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The Integration of Emotional, Immunological and Communication Responses to Medical Oncology Surveillance Appointments During Breast Cancer Survivorship

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Abstract

Background—Breast cancer survivors regularly interact with providers during routine surveillance medical oncology visits, discussing uncertainty / anxiety about cancer recurrence many years post-treatment. Because breast cancer onset frequently occurs in older women, survivors may have additional age-related illnesses and symptoms yet be uncertain about whether the cause of their symptoms is normal aging, another illness, or breast cancer recurrence. Physiologic responses such as immune alterations may predispose women to exacerbations of these illnesses. The survivor-provider relationship is also influential give the long standing nature of ongoing breast cancer surveillance post active treatment completion.

Objective—The purpose of this study was to evaluate relationships between emotional distress (uncertainty, anxiety, fear of recurrence), immunity (cytokine levels, lymphocyte counts), and communication events (women's plans for their visit, the ability to negotiate decision-making roles) immediately before and 24 hours after a regularly scheduled medical oncology surveillance visit.

Methods—We evaluated relationships between emotional distress (uncertainty, anxiety, fear of recurrence), immunity (cytokine levels, lymphocyte counts), women's plans for their visit, and their ability negotiate decision-making roles, before and after a medical oncology visit.

Results—Emotional responses (uncertainty, anxiety, fear of cancer recurrence) to an upcoming medical oncology were associated with change in immune status pre-post visit. Post-visit NK cells increased in 70% of women, and uncertainty/anxiety decreased. Most women had a plan for their oncology visit and 66% successfully negotiated decision-making roles with providers although these factors did not predict emotional or immune outcomes, perhaps due to longstanding relationships previously established with their medical oncology provider.

Conclusions—breast cancer survivors in this study, as in others, report uncertainty and anxiety related to the fear of cancer recurrence associated with routinely scheduled medical oncology

visits. Women also experienced alterations in immune responses to the stress of a routine medical oncology visit. The interaction between women and their oncology providers has the theoretical potential to allay both emotional and physiological responses to this stressor, contributing to the well-being and quality of life for older long-term breast cancer survivors

Implications for Practice—Because not all women respond in a similar fashion to an upcoming medical oncology surveillance visit there is a need to determine who may be most at risk for more acute alterations in immunity related to the fear of cancer recurrence that is inherent in ongoing surveillance after treatment for breast cancer. When the meaning of symptoms is understood, and existing symptoms are not erroneously attributed to breast cancer recurrence, quality of life is enhanced and women can move forward in their lives without significant emotional distress¹. Further, immediate answers to questions, thus resolving concerns and uncertainty about symptoms, may potentially avoid prolonged immune status changes that can result from worrying about and waiting for discussions of concerns until the next office appointment. This could be facilitated by nurse operated telephone based “help lines” where women could call in without fear of “bothering the doctor”. The goal here would be to provide immediate reassurance rather than let women worry for prolonged periods of time while waiting for their next (often annual) medical oncology appointment.

Keywords

breast cancer survivorship; cancer communication; emotional distress; immunity

Currently, it is estimated that 3.1 million breast cancer survivors live in the U.S. and 90% of women diagnosed with localized breast cancer are expected to survive 5 years or longer ². The steady decline in mortality due to breast cancer has resulted in more women living with and managing the acute and late emerging side effects of treatment. Further, breast cancer is often a disease of older women who manage additional chronic conditions. Eighty percent of breast cancer is diagnosed in women over age 50 with the median age at diagnosis 61 years ². Overall, and in response to the increasing number of cancer survivors, increased understanding of cancer survivorship has been a research priority of the National Cancer Institute’s Office of Cancer Survivorship as evidenced by sponsored conferences focusing on survivorship (7th biennial Cancer survivorship research conference held in 2014 and sponsored by the American Cancer Society, the National Cancer Institute’s Office of Cancer Survivorship, the Livestrong Foundation, and the Centers for Disease Control and Prevention) and calls to action addressing the unique concerns faced by survivors ³.

