the POST and TAU participants, we used chi-square tests for discrete variables and two-sided *t*-tests for continuous variables. An alpha level of 0.05 was used to determine statistical significance. All analyses were conducted using SAS software (version 9.4; SAS Institute, Cary, NC).

RESULTS

Of the 200 breast cancer survivors enrolled, 188 completed the baseline assessment (91 POST; 97 TAU). The participants were female (100%), were, on average, 60 years old at the time of enrollment ($SD = 11.0$ years), were predominantly white/non-Hispanic (86%), were married (58%), and most had attended at least some college (82%). Most women had Stage I cancer (45%) and were diagnosed six months or less prior to enrollment (63%). Finally, out of the 100 women randomized to TAU, chart review data revealed that 70 women received an SCP from the cancer center oncology team. Detailed demographic information can be found in Table 1 of the larger RCT paper.¹⁵

**Table 1.** Survivorship items discussed with patients by healthcare providers at last treatment visit: POST versus TAU

	Total		POST		TAU		P
	N	Percent	N	Percent	N	Percent	
Baseline (n=188)			N=91		N=97		
Medical Diagnosis and Treatment Summary	168	89.4	87	95.6	81	83.5	0.01
Medical Care Plan	180	95.7	90	98.9	90	92.8	0.12
Survivorship	131	69.7	73	80.2	58	59.8	0.01
Pain	168	89.4	84	92.3	84	86.6	0.30
Lymphedema (swelling in arms or legs)	122	64.9	71	78.0	51	52.6	0.0003
Tiredness or Fatigue	149	79.3	82	90.1	67	69.1	0.0004
Insomnia or Sleep Difficulties	125	66.5	77	84.6	48	49.5	<0.0001
Nausea/Vomiting/Diarrhea	105	55.9	58	63.7	47	48.5	0.08
Hot Flashes	134	71.3	74	81.3	60	61.9	0.002
Night Sweats	115	61.2	66	72.5	49	50.5	0.003
Anxiety	110	58.5	69	75.8	41	42.3	<0.0001
Depression	109	58.0	69	75.8	40	41.2	<0.0001
Cognitive Effects	95	50.5	64	70.3	31	32.0	<0.0001
Intimacy/Sexual Life	77	41.0	51	56.0	26	26.8	<0.0001
Body Image Concerns	97	51.6	53	58.2	44	45.4	0.07
Skin Changes	129	68.6	63	69.2	66	68.0	0.99
Hair Loss	69	36.7	38	41.8	31	32.0	0.33
Breast Reconstruction	71	37.8	29	31.9	42	43.3	0.26
Fear of Recurrence	108	57.4	60	65.9	48	49.5	0.01
Premature Menopause and/or Fertility Concerns	41	21.8	24	26.4	17	17.5	0.36
Finances/Employment/Practical Problems	45	23.9	27	29.7	18	18.6	0.04
Spirituality/Religiosity	31	16.5	15	16.5	16	16.5	0.74
Relationships/Social Support	91	48.4	56	61.5	35	36.1	0.001
Weight	115	61.2	67	73.6	48	49.5	0.001
Nutrition/Diet	122	64.9	74	81.3	48	49.5	<0.0001
Physical Activity/Exercise	147	78.2	83	91.2	64	66.0	<0.0001
Smoking/Tobacco Use	87	46.3	51	56.0	36	37.1	0.02
Alcohol Use	90	47.9	59	64.8	31	32.0	<0.0001
Side-effects of Cancer Medications	140	74.5	79	86.8	61	62.9	0.0002
	Mean	SD	Mean	SD	Mean	SD	P
Number of items checked "yes" per person	16.9	7.8	19.7	6.7	14.2	7.9	<0.0001

This table is limited to those who answered at least one Content Checklist question

Of the 29 items on the survivorship content checklist, the POST women reported discussing significantly more items (mean=19.7) as compared to 14.2 items among the TAU group ($P<0.0001$). Statistically significant discussion topics included, but were not limited to, medical diagnosis and

treatment summary ($P=0.01$), lymphedema ($P=0.0003$), anxiety ($P<0.0001$), depression ($P<0.0001$), and cognitive effects ($P<0.0001$; See Table 1). Similar analyses were conducted comparing the 70 women in the TAU who received a standard care SCP with the women who received the POST



