

AD_____

Award Number: W81XWH-06-1-0401

TITLE: Determinants of Weight Gain in Women with Early-Stage Breast Cancer

PRINCIPAL INVESTIGATOR: Chi-Chen Hong, Ph.D.

CONTRACTING ORGANIZATION: Health Research Inc.
Buffalo NY 14263

REPORT DATE: April 2008

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.				
1. REPORT DATE (DD-MM-YYYY) 30-04-2008		2. REPORT TYPE Annual		3. DATES COVERED (From - To) 1 APR 2007 - 31 MAR 2008
4. TITLE AND SUBTITLE Determinants of Weight Gain in Women with Early-Stage Breast Cancer .			5a. CONTRACT NUMBER	
			5b. GRANT NUMBER W81XWH-06-1-0401	
			5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Chi-Chen Hong, Ph.D. Email: chi-chen.hong@roswellpark.org			5d. PROJECT NUMBER	
			5e. TASK NUMBER	
			5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Health Research Inc. Buffalo, NY 14263			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research And Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSOR/MONITOR'S ACRONYM(S)	
			11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited.				
13. SUPPLEMENTARY NOTES				
14. ABSTRACT. Weight gain after breast cancer diagnosis is common, and has been associated with poorer prognosis. The goals of the study are to examine weight gain relation to treatment-related changes in sex hormone levels, and in relation to genetic polymorphisms in sex hormone pathways, accounting for potential interactions with energy balance, psychosocial factors, tumor characteristics, cancer treatment, and medication use. A prospective longitudinal study of weight gain is being conducted in 215 stage I to IIIA breast cancer patients. During the second year of this grant, a supplementary questionnaire was developed to examine temperature perception after breast cancer diagnosis and treatment and in collaboration with the departments of Clinical Research Services and the Information Technology, study databases were developed for data entry of this questionnaire. Recruitment and followup of participants have continued, with a total of 226 patients recruited into the study. Of these 31 patients have withdrawn from the study and 5 were lost to followup leaving a total of 190 participants. We are in the process of double entering of all data collected by survey and checking and clarifying any differences that exist. Participant recruitment using consent forms with DOD language began January 2007 after obtaining institutional IRB and USAMRMC Human Research Protections approval. Sixty-six participants have been re-enrolled using this consent form, with 9 refusing re-consent, and 16 still in the process of being reconsented. The study will help identify women who are most susceptible to weight gain after being diagnosed with breast cancer, based on biologic characteristics as well as modifiable factors.				
15. SUBJECT TERMS Sex hormone, genetic polymorphisms, weight gain, cohort study, diet, physical activity, psychosocial factors.				
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 35
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U		
				19b. TELEPHONE NUMBER (include area code)

Table of Contents

	<u>Page</u>
Introduction.....	4
Body.....	4
Key Research Accomplishments.....	8
Reportable Outcomes.....	9
Conclusion.....	13
References.....	13
Appendices.....	14

1. Introduction

Weight gain after breast cancer diagnosis is very common, occurring in 50-95% of early stage patients undergoing adjuvant chemotherapy, and has been associated with poorer prognosis. Potentially important contributors to this weight gain may be treatment-related reductions in ovarian function and/or increases in cortisol level due to physical and psychological stress. Since sex hormones and glucocorticoids regulate body weight and adipose tissue distribution, we hypothesize that sex hormones and cortisol play a role in treatment-induced weight gain, and that complex interactions exist with genetic susceptibility, lifestyle, and psychosocial factors. The goals of the study are to examine post-diagnostic weight change and: 1) changes in sex hormone and cortisol levels; 2) genetic polymorphisms in sex hormone pathways; 3) energy intake, physical activity, and psychosocial factors; and 4) characteristics of the cancer and treatments received. A prospective longitudinal study of weight gain is being conducted in 215 patients, aged 35 to 75 years, with non-metastatic breast cancer (Stage I to IIIA). After informed consent, we are collecting serial biospecimens and survey data, to measure hormone levels and genetic polymorphisms, and to assess menopausal status, anthropometry, diet, physical activity, and psychological variables (fatigue, depression, social support) at baseline, 6, and 12 months. These factors will be evaluated in relation to weight changes during and following therapy. This study will be the first to comprehensively examine predictors and modulators of post-diagnostic weight gain in women with breast cancer using a multidisciplinary approach encompassing hormonal changes, genetic polymorphisms, and psychosocial factors. The outcome of this research may shed light on why so many women suffer weight gain after breast cancer and will help guide the development of interventions targeting modifiable risk factors.

2. Body

Task 1: Study Protocol Revisions, Months 1 to 24

Study protocols and the consent form were revised to include DOD elements and were submitted to the USAMRMC Office of Research Protections, Human Research Protections Office (ORP HRPO) for review. Local IRB approval and approval from USAMRMC ORP HRPO was obtained January 8th, 2007.

In the last year, beginning 10/31/2007 the eligibility criteria for the study protocol was broadened and amended from women aged 35 to 75 to women 18 years and older.

Task 2. Develop databases with Clinical Research Service and Information Technology department at RPCI, months 1-24.

In collaboration with the Clinical Research Services and Information Technology department at Roswell Park, a tracking database has been developed which tracks for each potential participant their study eligibility and participation status. For each participant, the system also tracks specimen collection, as well as allows for entry of all data collected by survey. The database developed uses the eResearch Technology (eRT), eData Management, eStudy Conduct, eSafety Net software products as well as various other RPCI custom applications connected to eRT via Microsoft ODBC technology. The database is currently interfaced to RPCI's hospital information system (demographics), and the RPCI Cerner lab system (lab

results), which allows all of this information to transfer electronically. The database management system is Oracle 9i. Backups of the study data to tape are performed nightly and stored in a separate physical location from the servers themselves.