Background

Breast cancer survivorship is a process of integrating past disease experiences with current lifestyle and future events. Given that women interact with multiple healthcare providers and often have multiple comorbid conditions, providing optimal cancer survivorship care is a complex endeavor that must integrate emotional, physiologic, and communication components. Uncertainty theory suggests that when this is done positively a new view of life is created, based on opportunity and hope rather than anxiety and uncertainty ^{4, 5}. The experience is also well described by the Reservoir Model – stressful events accumulate

(“add up”) over time but can be dissipated as individuals apply stress reducing mechanisms to their daily lives ⁶.

Overall, little is known about how naturally occurring stressful events (as opposed to laboratory induced stressors of public speaking or solving mathematical problems) such as regularly scheduled medical oncology appointments are associated with immune responses for breast cancer survivors. Even less is known about the association of survivor-provider communication with emotional and physiologic outcomes among breast cancer survivors. Therefore the purpose of this study was to evaluate relationships between emotional distress (uncertainty, anxiety, fear of recurrence), immunity (cytokine levels, lymphocyte counts), and communication events (women’s plans for their visit, the ability to negotiate decision-making roles) immediately before and 24 hours after a regularly scheduled medical oncology surveillance visit.

Emotional Considerations During Breast Cancer Survivorship

Although 5 year survival is still considered a major milestone for recovery, most breast cancer survivors attend routine medical follow-up visits throughout survivorship and remain nervous about these visits ^{7, 8}. Indeed, while most breast cancer survivors do not experience diagnosed depression greater than others in the population, it is known that intermittent acute distress and psychological distress about cancer recurrence persist post diagnosis ^{7, 9, 10}. Breast cancer survivors emphasize the cyclical anxiety and uncertainty occurring before medical visits ^{11, 12}. Women report “waiting” for the next office visit, the next medical test, and the next visit with their provider ¹¹ in an ongoing state of uncertainty and “needing to know” ¹². This concern is valid, since breast cancer recurrence can occur 10 or more years after initial treatment, and the risk of a new cancer remains elevated for life ¹³.

Complicating provider assessment of emotional distress, studies addressing the stress of women living with the risk of breast cancer recurrence report that subjective survivor reports of emotional well-being do not always correlate with objective measures of physiologic well-being ^{14, 15}. These studies suggest that patients can adopt a pleasant affect toward medical providers yet remain highly anxious, thus providers may not always be aware of emotional distress ¹⁵.

Physiologic considerations during breast cancer survivorship

Studies of physiologic responses to stressors have often been conducted in vitro, identifying cellular pathways and responses, but not addressing external processes such as patient worry and patient-provider communication that may impact responses to an identified stressor ¹⁶. Physical responses to real world stressors such as an upcoming medical oncology visit and the associated fear of cancer recurrence are less well understood than emotional responses. Previous research links stressful events to altered immunity in both animal models ¹⁷ and cardiac patients ¹⁸. Other research indicates that emotional stress is associated with decreases in NK activity and Th1 cytokines IL-2 and IFN- γ among daughters of women with breast cancer ¹⁹. Decreased IL-2 production and NK production have also been associated with increased norepinephrine and cortisol implying neuroendocrine mediation (Cohen et al., 2002). Overall, altered immunity and associated emotional stressors may

impact cancer development as well as short and long-term health. This is due to the suppression of innate immunity during acute stress, suppressing T lymphocyte helper type1 (Th1) mediated responses (decreases in Th1 cytokines such as IFN- γ and IL-2, reduced IL-2 receptor expression and decreases in the normal Tc and NK absolute counts and cell activity) that protect against infections and some tumors, and the increased T lymphocyte helper type2 (Th2) responses (increases in Th2 cytokines such as IL-4 and IL-5) that may exacerbate comorbid conditions frequently associated with older age (e.g. cardiovascular disease, osteoporosis, rheumatoid arthritis, diabetes) ^{20–22}.