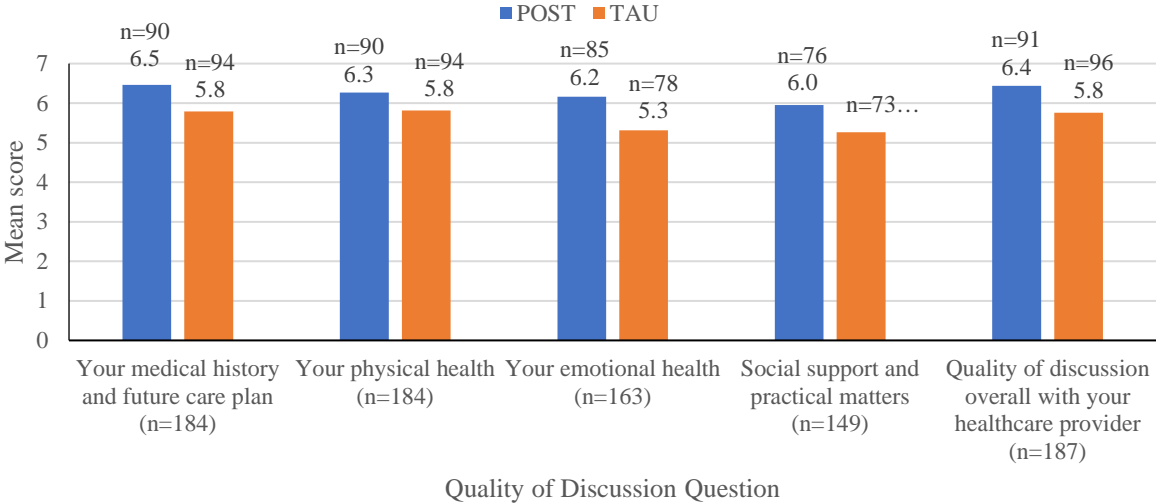
SCP. These analyses concluded that POST women still reported discussing more items with their physicians compared to the 70 TAU women who received an SCP. Compared to the 19.6 item average for the POST women, the TAU women reported discussing 14.3 items, on average (Detailed results can be found in Table 2).

Mean quality of discussion scores were calculated for the overall score and 4 subscales. On average,

POST women rated significantly higher (better) overall quality of discussion with their providers (mean=6.4) compared to TAU (mean=5.8; $P=0.0003$) as well as better quality of discussion across four specific areas of functioning including medical history and future care plan ($P=0.0005$), physical health, ($P=0.01$), emotional health ($P=0.0004$), and social support and practical matters ($P=0.01$; See Figure 1.)

Table 2. Survivorship items discussed with patients by healthcare providers at last treatment visit: POST versus only women in TAU who received an SCP

	Total		POST		TAU		P
	N	Percent	N	Percent	N	Percent	
Baseline (n=158)			N=90		N=68		
Medical Diagnosis and Treatment Summary	145	92	86	96	59	87	0.09
Medical Care Plan	153	97	89	99	64	94	0.21
Survivorship	117	74	72	80	45	66	0.13
Pain	140	89	83	92	57	84	0.15
Lymphedema (swelling in arms or legs)	105	66	70	78	35	51	0.0004
Tiredness or Fatigue	130	82	81	90	49	72	0.01
Insomnia or Sleep Difficulties	109	69	76	84	33	49	<0.0001
Nausea/Vomiting/Diarrhea	91	58	57	63	34	50	0.23
Hot Flashes	115	73	73	81	42	62	0.01
Night Sweats	98	62	65	72	33	49	0.004
Anxiety	95	60	68	76	27	40	<0.0001
Depression	95	60	68	76	27	40	<0.0001
Cognitive Effects	86	54	63	70	23	34	<0.0001
Intimacy/Sexual Life	67	42	50	56	17	25	<0.0001
Body Image Concerns	84	53	52	58	32	47	0.22
Skin Changes	109	69	62	69	47	69	0.99
Hair Loss	56	35	37	41	19	28	0.21
Breast Reconstruction	57	36	28	31	29	43	0.32
Fear of Recurrence	94	59	59	66	35	51	0.02
Premature Menopause and/or Fertility Concerns	34	22	23	26	11	16	0.40
Finances/Employment/Practical Problems	37	23	26	29	11	16	0.08
Spirituality/Religiosity	24	15	14	16	10	15	0.85
Relationships/Social Support	80	51	55	61	25	37	0.01
Weight	98	62	66	73	32	47	0.001
Nutrition/Diet	106	67	73	81	33	49	<0.0001
Physical Activity/Exercise	129	82	82	91	47	69	0.001
Smoking/Tobacco Use	78	49	50	56	28	41	0.18
Alcohol Use	80	51	58	64	22	32	0.0001
Side-effects of Cancer Medications	121	77	78	87	43	63	0.001
	Mean	SD	Mean	SD	Mean	SD	P
Number of items checked "yes" per person	17.3	7.6	19.6	6.7	14.3	7.6	<0.0001