Within the last year we developed a supplementary questionnaire to collect information on temperature perception in breast cancer patients (see section 4.3.2.2. below and Appendix 1) that was initiated July 2007. The questionnaire also collects additional information on vitamin supplement use and use of herbals and other compounds after breast cancer diagnosis. As a result, our study databases were recently updated to allow double entry of this data and we are currently in the process of entering the backlog of data collected with the supplementary questionnaire.

Task 3. Train study personnel to consent patients, months 1 to 6

At the start of the study a project co-ordinator was hired and trained to consent patients into the study from the breast clinic at Roswell Park Cancer Institute. In addition, a half-time study coordinator was hired in September 2006 to aid in the conduct of this study.

Task 4. Study Recruitment, Months 6-18; Participant Followup, Months 7 to 30.

Recruitment of participants who participate in the Institutes DataBank and BioRepository using consent forms with DOD language was initiated in Jan, 2007. To date (5/14/08), 226 participants have been enrolled. From this group there were a total of 31 withdrawals and 5 individuals were lost to followup leaving 190 active participants. Reasons for withdrawal from the study are provided in Table 2.

Table 1. Study Recruitment by Ethnicity

Ethnicity	Total Recruited	Withdrawn	Lost to Followup
Caucasian	199	28	3
Black	20	2	1
American Indian	2		
White/Hispanic	2		
Black/Hispanic/Other	1		1
White/Asian	1		
Black/Caucasian	1	1	

Table 2. Reasons for Withdrawal from the Study

Reason	Number
Patient no longer receiving care at Roswell Park Cancer Institute, and so is no longer interested in participating in the study.	6
Patient feels overwhelmed; dealing with too many things.	12
Patients found to be ineligible for the study after enrolling	3
Not interested in participating with no specific reason provided for decision.	10

Recruitment into the study, prior to DOD approval, began April 2006. The intent was to recontact these participants using the DOD approved consent forms. To date (5/14/08), of 91 individuals that needed to be recontacted, 66 have been recontacted, 9 have refused, and 16 are still in the process of being recontacted for recontacts.

Questionnaires provided for self-completion at home

We are in the process of collecting data on dietary intake, physical activity, and psychosocial factors through questionnaires administered at baseline, 6 months, and at 12 months. To date 84% of participants have filled out and returned their baseline questionnaire. The return rate are somewhat lower at 6 and 12 months of followup, being 72% and 67% respectively, with 75% of those eligible for followup data collection returning at least one followup questionnaire. Although the proportion of 75% includes patients who are recently eligible for followup and therefore may not have had sufficient time yet to return their questionnaire, we are in the process of changing our followup protocol to include more frequent contact with participants who do not return their study questionnaire within a month after their provision so that the response rate for the survey component of the study can be improved.

Measurement of weight, height, and body composition

Protocols to measure body composition and weight in the Roswell Park Breast clinic was established using the Tanita Body Composition analyzer, which uses the tetrapolar bioelectrical impedance technique. As well, protocols were established with clinical staff in the Breast Clinic to measure waist and hip circumferences on all newly diagnosed breast cancer patients at baseline and at followup visits. At baseline, 94% of all participants have provided body composition data using the Tanita scale. For the remaining participants, use of the Tanita scale was either contraindicated, the patient was unable to stand on the scale, or the patient refused the measurement. At 6 months and 12 months of followup, the proportion of those measured by the Tanita scale were lower at 79% and 83% respectively, with 90% of all participants eligible for followup providing at least 1 followup Tanita measurement. Going forward, our study staff will begin escorting participants personally to the breast clinic to ensure that those eligible for a followup measurement will have these data collected.

Collection of blood and urine samples

Protocols for the collection and processing of fasting blood samples prior to surgery/treatment were developed and include banking of serum, plasma, buffy coat, and red blood cells. As well, presurgical overnight urine specimens were collected, which is accompanied by a specimen questionnaire that was developed, which asks about lifestyle, diet, and medication use in the last 2 days. Currently, fresh whole blood is sent to Labcorp for determination of HbA1C results. Serum and plasma are being stored to allow for future determination of sex hormone and cortisol levels. Originally we had planned to begin shipping serum samples periodically to Labcorp to determine hormone levels beginning in month 6, but to reduce laboratory error we will instead wait until followup is complete and have baseline, 6 months, and 1 year samples assayed simultaneously. To date, 98% of all participants have provided a baseline blood sample. At 6 months and 12 months, 85% and 86% of those eligible for followup have provided a blood sample, with 93% of these participants providing at least 1

followup blood sample. For urine samples, 92% of patients provided pretreatment samples (after subtracting those withdrawn from the study) and of these 88% of those eligible for at least one followup urine collection have provided at least one followup urine sample.

Task 5. Data Management, Months 6 to 31.

We are in the process of double entering all our data into study databases. This is done by at least 2 different individuals, and periodically the two sets of data entered are compared and differences are flagged for further followup.

Within this last year, two research associates were hired to help with data entry. Up to November 2007, data entry for the study had been performed largely by student volunteers and the progress was slow and the study was behind on this task. In response, two half-time research associates were hired between November and December 2007 to aid in data entry and in patient followup. Two persons were required since duplicate data entry had to be performed by different people. In addition to data entry, the two half-time research associates aid in the followup of incomplete questionnaires with participants during evening hours when participants are most likely to be at home, as well as in the scheduling of patients for followup appointments. The additional personnel were needed to handle the increased number of participants requiring active followup.