Because breast cancer survivors consider follow-up medical office visits as stressful “high stakes” events, changes in immunity (e.g. altered cytokine levels and lymphocyte counts) may be seen ^{23–25}. Other immune responses such as elevated baseline cortisol levels and blunted cortisol reactivity to the acute stress of routine mammograms in long-term breast cancer survivors have been reported ²⁶. Further, the subjective perception of stress including the presence of intrusive thoughts, and prolonged exposure to a stressor has been linked to reduced counts and activity of circulating lymphocytes and may predict cancer recurrence for some ^{14, 23, 27}. Because older persons and persons with co-morbid diseases have immune systems that are less robust than younger persons making them vulnerable to the adverse effects of altered immunity (e.g. minor illness and worsening autoimmune diseases such as arthritis) ²³ and survivors are living longer with age related co-morbid illnesses, evaluating the effect of altered immunity on short and long term health becomes important.

Communication considerations during breast cancer survivorship

Communication with Providers—The importance of communication was noted by Hippocrates who wrote: “I will remember that there is art to medicine as well as science, and that warmth, sympathy, and understanding, may outweigh the surgeon’s knife or the chemists drug” ²⁸. Patient-provider communication has been associated with both the emotional well-being of cancer survivors ⁸ as well as altered immunity (increased cortisol) ²⁹.

Communication with healthcare providers has been shown to reduce uncertainty and distress for breast cancer survivors and as such can be considered a stress reducing mechanism ⁸. When the conversation is perceived by survivors to be more patient centered distress and uncertainty are also reduced ^{7, 30}. As an example, during routine breast exams during surveillance medical oncology office visits women may be anxious about whether the doctor “found a new lump” knowing that an abnormal clinical breast exam is known to be a strong indicator of cancer recurrence ³¹. Results are available immediately, and are part of the communication between patient and provider. Thus, communication with providers plays a major role in reducing the fear of cancer recurrence by the provision of information and reassurance about the meaning of symptoms ⁸. In addition, the ability of patients to present experienced symptoms and concerns and have them fully addressed by providers with explanation and information (a patient-centered approach), can potentially reduce uncertainty and anxiety about the meaning of symptoms with respect to cancer recurrence ⁷.

The survivor-provider relationship—The survivor-provider relationship is influential given the long standing nature of ongoing breast cancer surveillance throughout survivorship. Often there is an established patient-provider relationship and women feel comfortable presenting their questions and concerns to providers. Women may plan for their visit, developing specific questions and issues they wish to discuss with providers. Previous research has shown that among breast cancer survivors attending routine follow-up surveillance oncology visits 63% had a very specific plan and an additional 24% had a general plan for their visit ⁷. Medical oncology providers can allay uncertainty and anxiety by effective patient-centered communication (for example acknowledging and addressing symptoms), facilitating decision-making role preferences, and providing information that can allay fears of recurrence.

Communication problems—Communication problems also exist. Providers can only address symptoms, anxiety and uncertainty of breast cancer survivors if they are aware of these issues. Women must be willing to communicate their concerns to providers, and providers must be willing to address concerns. However, some breast cancer survivors may be unwilling to share information, for example women report enduring symptoms such as fatigue that they have not discussed with providers ⁷. Negotiating decision making roles is another area that may result in less than optimal communication processes. While most breast cancer survivors are able to negotiate the decision-making role they desire (active, passive, or collaborative) some are unable to do so. Previous research has shown that as many as 52% of women must adopt a more passive or active decision-making interaction role with providers than they initially desired ⁸.

Methods

Procedures

After obtaining IRB approval, recurrence-free breast cancer survivors two or more years beyond original treatment were identified using appointment schedules from the recruitment site, then telephoned by medical oncology office staff to introduce the study. If women were willing to learn more about the study, names were given to the principal investigator who called and explained the study in greater detail and obtained verbal consent. On the day of their regularly scheduled surveillance appointment, women were asked to arrive 30 minutes early for their appointment. Women were met in the medical oncology office, written consent obtained, and self-report measures obtained by a trained research assistant. Immediately prior to the visit, measures of immunity were obtained in conjunction with regular blood work, as a normal part of the visit. Post-visit immune markers were collected by a trained phlebotomist research assistant the following morning in the woman's home, as was self-report data. Collecting data within a standardized 3 hour time (9AM-12 Noon) controlled for diurnal variation. Blood specimens were delivered to the testing lab and self-report surveys were placed in an envelope, sealed, and returned directly to the PI.