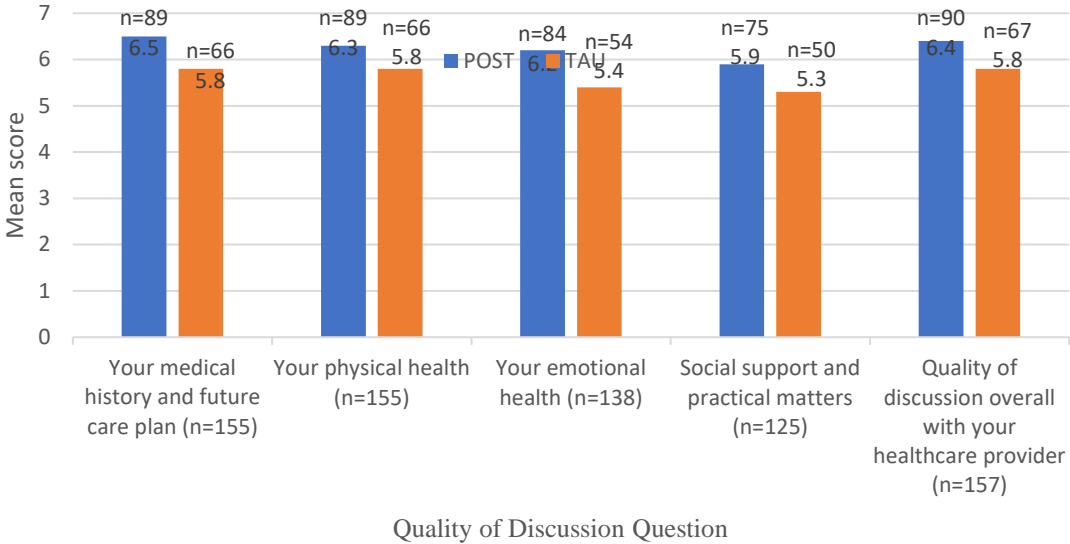


The total 'n' for each subscale indicates the number of people who answered the question. All comparisons shown were statistically significant (P<.05).

Figure 1. Mean quality of discussion with healthcare provider among POST versus TAU women

All analyses were repeated comparing the 70 women in the TAU who received an SCP with the POST women. When the analyses were run again, we found that the POST remained superior to TAU across QOD overall (P=0.003) and its subscales: medical

history and future care plan (P=0.001), physical health (P=0.04), emotional health (P=0.002), and social support and practical matters (P=0.02; Detailed results can be found in Figure 2).



The total 'n' for each subscale indicates the number of people who answered the question. All comparisons shown were statistically significant (p<.05).

Figure 2. Mean quality of discussion with healthcare provider among POST and TAU women who received an SCP



DISCUSSION

The primary purpose of this study was to evaluate whether the POST intervention affected patients' perceptions of their oncology care, assessed by patient reported quality and content of discussion, more so than TAU. However, because we noted from chart review data that out of the 100 women enrolled into the TAU condition, 70 received an SCP from their oncology care team, a secondary goal of this paper was to compare the women given POST SCP to the women in the TAU who received a standard care SCP. There were several notable findings indicating that the POST intervention was more successful than TAU in enhancing perceptions of oncology care at the end of treatment.