Task 6. Measurement of hormone levels, Months 12 to 31.

This task has not yet begun. Currently, fresh whole blood is sent to Labcorp for determination of HbA1C results. Serum and plasma are being stored to allow for future determination of sex hormone and cortisol levels. Originally we had planned to begin shipping serum samples periodically to Labcorp to determine hormone levels beginning in month 6, but to reduce laboratory error we will instead wait until followup is complete and have baseline, 6 months, and 1 year samples assayed simultaneously. We anticipate beginning these assays in the later half of this year.

Task 7. Postdoctoral Training, Months 1-36

Developmental meetings are held weekly and on an as needed basis to discuss progress and career development with Dr. Christine Ambrosone, the primary mentor. Frequent meetings are also held with other mentors on an as needed basis to address issues associated with the conduct of the study.. I have attended several scientific conferences as part of my training including the 2007 and 2008 annual meeting of the American Association for Cancer Research and was the co-chair both years for the Annual Grant Writing Workshop for Associate Members, Professional Advancement Session. In 2008, I was invited by AACR to be a junior facilitator at the Leila Diamond Networking Breakfast hosted by Women in Cancer Research at the 2008 AACR Annual Meeting. I attended the AACR Molecular Epidemiology Working Group (MEG) sponsored special conference on 'Approaches to Complex Pathways in Molecular Epidemiology' from May 30 to June 2nd, 2007 and attended the 2007 AACR Frontiers in Cancer Prevention Research meeting held from December 5-8, 2007. I continue to attend (and coordinate) the biweekly Work-in-Progress meetings in epidemiology and chemoprevention that occur within the

Department of Cancer Prevention and Control at Roswell Park Cancer Institute, as well as weekly Faculty Forum, Cancer Prevention Grand Rounds, and Medical Grand Rounds seminars. My training has also been enhanced by participating as a peer-reviewer for the DoD BCRP Idea and Synergism grant mechanisms as well as a reviewer for the Breast Cancer Campaign in the United Kingdom. I have been invited back in 2008 to participate as a peer-reviewer for the BCRP Idea and Synergism Awards.

Task 8. Mount Sinai Center Visit, Month 12

I have not yet visited Dr. Bovbjerg yet at the Mount Sinai Center in NY. We plan to have more followup psychosocial data collected before planning this visit.

Task 9. Interim Analyses, Months 12-30

We have done analyses to look at data quality and followup rates, but analyses focused on our main hypotheses have not yet begun.

Task 10. DNA extraction and Genotyping, Months 14 to 22.

As part of the blood collection protocol, buffy coats are being banked and stored to allow for DNA extraction and genotyping. We will begin DNA extraction and genotyping shortly as we are now approaching our recruitment target of 219 (after excluding withdrawals) study participants with stage I to IIIa cancers.

Task 11. Merge genotyping data with data questionnaires and medical records. Month 23.

Not yet performed. We have not yet merged medical records data yet with our survey data, although the clinical data is routinely collected by the Breast Surgery department and is readily available when needed. This task is scheduled for Months 23 to 30 of the grant.

Task 12. Final data analysis, interpretation and reporting, Months 31 to 36.

Not yet performed.

3. Key Research Accomplishments.

None yet.

4. REPORTABLE OUTCOMES

4.1. Establishment of Serum and Urine Repository

This research grant has allowed for the creation of a serum and urine repository for the conduct of survivorship studies of breast cancer patients. This biorepository is unique in that it collects biospecimens annually and therefore lends itself well to studies aimed at detecting changes that occur during and after breast cancer treatment.

4.2. Establishment of Study Database

In collaboration with the Clinical Research Services and Information Technology department at Roswell Park, a comprehensive database has been developed which allows for double entry of all data collected by survey. The database developed uses the eResearch Technology (eRT), eData Management, eStudy Conduct, eSafety Net software products as well as various other Roswell Park Cancer Institute custom applications connected to eRT via Microsoft ODBC technology. The database is currently interfaced to RPCI's hospital information system (demographics), and the RPCI Cerner lab system (lab results), which allows all of this information to transfer electronically. The database management system is Oracle 9i. Backups of the study data to tape are performed nightly and stored in a separate physical location from the servers themselves.

4.3. Employment or Research Opportunities

4.3.1. Employment

Based in part on the success of the survivorship cohort developed with this grant and its broad potential as a basis for developing a number of research projects focused on survivorship research in breast cancer patients, I was promoted to an Assistant Member position at Roswell Park Cancer Institute (RPCI) effective Jan 03/08, which is equivalent to a tenure track Assistant Professor at universities. In addition, based on the research funding provided by the DoD and Komen for this project, I was invited to be a member of the Cancer Center Support Grant at RPCI. I also have an appointment as a Research Assistant Professor at the Department of Social and Preventive Medicine at SUNY University at Buffalo, and my application to be an Assistant Professor in the Department of Cancer Pathology and Prevention at Roswell Park has been recently approved.

4.3.2. New Research Opportunities Derived from this Grant

4.3.2.1. Expansion of Determinants of Weight Gain Study to the Abraham Cancer Center at the University of Pennsylvania

Based on the research ideas pursued in our grant to examine determinants of weight gain in breast cancer patients, we have formed a collaboration with researchers at the Abramson Cancer Center of the University of Pennsylvania to duplicate the study at their cancer center and to pool our study populations for this and other survivorship studies developed. The intent will be to apply for a RO1 grant in October 2008, with co-principal investigators, to have a two-site

study examining the issue of weight gain in breast cancer patients. We are in the process of revising and submitting the protocol for IRB approval at the University of Pennsylvania. Once approved, our intent will be pilot the study at the Abramson Cancer Center to ensure feasibility and to generate pilot recruitment data for our grant submission. The study at Abramson will be lead by Dr. Carrie Stricker, a PhD level Oncology Nurse Practitioner and Assistant Professor at the School of Nursing.