Sample and Setting

Twenty seven community dwelling breast cancer survivors were recruited. Inclusion criteria were: (a) cognitively intact women age 40 and older (because younger women of child

bearing age often have different issues and concerns such as fertility related to treatment, as well as more aggressive disease and less age associated co-morbid conditions are potentially associated with immunity); (b) a previous diagnosis of breast cancer Stage 1 or greater, c) no history of cancer recurrence; (d) minimum two years post treatment; and (e) adequate veins for venipuncture. Two year survival allowed the acute side effects of initial treatment to abate and chronic symptoms that may create thoughts of cancer recurrence to emerge. Self-reported vein adequacy was used to exclude women who might attach undue stress to the post-visit venipuncture, thus confounding results. Women taking prescription anti-inflammatory medications were also excluded. Women were given a \$20 gift card to a local supermarket in appreciation for their participation.

Measures

Demographic information—Demographic data included age, marital status, employment, education, income, and length of time women had received care from their medical oncologist. Table 1 presents a summary of instrument internal consistency and descriptive results.

Current health status—Current Health Status was measured with a 27-item self-report questionnaire that included chronic co-morbid conditions and recent minor illnesses.

Symptoms—The Symptom Distress Scale ³² was used to determine the number of experienced symptoms and associated symptom bother. Symptoms indicate possible concerns women would bring to the attention of providers and potential triggers of the fear of cancer recurrence if women did not understand the meaning of their symptoms. Respondents indicated the symptoms they experienced, then indicated the amount of severity and bother on a five point Likert-type scale (1=slight to 5 = very severe). Scores were summed with higher scores indicating more symptom bother. Validity in cancer patients was previously demonstrated by a positive correlation with the Profile of Mood States ³³.

Emotional Responses to Stressors

Uncertainty: Survivor uncertainty was measured using the 22 item Uncertainty in Illness Scale- Survivor version ³⁴. Respondents indicated their level of agreement on a five point Likert-type scale ranging from strongly agree to strongly disagree. Scores were summed with higher scores reflecting greater uncertainty. Validity in cancer patients was previously demonstrated by positive associations with emotional distress, fears of recurrence, and symptom bother ⁸.

Anxiety: The State-Trait Anxiety Inventory (STAI) ³⁵ was used to measure transient anxiety (state). Respondents indicated their agreement with items measuring feelings of apprehension, tension, nervousness, comfort, and decision-making. Scores were summed for each subscale with higher scores indicating more anxiety. In addition, we included a single item question specifically asking about anxiety related to the upcoming medical visit.

Concern about recurrence: Thoughts of recurrence were measured using the Concerns about Recurrence Scale (CARS) ³⁶. The CARS assesses the nature and extent of women's fears about breast cancer recurrence. The two-part survey uses a five point Likert-like scale ranging from 0 (not at all) to 4 (extremely) response format to indicate the extent of worry related to each item. Four questions focused on time spent thinking about recurrence, frequency of thoughts, and intensity of fears followed by 26 items assessing the nature of women's fear of recurrence. Higher summed scores indicated greater concern about recurrence.

Validity of the CARS was previously demonstrated in breast cancer survivors with convergent validity was demonstrated using the Intrusive Thoughts ($r = .64$, $p < .001$) and Avoidance ($r = .50$, $p < .001$) subscales of the Impact of Events Scale ³⁷ and the Distress ($r = .54$, $p < .001$) and Wellbeing ($r = -.44$, $p < .001$) subscales of the Mental Health Inventory (Veit & Ware, 1983).