First, we found that significantly more women who received the POST reported discussing survivorship-related topics (i.e., 20 topics) with their oncology provider at the end of treatment, as compared to women who received TAU (Table 1). Topics included but were not limited to cancer diagnosis, anxiety, depression, cognitive effects, and side effects to cancer medications. Once we repeated the analyses comparing the 70 women to the 100 POST women, only 16 topics remained significantly in favor of the POST intervention. The topics that went from significant to non-significant included medical diagnosis and treatment summary, survivorship, finances/employment/practical problems, and smoking/tobacco use. One reason for these findings may be that the POST SCP was more comprehensive, covering more topics, than the SCPs used in TAU. A more detailed SCP may have cued the study nurse to discuss more topics at the final survivorship care-planning visit. Also, the oncology providers in the TAU condition were not part of a research study and, therefore, may not have been able to dedicate as much time to each patient to discuss various topics covered in the SCPs.

We also examined patients' ratings of the quality of discussion with their providers at the end of treatment. Women who received the POST SCP reported a better quality of discussion overall and across all subscales (See Figure 1). This remained true even when comparing the POST women to the 70 women in TAU who received a care plan (See Figure 2). This highlights the need for an individualized care plan, such as the POST, because of its enhancement of the patients' appreciation that their providers did a good job discussing their survivorship needs. This is important as 22% of breast cancer survivors continue to experience anxiety and depression,¹⁶ throughout their survivorship journey. Thus, we speculate that it is important that patients feel as though they have fulfilling conversations with their providers to mitigate this anxiety.

This study had several limitations. The scope of the present study was limited to women with breast cancer. Therefore, our findings may not be generalizable to other cancer types or males. Our sample also was predominantly white/non-Hispanic (86%); we recommend that future studies focus on women of color and their perceptions of oncology care as they enter survivorship. As previously noted, several of the assessments used in the study were not validated tools because they were developed from a grant funded by the NCI and, therefore, we avoided using validated measures to limit participant burden. In addition, due to the multiple comparisons that were conducted within this analysis, we did not adjust the p-value cut off. Therefore, one should consider the likelihood of increased Type I error (incorrectly rejecting a true null hypothesis) in the results. Lastly, 70 women in the TAU received a care plan. Originally, we intended to compare the POST to an absence of care planning. However, after receiving the grant, the hospital where the study was conducted introduced requirements that all women ending treatment for breast cancer receive SCPs. The research team changed the study to examine TAU and chart review data documented that 70% of the women in the TAU received SCPs. Results showed that the POST remained superior for several content areas that were discussed with the women at the end of treatment as compared to the SCPs received in the TAU. More importantly, the POST's impact on ratings of quality of discussion remained superior when comparing the two groups of women who received SCPs.

CONCLUSION

In conclusion, these findings support our hypothesis that the POST intervention improved patient perceptions of their oncology care. Specifically, the POST women remembered discussing more survivorship topics than the women in TAU as well as compared to those women who received an SCP as part of their TAU. They also rated quality of discussion with their provider significantly better than TAU. We found that not only was the POST SCP superior to the absence of care planning, it was also superior to the standard practice care plan. In sum, having an oncology nurse provide a tailored, comprehensive SCP, like the POST, to women ending treatment for breast cancer may help women transition into survivorship feeling more knowledgeable about important survivorship topics and satisfied with their oncology care. In addition, we believe women who receive a tailored SCP in the future will also feel as though they had high quality discussions about their road to survivorship. There-



fore, we speculate that long-term effects of an individualized SCP will improve survivors' feelings of confidence toward survivorship which may enhance their overall quality of life.

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CONFLICT OF INTEREST

Intellectual property, licensing and revenue income from the POST program are shared between Tridium (formerly known as Polaris Health Directions) and the University of Massachusetts Medical School. Dr. Boudreaux and Dr. O'Hea have also consulted for Tridium and Dr. Harralson is employed by Tridium. The content is solely the

responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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