4.3.2.2. Development of Two Research Studies to Examine Body Temperature Perception and Immune Function following Breast Cancer Diagnosis.

The establishment of this cohort of breast cancer survivors has led to a collaboration with Dr. Elizabeth Repasky within the Department of Immunology at the Roswell Park Cancer Institute to explore the hypothesis that a distinct subgroup of breast cancer patients experience symptoms of

being persistently cold after breast cancer treatment and that these symptoms are distinct from the more widely studied phenomenon of “hot flashes” as a result of treatment-induced menopause.

In the last year we developed a questionnaire that collects information on women’s experiences with “hot flashes and sweats”, and with feelings of “feeling inappropriately and excessively cold”. The questionnaire collects information about experiences within the past 7 days as well as the past 6 months and was patterned on the Functional Assessment of Cancer Therapy –

Fatigue Subscale (FACT-F) and the Multidimensional Assessment of Fatigue (MAF) scales, which are existing validated questionnaires on experiences with fatigue. Information collected includes prevalence and degree of symptoms, severity, severity compared to before their diagnosis with breast cancer, frequency, impact on daily activities, perceived reasons for their experience, and

Figure 1. To what degree have you experienced: ■ hot flashes and/or sweats? ■ feeling inappropriately cold or chilled when others feel fine or hot?

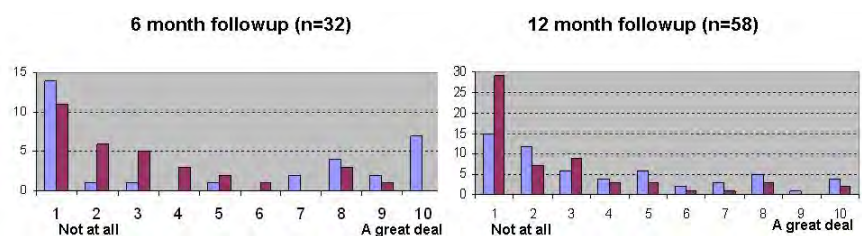


Figure 2. Over the past 7 days, how often have you: 1) had hot flashes and/or night sweats? 2) felt cold or chilled?

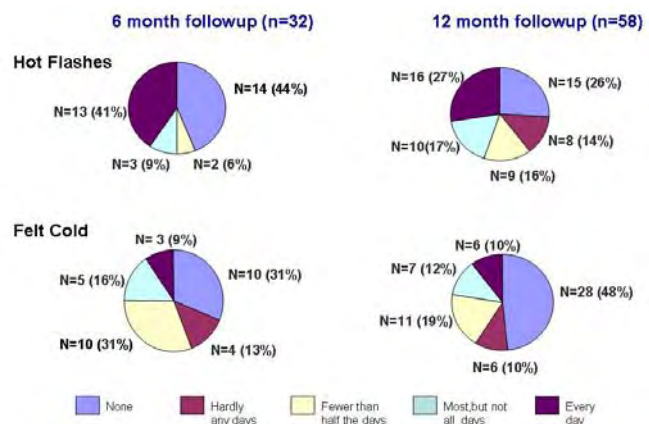
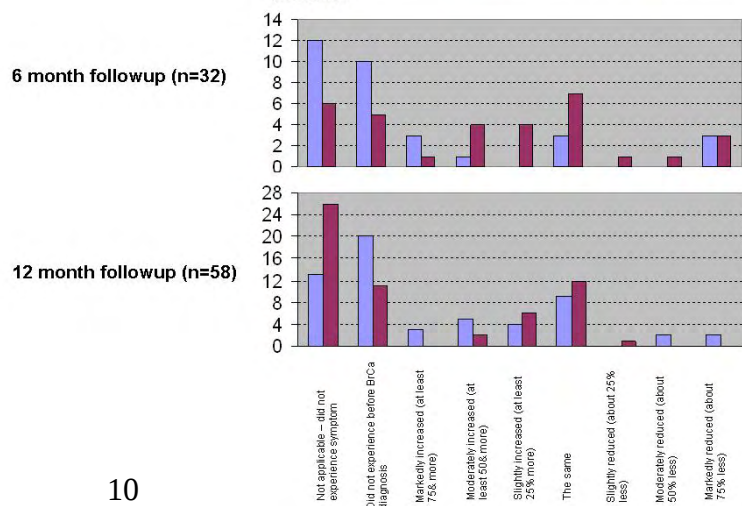


Figure 3. Compared to before you were diagnosed with breast cancer, how severe are your ■ hot flashes and/or sweats? ■ your feelings of being cold or chilled?



treatments that women have used to try and cope with their symptoms.