Physiologic Responses to Stressors

Immunity: Cytokine levels and lymphocyte counts were obtained to assess immune status. Cytokine levels were measured using a multi-analytic fluorescent detection method in contrast to the more familiar enzyme linked immunosorbent assays (ELISA) ³⁸. This procedure allows the simultaneous detection of multiple serum cytokines as opposed to ELISA assays that detect one cytokine per assay. (Cytokines: IL1, 2, 4, 6, 8, 10, 12, IFN γ , TNF α , CD40 ligand, and IL2 receptor). Lymphocytes were analyzed using flow cytometry for total lymphocyte counts. The CD3 T cell marker was used to differentiate NK cells from T-cytotoxic cells. Selected cytokines and lymphocytes were determined by the assay given that these tests were not obtained individually due to cost.

Patient-Provider Communication

Visit plan: Data were obtained on participants' plan for their upcoming medical visit. Items included: "How do you plan to use the time you spend with your provider today," and "Is there anything you plan to (or want to) discuss with your provider today?" These data were used to create a three level variable that we labeled "plan specificity" with lower scores representing a more specific plan for the upcoming visit.

Decision-making role: The Control Preferences Scale ³⁹ was used to determine the women's desired healthcare decision-making role compared to how healthcare decisions were actually made in their medical surveillance visit. Decision-making role preference was scored on a 1 – 5 scale, with higher scores indicating more active decision making. Item statements include: "I prefer to leave all decisions regarding my treatment to my doctor, PA, or nurse practitioner." (score = 1) and "I prefer to make the final selection about which treatment I will receive." (score = 5). We asked respondents to select the one statement that most closely described their desired decision making preference before the medical visit, then after the medical appointment select the statement that most closely described how healthcare decisions were actually made (attained decision-making role). We subtracted a woman's desired decision-making role score from the attained decision-making role score to determine a discrepancy score ⁸. The discrepancy score reflects the magnitude and direction

of the incongruity between the respondent's desired and attained role in decision-making. Negative discrepancy scores can be interpreted as a woman desired a more active role than she attained during her visit. Positive scores indicate that a woman desired a more passive decision-making role than she attained. A score of zero indicates there was no difference between attained and desired decision-making role. Previous research supports a respondents' ability to choose decisional preference for decision-making roles on a continuum among breast cancer survivors^{8, 40} and among colorectal cancer patients⁴¹.

Results

Data were analyzed using IBM SPSS Statistics™ version 22. Because data were collected in person, study booklets were checked prior to a woman leaving the medical office and for post visit data prior to the research assistant leaving a woman's home. Thus, there was minimal missing data in this study. When data was missing for self-reported measures missing values were replaced with the mean. No missing physiologic data was replaced, (one post visit sample was not suitable for testing).

Age ranged from 43 to 81 years, with an average age of 60.5 years. Most participants were married and the vast majority had education beyond high school. One third of women reported a minor illness within the last month (Table 2). Women reported on average four co-morbid illnesses and endorsed an average of five symptoms related to previous cancer treatment. The most frequently endorsed illnesses were hypertension, anxiety, and arthritis. The most frequently endorsed treatment related side effects were fatigue, underarm tenderness or numbness, and weight gain. Trouble thinking was also endorsed by 41% of women. The most bothersome (and difficult to manage) treatment related symptoms were weight gain, trouble thinking and arm weakness and mobility issues. Concerns about cancer recurrence in this sample were moderate (mean 46, range 4–102, SD 26.5) (Table 1).

Emotional Response

We operationalized an emotional stressor in this study as a regularly occurring medical oncology surveillance visit, potentially precipitating emotional distress and anxiety about breast cancer recurrence as well as immune alteration. Findings showed that there was a strong correlation between concern about cancer recurrence and a single item asking about the extent of self-reported anxiety about the upcoming medical visit ($r=.68$, $p=.00$).

To examine which variables demonstrated change over time between pre and post-visit data collection, correlated samples *t* tests were used. Findings showed that breast cancer survivors reported decreased uncertainty ($t=19.98$, $df=26$, $p=.000$) and state anxiety ($t=21.28$, $df=26$, $p=.000$) post visit.

Physiologic Responses

Natural Killer (NK) cells increased in 70% of women ($t=-2.11$, $df 24$, $p=.045$) suggesting previous immune alteration (decreased innate immunity prior to the visit). In addition, one third of women reported a minor illness in the month prior to their visit, further supporting pre-visit immune alteration. Other immune markers showed inconsistent and nonsignificant change pre-post medical oncology visit.

Patient Provider Communication

The Survivor-Provider relationship—On average women had been interacting with the same provider for care for 4.2 years (range 2–15 years) (Table 2). When asked how they planned to spend the time with their provider during their medical oncology visit, 70% indicated they had something very specific to discuss with providers at their visit such as stopping medications, questions about genetic testing, or breast reconstruction. Another 11% had a moderately specific plan such as obtaining the results of lab tests or discussing their overall health. The remaining women did not have a plan for their visit.

Not all women were able to attain their preferred decision-making role with their provider. Calculating the difference between preferred and attained role (with 0 indicating no difference between desired and attained role) showed that 66% were able to successfully negotiate their desired decision-making role. However, one third of women reported that during the visit they were more active or more passive than they originally desired, indicating an inability to successfully negotiate their desired role (Table 3).

Emotional, Physiologic and Communication Associations

To explore whether change in emotional responses predicts change in immunity before and after a medical oncology office visit, we initially used log transformations for ease in interpreting standardized coefficients of change in pre-post immunity. Using a conditional change approach estimating change in post-visit values conditional on pre-visit values our findings consistently demonstrated that greater fear of cancer recurrence was highly associated with increased change in levels of interleukins post-visit (Table 4). Associations were also found between changes in pre/post state anxiety and three pro-inflammatory cytokines: CD40L, TNFa, and IL2r (can be both pro and anti-inflammatory, ultimately impacting T cell responses) and for CD19 cell counts (that activate B cells eliciting antibody production). Change in uncertainty and state anxiety predicted changes in CD40L. Although previous analyses showed that the number of absolute NK cells rose post visit, self-reported measures of distress were not associated with this alteration in immunity. Overall, emotional responses (uncertainty, anxiety, fear of cancer recurrence) to an upcoming medical oncology were associate with change in immune status pre-post visit.

To explore whether or not a woman's plan for her visit and her ability to successfully negotiate her desired decision-making role predicted change in physiologic and emotional outcomes we used regression analyses. Setting significance at .10 due to the exploratory nature of this study, the overall all model was significant ($F 3.23, df 22, p=.06$). Closer examination of the coefficients however showed that while a more specific plan predicted greater change in uncertainty (Standardized $B = -.506, p=.02$) the ability to negotiate decision-making roles did not predict change in uncertainty. Neither the specificity of the visit plan nor the ability to successfully negotiate desired decision-making roles predicted change in anxiety from before to after the medical oncology visit. Finally, specificity of the visit plan and negotiation of decision-making roles did not predict change in immune status.

Conclusion

Overall, findings support the association of emotional aspects of ongoing cancer surveillance with physiologic responses to regularly scheduled medical oncology surveillance visits. There was a consistent association between fear of cancer recurrence and immune alterations, namely for interleukins and cytokines. However, change in the direction of immune alteration was inconsistent. Some women had increasing values of pro-inflammatory interleukins and increasing numbers of lymphocytes while others showed decreasing or no change in levels of lymphocytes and/or interleukins. This inconsistency suggests individual variation in how women experience the stress of an upcoming medical oncology office visit and the associated fear of recurrence. For some women, an increase in pro-inflammatory markers post visit may suggest that medical oncology visits trigger cognitive processes that can cause women to reflect on their cancer experience longer than previously thought (e.g. rumination prolonging immune alterations), despite receiving good news. Because not all women respond in a similar fashion to an upcoming medical oncology surveillance visit there is a need to determine who may be most at risk for more acute alterations in immunity related to the fear of cancer recurrence that is inherent in ongoing surveillance after treatment for breast cancer.