From July 2007 to April 2008, we piloted this questionnaire in an ongoing prospective study of weight gain in women newly diagnosed with early-stage breast cancer. The self-administered questionnaire was filled out by 32 study participants 6 months following their initial diagnosis of breast cancer, and by 58 participants one year following their diagnosis. Our initial findings, shown in Figures 1 and 2, indicate that more than half of women diagnosed with early-stage breast cancer indicate that they felt cold to some degree in the past 7 days at either 6 or 12 months after their breast cancer diagnosis (69% at 6 months and 52% at 12 months). In contrast, 56% and 74% of women reported experiencing hot flashes at 6 and 12 months, respectively, after being diagnosed with breast cancer. When women who reported experiencing “feeling cold or chilled” in the past 6 months were asked to compare the severity of their current experience to that before their breast cancer diagnosis (see Figure 3), most women either indicated that it was “the same”, “slightly increased (at least 25% more)”, or that they “did not experience feeling cold or chilled before (their) breast cancer diagnosis”. These data suggest that a subset of women do appear to feel inappropriately cold following their diagnosis and treatment for breast cancer, and that these symptoms are distinct from their experiences with “hot flashes”.

In addition we examined body temperature changes in 56 breast cancer patients diagnosed at RPCI between Jan 2001 and Dec 2003 to determine whether body temperature

changed after breast cancer diagnosis, and found significant declines over a 1 year follow-up period. Body temperatures were abstracted from medical charts and a statistically significant decline in unadjusted body temperature was observed at 6 (-0.22°C, p=0.01) and 12 (-0.29°C, p=0.003) months after diagnosis (see Table 1). Declines at 12 months were found to be significantly associated with younger age at diagnosis after adjusting for menopausal status, date of diagnosis, and cancer treatments received, but body temperature was not shown to vary with radiation treatment, chemotherapy treatment or hormonal therapy. These results suggest that changes in body temperature regulation may indeed occur in breast cancer patients after their diagnosis, although the cause is unclear.

Based on our initial findings determined retrospectively, as well as with the cohort of patients established prospectively, our preliminary data indicate that breast cancer patients experience a drop in body temperature after breast cancer diagnosis and treatment and that a subset of these patients experience feeling persistently cold. Elevated levels of proinflammatory cytokines have been linked with many treatment-related symptoms reported for breast cancer, implicated in breast cancer carcinogenesis and progression, potential indicators of immune function, and have a role in regulating body temperature as endogenous pyrogens; thus, we hypothesize that body temperature and/or experiences of feeling persistently cold will be associated with levels or changing levels of these cytokines. We have applied for a DoD Idea award to examine this highly novel and previously untested hypothesis that *normal* variation in body temperature observed among breast cancer patients before and/or after cancer diagnosis

Table 1. Mean Body Temperature at Diagnosis and 6 and 12 months				
	Body Temperature °C (95% CI)	Temperature Difference from Dx °C (95% CI)	Paired t-test	P
Diagnosis (Dx)	36.75 (36.62, 36.89)			
6 months	36.53 (36.39, 36.67)	-0.22 (-0.39, -0.05)	-2.63	0.01
12 months	36.46 (36.32, 36.60)	-0.29 (-0.48, -0.10)	-3.09	0.003

Table 2. Differences in Body Temperature 6 and 12 months after Breast cancer Dx According to Age						
6 Months after Dx					12 Months after Dx	
Age (yrs)	N	Temp Difference from Dx °C (95% CI)	F	P	Temp Difference from Dx °C (95% CI)	P
40-50	21	-0.40 (-0.85, 0.05)	0.77	0.47	-0.51 (-0.98, -0.03)	3.76
51-60	23	-0.03 (-0.52, 0.45)			0.05 (-0.46, 0.57)	0.03
60+	12	-0.07 (-0.67, 0.53)			0.51 (-0.12, 1.14)	
		P-trend=0.57			p-trend=0.008	

may be an indicator of underlying immune function. A second application for a DoD Concept award has been submitted to determine if normal variations in body temperature before and/or after cancer diagnosis may be associated with risk of breast cancer recurrence and/or overall long-term survival. An RO1 submission is planned for February 2009 examining these research questions.

Pending Grants:

DOD, Concept (Hong, PI, 20%)

11/01/08 – 10/31/09
\$145,352 (total)

Body Temperature and Breast Cancer Prognosis: A Potential Link

Study Goals: To conduct the first hospital-based retrospective analysis using body temperature data abstracted from patient medical records, clinical data maintained by the breast surgery department, and recurrence and mortality data provided by the hospital tumor registry to determine if 1) pre-treatment and/or post-treatment body temperatures, or post-treatment changes in body temperature, are predictive of breast cancer recurrence or survival. The study hypothesizes that body temperature may be associated with underlying immune function of breast cancer patients.

DOD, Idea (Hong, PI, 20%)

04/01/09 – 03/31/13
\$1,086,791 (total)

Testing a new hypothesis linking body temperature perception and immune function following breast cancer diagnosis.

Study Goals: Based on the multiple roles played by proinflammatory cytokines in immunologic function and temperature regulation, and their potential role in breast cancer carcinogenesis and progression, we are exploring the highly novel and previously untested hypothesis that symptoms of being excessively cold, felt in a subgroup of breast cancer patients, may be related to pro-inflammatory cytokine levels and that these relationships may be indicative of the patient's underlying immune capacity.