The most consistent physiologic change in this study was a rise post visit in NK cell counts. Because NK cell counts are known to decrease under stressful conditions, for the women whose NK counts rose post visit, it is likely that these women had stress responses to their upcoming medical visit that occurred prior to the day of the visit although again, only 70% of women experienced this impact, indicating that for some women there was no impact of the visit on this measure. It should be noted that the inability to determine significant change in immune markers is likely due to the smaller sample size and the exploratory nature of this study. Further, given the immediate pre-post nature of data collection we cannot determine when these women began to experience emotional distress and immune changes, nor when immune alterations returned to usual baseline levels post visit. The increase in NK cells implies an earlier pre-visit stress response presumably to the upcoming office visit given that resolution began immediately post visit, (although it is possible that other life stressors contributed to this alteration).

Limitations include the comparatively optimal longstanding patient-provider relationship women had with their providers, the immediate pre-post nature of the data such that we could not determine what an individual woman's baseline values were and when immune alteration begins and returns to baseline, variability in normal values for immune measures adding challenge to interpretation, and the smaller sample size which did not include men. Future research might focus on those who have reported more extreme emotional distress and/or markedly unsatisfactory communication interactions to obtain a more clear understanding of the associations between emotional, physiologic alterations in immunity and communication with providers for long-term recurrence free breast cancer survivors. Additional considerations would be to explore the experiences of male survivors.

Implications for Practice

Stress related changes in immune status often result in a Th1 to Th2 shift, indicating a change from cellular innate immunity to adaptive immunity. In this sample arthritis and hypertension were highly endorsed by women. The finding that women in this sample, as in the general population, were older with multiple co-morbid illnesses and that one third of women had experienced a minor illness in the month prior to their appointment, suggest potential alterations in immunity beyond what we were able to evaluate give the timing of data collection and the smaller size of this sample.

Healthcare providers have the obligation to identify women who are experiencing distress and attempt to ameliorate changes in immunity because of the possible temporary lack of protection from minor illnesses (that may be more dangerous when coupled with pre-existing illnesses such as heart disease or diabetes) and the potential exacerbation of antibody dependent autoimmune illnesses such as arthritis and diabetes. Knowing that most women experience uncertainty and anxiety prior to a scheduled visit, providers have the opportunity to allay a woman's concern about the meaning of her symptoms with respect to cancer recurrence. In this study anxiety and uncertainty were reduced overall post-visit suggesting that women were told by their providers that their breast cancer had not recurred, in a believable fashion. Further, the fact that most women were familiar with interacting with these providers for many years, and had a plan for their visit suggests that women felt comfortable raising concerns with their providers.

When the meaning of symptoms is understood, and existing symptoms are not erroneously attributed to breast cancer recurrence, quality of life is enhanced and women can move forward in their lives without significant emotional distress¹. Further, immediate answers to questions, thus resolving concerns and uncertainty about symptoms, may potentially avoid prolonged immune status changes that can result from worrying about and waiting for discussions of concerns until the next office appointment. This could be facilitated by nurse operated telephone based "help lines" where women could call in without fear of "bothering the doctor". The goal here would be to provide immediate reassurance rather than let women worry for prolonged periods of time while waiting for their next (often annual) medical oncology appointment.

While most women were able to achieve their desired decision-making roles, similar to other research, a portion of women reported adopting a more passive or active role than initially desired.^{7, 30} This finding suggests that providers could adopt a more patient-centered approach to discussions of further testing and/or treatment for late emerging side effects of treatment, and allow women to adopt their chosen role no matter whether they desire an active or passive decision-making role.⁸ The common assumption that a more active patient will lead to better health outcomes may not reflect the role some women wish to adopt during post-treatment surveillance. Yet, successful negotiation of decision-making roles did not predict reduction in emotional distress nor resolution of immune measures in this study. This finding could imply that roles were negotiated (successfully or unsuccessfully) in previous years given the long term nature of these patient provider relationships, and as such

had no bearing on emotional or physiologic outcomes because the manner of interaction had been previously established.

In summary, breast cancer survivors in this study, as in others, reported uncertainty and anxiety related to the fear of cancer recurrence associated with routinely scheduled medical oncology surveillance visits. Women also experienced alteration in immunity presumably related to the stress of a routine medical oncology visit and the associated fear of cancer recurrence. Consistent with uncertainty theory and the theory of The interaction between women and their oncology providers has the theoretical potential to allay both emotional and physiological responses to this stressor, contributing to the well-being and quality of life for older long-term breast cancer survivors.

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Table 1

Reliability, Range, Mean, and Standard Deviation of Instruments

Measure	Reliability (Cronbach's alpha)	Range	Mean	Std. Dev.
Symptom Distress Scale	0.91	4 – 112	38.22	25.49
Uncertainty in Illness Scale	0.89			
Pre-visit		22 – 74	48.21	11.82
Post-visit		22 – 73	45.67	12.12
State Anxiety	0.92			
Pre-visit		20–52	31.79	7.96
Post-visit		20 – 49	28.64	7.78
Concerns About Recurrence Scale	0.96	4 – 102	46.39	26.57

Table 2**Participant characteristics**

	N	%
Relationship Status		
Married	20	74.1
Partnered > 6 mos.	1	3.7
Separated or Divorced	4	14.8
Widowed	1	3.7
Never married	1	3.7
Education - # years college		
0 years	1	3.7
1 – 3 years	5	28.5
4 years	13	48.1
5 years	4	14.8
6 – 7 years	3	11.1
Employment Status		
Full-Time	9	33.3
Part-Time	4	14.8
Retired / unemployed	14	51.9
Years visiting this provider		
2 years	5	18.5
3 years	10	37.0
4 years	4	14.8
6 – 8 years	3	11.1
> 10 years	2	7.4
Visit Plan Specificity		
Highly Specific	19	70
Moderately Specific	3	11
Nonspecific (No plan)	4	15
Health Status		
Arthritis	12	44.4
High blood pressure	11	40.7
Nerves / Anxiety	11	40.7
Minor illness in last month	9	33.3
Thyroid problems	8	29.6
Constipation	7	25.9
Cataracts	6	22.2
Diabetes	5	18.5
Stomach problems (not ulcers)	5	18.5
Cancer Treatment Side Effects / Symptoms		
Fatigue	15	55.6
Tenderness underarm or treated area	14	51.9

	N	%
Numbness underarm or treated area	14	51.9
Weight gain	13	48.1
Sensitive skin underarm or treated area	12	44.4
Change in appearance	12	44.4
Trouble thinking	11	40.7
Limited shoulder motion treated side	9	33.3
Arm/shoulder stiffness	8	29.6
Pain	8	29.6
Arm weakness	6	22.2
Changes in scar or treated breast	6	22.2
Treatment area dryness or hardness	5	18.5

Table 3

Difference in attained versus desired decision-making role (attained – desired)

Difference score	N	%	Interpretation
– 2.00	1	3.7	Desired much more active role than attained
– 1.00	3	11.1	Desired slightly more active role than attained
0.00	18	66.7	Attained desired role
1.00	4	14.8	Desired slightly more passive role than attained

Note: Desired and attained decision making role could range from 1–5 (passive to active)

Table 4

Standardized regression coefficients for predicting Biomarker Post (y_2) from Self-Report Measure Pre (x_1), conditional on Biomarker Pre (y_1)

	State Anxiety	Uncertainty	Fear of Cancer Recurrence	p(cha)
CD19	.38			.014
CD40L	-.475			.046
CD40L		-.501		.021
IFNg			.41	.044
IL-10			.32	.021
IL-12			.45	.030
IL-1b			.38	.033
IL-2			.45	.030
IL-2r	-.609			.007
IL-4			.48	.028
IL-5			.32	.027
TNFa	-.506			.032