4.3.2.3. Research Study to Examine Determinants of Urinary Isothiocyanate Levels

Dietary and urine biospecimens collected in this study is currently being analyzed by a Postdoctoral Fellow, Dr. Li Tang, under the mentorship of Dr. Christine Ambrosone to examine determinants of dietary isothiocyanates levels in urine samples. Dietary isothiocyanates (ITCs) are a group of promising cancer-chemopreventive agents widely found and consumed in cruciferous vegetables. In order to fully understand the cancer-protective effect of ITCs in humans, accurate capture of dietary ITC intake is critical. This study is the result of a collaboration between Drs. Li Tang, Christine Ambrosone, Yuesheng Zhang, Susan McCann, Lara Sucheston, and myself at Roswell Park Cancer Institute. The study focuses on using 150 banked pre-treatment urine and plasma samples along with linked questionnaire data from the study cohort established with the DoD Determinants of Weight Gain grant. The study will use urinary total ITC levels as a biomarker of ITC exposure to evaluate three important issues: 1) to determine the relationship between total urinary ITCs and dietary intake of ITCs as well as cruciferous vegetable intake estimated from a food frequency questionnaire; 2) to define the

ranges of dietary, plasma, and urinary total ITCs in a Caucasian population located in the United States; 3) to examine the effect of polymorphisms of genes (GST, γ -GT, CG, and NAT) on ITC metabolism. To the best of our knowledge, the proposed study has never been performed and will provide important information for future studies examining the role of ITCs in cancer prevention and in survival. Funding for this research is being provided by an institutional NCI R25 Cancer Prevention Postdoctoral Training Grant.

5. Conclusion

In the second year of this grant, a supplementary questionnaire was developed to capture data on temperature dysregulation in breast cancer survivors 6 months and 12 months after their initial diagnosis. A DoD Idea grant application has been submitted to pursue this research avenue. The supplementary questionnaire developed also included collecting data on use of supplements and herbals after breast cancer diagnosis. In collaboration with the departments of Clinical Research Services and the Information Technology, study databases were amended to allow for double entry of the new data being collected. Two additional study personnel were hired to aid in data entry and participant followup. We are still engaged in reconsenting participants who were recruited into the study prior to January 2007, when consent forms with DoD language was introduced. In the upcoming year we will begin DNA extractions and hormone assay measurements. Findings from this study will help identify women who are most susceptible to weight gain after being diagnosed with breast cancer, based on biologic characteristics as well as modifiable factors. From a public health viewpoint, findings from this study may indicate ways to improve women's health after breast cancer and to optimize their long-term survival.

6. References

None

7. Appendix

Supplementary Questionnaire

Women's Health

After Breast Cancer



The questions in this survey are concerned with factors affecting health so that we may study how a woman's health changes after she is diagnosed with breast cancer.

Please note that the answers you provide will be kept confidential.

Participation in this survey is voluntary, but your answers are critical to enhanced understanding of this process. Please answer all of the questions with as much detail as possible. If you are unsure of an answer, please offer as much information as you can give.

Please feel free to speak with family, friends, or other persons, such as your physician, who may be able to help you with your answers. You do not have to do the entire questionnaire all at once – take breaks when you need to!

If you have any questions, please feel free to call the researchers **Dr. Chi-Chen Hong** at (716) 845-7785 or **Dr. Christine Ambrosone** at (716) 845-3082. You can also call us toll free at 1-877-275-7724. Please mention the **Women's Health after Breast Cancer Study**.

Study ID _____

Supplementary Questionnaire

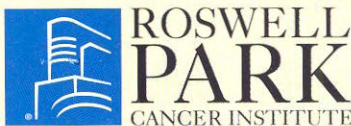
*Be a part of cancer research
and make a difference!*

For more information
about the study contact us:

Toll Free:
1-877-ASK RPCI
(1-877-275-7724)

Local:
(716) 845-7785

Please mention the
**WOMEN'S HEALTH
AFTER BREAST CANCER STUDY**



ROSWELL PARK CANCER INSTITUTE
Division of Cancer Prevention and Population Sciences
Elm & Carlton Streets • Buffalo, New York 14263
A National Cancer Institute-Designated Comprehensive Cancer Center

1. Do you smoke now?

☐ No, not at all

☐ Yes, every day

☐ Yes, some days

a) On how many of the past 30 days did you smoke a cigarette? |__|__| Days

b) On average, how many cigarettes do you smoke each day? |__|__| Cigarettes

MULTIVITAMIN USE

Please assemble all your vitamins for this section.

**MULTIVITAMINS CONTAIN 10 OR MORE VITAMINS AND/OR MINERALS.
AN EXAMPLE IS CENTRUM®**

2. Since your diagnosis with breast cancer, did you take a MULTIVITAMIN at least once a week?

☐ No →

☐ Yes, but less than once a week

Go to question 6 on page 3

☐ Yes, at least once a week

→ **Days per week?**

☐ 1-2

☐ 3-4

☐ 5-6

☐ 7

3. Since your breast cancer diagnosis, what brand of MULTIVITAMIN do you take? Mark only one.

☐ Centrum®

☐ Centrum Silver®

☐ One-A-Day® Maximum with minerals

☐ One-A-Day® Essential (no minerals)

☐ One-A-Day® Women's

☐ One-A-Day® 50 Plus

☐ Theragran-M® with minerals

☐ Theragran® (no minerals)

☐ **My brand is not listed above** _____
(name of your multivitamin)

4. Look at the label on your *MULTIVITAMIN* and tell us how much of each vitamin or mineral listed below is in your *MULTIVITAMIN*.

Vitamin A in your Multivitamin ☐ None ☐ 10,000 IU ☐ 5000 IU ☐ 15,000 IU ☐ 7500 IU ☐ A different amount _____ IU	Vitamin B12 in your Multivitamin ☐ None ☐ 100 mcg ☐ 6 mcg ☐ 250 mcg ☐ 50 mcg ☐ A different amount _____ mcg
Beta carotene in your Multivitamin ☐ None ☐ 10,000 IU _____ ☐ 5000 IU ☐ 15,000 IU ☐ 7500 IU ☐ A different amount _____ IU mg	Vitamin E in your Multivitamin ☐ None ☐ 400 IU ☐ 30 IU ☐ 600 IU ☐ 100 IU ☐ 1000 IU ☐ 200 IU ☐ A different amount _____ IU _____ mg
Vitamin C in your Multivitamin ☐ None ☐ 500 mg ☐ 60 mg ☐ 1000 mg ☐ 100 mg ☐ A different amount _____ mg ☐ 250 mg	Calcium in your Multivitamin ☐ None ☐ 800 mg ☐ 100 mg ☐ 1000 mg ☐ 250 mg ☐ A different amount _____ mg ☐ 500 mg
Thiamin (B1) in your Multivitamin ☐ None ☐ 100 mg ☐ 1.5 mg ☐ A different amount _____ mg ☐ 50 mg	Iron in your Multivitamin ☐ None ☐ 27 mg ☐ 10 mg ☐ 50 mg ☐ 18 mg ☐ A different amount _____ mg
Vitamin B6 in your Multivitamin ☐ None ☐ 50 mg ☐ 2 mg ☐ 100 mg ☐ 20 mg ☐ A different amount _____ mg	Zinc in your Multivitamin ☐ None ☐ 60 mg ☐ 15 mg ☐ 100 mg ☐ 30 mg ☐ A different amount _____ mg
Folic acid in your Multivitamin ☐ None ☐ 800 mcg ☐ 400 mcg ☐ A different amount _____ mcg ☐ 600 mcg	Selenium in your Multivitamin ☐ None ☐ 100 mcg ☐ 25 mcg ☐ A different amount _____ mcg ☐ 50 mcg

5. Does your *MULTIVITAMIN* contain any of the following?

Mark all that apply.

- | | |
|--|---|
| ☐ Bioflavonoids | ☐ Ginseng |
| ☐ Black cohosh | ☐ Lutein |
| ☐ Dong quai | ☐ Lycopene |
| ☐ Garlic | ☐ Soy or isoflavones |
| ☐ Ginkgo biloba | |

VITAMINS, MINERALS AND OTHER SUPPLEMENTS (Excluding Multivitamins)

6. During your treatment for breast cancer, did you ever take any vitamins or minerals OTHER THAN A MULTIVITAMIN?

- ☐ No →
☐ Yes, but less than once a week } → **Go to question 7 on page 6**
☐ Yes, at least once a week
 ↓

**After your diagnosis with breast cancer, did you take any of the following supplements?
DO NOT INCLUDE MULTIVITAMINS.**

Vitamin A		
☐ Yes, at least once a week → ☐ No or less than once a week Go to next supplement	Days per week? ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	Amount per day? ☐ 5000 IU ☐ 10,000 IU ☐ 15,000 IU ☐ 20,000 IU ☐ 25,000 IU ☐ Other _____ IU _____mcg ☐ Don't know
Beta Carotene		
☐ Yes, at least once a week → ☐ No or less than once a week Go to next supplement	Days per week? ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	Amount per day? ☐ 15 mg ☐ 5000 IU ☐ 10,000 IU ☐ 15,000 IU ☐ 20,000 IU ☐ Other _____ IU _____mcg ☐ Don't know
Vitamin C		
☐ Yes, at least once a week → ☐ No or less than once a week Go to next supplement	Days per week? ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	Amount per day? ☐ 250 mg ☐ 300 mg ☐ 500 mg ☐ 1000 mg ☐ 1500 mg ☐ Other _____ mg ☐ Don't know
Vitamin D		
☐ Yes, at least once a week → ☐ No or less than once a week Go to next supplement	Days per week? ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	Amount per day? ☐ 200 IU ☐ 400 IU ☐ 600 IU ☐ 800 IU ☐ Other _____ IU _____mcg ☐ Don't know

Vitamin E☐ Yes, at least once a week →Days per week? →Amount per day?☐ No or less than once a week
Go to next supplement

- ☐
- 1-2
-
- ☐
- 3-4
-
- ☐
- 5-6
-
- ☐
- 7

- ☐
- 100 IU
-
- ☐
- 200 IU
-
- ☐
- 400 IU
-
- ☐
- 600 IU
-
- ☐
- 800 IU
-
- ☐
- 1000 IU
-
- ☐
- Other _____ IU _____ mg
-
- ☐
- Don't know

Thiamin (B1)☐ Yes, at least once a week →Days per week? →Amount per day?☐ No or less than once a week
Go to next supplement

- ☐
- 1-2
-
- ☐
- 3-4
-
- ☐
- 5-6
-
- ☐
- 7

- ☐
- 50 mg
-
- ☐
- 100 mg
-
- ☐
- Other _____ mg
-
- ☐
- Don't know

Niacin (B3)☐ Yes, at least once a week →Days per week? →Amount per day?☐ No or less than once a week
Go to next supplement

- ☐
- 1-2
-
- ☐
- 3-4
-
- ☐
- 5-6
-
- ☐
- 7

- ☐
- 50 mg
-
- ☐
- 100 mg
-
- ☐
- 250 mg
-
- ☐
- 500 mg
-
- ☐
- Other _____ mg
-
- ☐
- Don't know

Vitamin B6☐ Yes, at least once a week →Days per week? →Amount per day?☐ No or less than once a week
Go to next supplement

- ☐
- 1-2
-
- ☐
- 3-4
-
- ☐
- 5-6
-
- ☐
- 7

- ☐
- 50 mg
-
- ☐
- 100 mg
-
- ☐
- 200 mg
-
- ☐
- Other _____ mg
-
- ☐
- Don't know

Folic acid (folate)☐ Yes, at least once a week →Days per week? →Amount per day?☐ No or less than once a week
Go to next supplement

- ☐
- 1-2
-
- ☐
- 3-4
-
- ☐
- 5-6
-
- ☐
- 7

- ☐
- 400 mcg
-
- ☐
- 600 mcg
-
- ☐
- 800 mcg
-
- ☐
- Other _____ mcg
-
- ☐
- Don't know

Vitamin B12☐ Yes, at least once a week →Days per week? →Amount per day?☐ No or less than once a week
Go to next supplement

- ☐
- 1-2
-
- ☐
- 3-4
-
- ☐
- 5-6
-
- ☐
- 7

- ☐
- 50 mcg
-
- ☐
- 100 mcg
-
- ☐
- 250 mcg
-
- ☐
- 500 mcg
-
- ☐
- 1,000 mcg
-
- ☐
- 1,500 mcg
-
- ☐
- Other _____ mcg
-
- ☐
- Don't know

Calcium, Tums, or antacids with calcium (regular strength=200 mg, maximum strength=400 mg)		
☐ Yes, at least once a week →	<u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	<u>Amount per day?</u> ☐ 100 mg ☐ 200 mg ☐ 500 mg ☐ 800 mg ☐ 1000 mg ☐ Other _____ mg ☐ Don't know
☐ No or less than once a week Go to next supplement		
Iron		
☐ Yes, at least once a week →	<u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	<u>Amount per day?</u> ☐ 10 mg ☐ 18 mg ☐ 27 mg ☐ 50 mg ☐ Other _____ mg ☐ Don't know
☐ No or less than once a week Go to next supplement		
Magnesium		
☐ Yes, at least once a week →	<u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	<u>Amount per day?</u> ☐ 100 mg ☐ 250 mg ☐ 500 mg ☐ 1000 mg ☐ Other _____ mg ☐ Don't know
☐ No or less than once a week Go to next supplement		
Zinc		
☐ Yes, at least once a week →	<u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	<u>Amount per day?</u> ☐ 15 mg ☐ 30 mg ☐ 60 mg ☐ 100 mg ☐ Other _____ mg ☐ Don't know
☐ No or less than once a week Go to next supplement		
Selenium		
☐ Yes, at least once a week →	<u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	<u>Amount per day?</u> ☐ 50 mcg ☐ 100 mcg ☐ 200 mcg ☐ Other _____ mcg ☐ Don't know
☐ No or less than once a week Go to next supplement		
Chromium		
☐ Yes, at least once a week →	<u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7	<u>Amount per day?</u> ☐ 50 mcg ☐ 100 mcg ☐ 200 mcg ☐ 400 mcg ☐ Other _____ mcg ☐ Don't know
☐ No or less than once a week Go to next supplement		

7. These next questions ask you about HERBALS and OTHER COMPOUNDS, which include pills, powders, tinctures, and teas taken since you were diagnosed with breast cancer.

Acidophilus pills ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	Ginkgo Biloba ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement
Black Cohosh ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	Ginseng ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement
Co-enzyme Q10 (CoQ10) ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	Grapeseed, Pycnogenol or Proanthocyanidin ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement
Cranberry pills ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	Glucosamine ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement
Dong Quai ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	Chondroitin ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement
Fish oil, EPA, omega-3, flaxseed or cod liver oil ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	Lutein ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement
Garlic pills ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	Lycopene ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement

Melatonin ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	St. John's Wort ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement
Soy supplements (not milk) or isoflavones ☐ Yes, at least once a week → <u>Days per week?</u> ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7 ☐ No or less than once a week Go to next supplement	

8. Have your doctors given you any recommendations concerning your use of vitamins or supplements after your diagnosis for breast cancer?

- ☐ No, we did not discuss the topic.
- ☐ No, we did discuss the topic of vitamin and supplement use, but my doctors did not make any specific recommendations.

- ☐ Yes —→ ☐ My doctors recommended that I not take any vitamins and/or supplements during and after my treatment.
- ☐ My doctors recommended that I not take any vitamins and/or supplements during treatment, but can take them afterwards.
- ☐ My doctors recommended that I not take any vitamins and/or supplements other than a multivitamin.
- ☐ My doctors recommended that I use vitamins and/or supplements both during and after my treatment.
- ☐ Other. Please specify _____
- _____
- _____

9. How have you responded to these recommendations?

- ☐ I followed my doctors' recommendation.
- ☐ I did not follow my doctors' recommendation.
- ☐ Other. Please specify _____
- _____
- _____

FOOD HABITS

These questions are about the types of foods you ate over the last 6 months.

10. Did you eat chicken or turkey?

☐ No

☐ Yes →

When you ate chicken or turkey, how often did you eat the skin?

☐ Almost always

☐ Often

☐ Sometimes

☐ Rarely

☐ Never

11. Did you eat beef, pork, ham or lamb?

☐ No

☐ Yes →

When you ate beef, pork, ham or lamb, how often did you eat the fat?

☐ Almost always

☐ Often

☐ Sometimes

☐ Rarely

☐ Never

12. Did you eat hamburger or other ground meat?

☐ No

☐ Yes →

When you ate hamburger or other ground meat, was it usually...? *Mark one or two*

☐ Regular

☐ Lean

☐ Extra lean

☐ Ground chicken or turkey

☐ Don't know

13. Did you put milk, cream, or creamer on cereal?

- ☐ No
☐ Yes →

When you put milk, cream or creamer on cereal, what type did you usually use? *Mark one or two*

- ☐ Cream or half and half
☐ Whole milk
☐ 2% milk
☐ 1% milk or buttermilk
☐ Nonfat or skim milk
☐ Acidophilus milk
☐ Soymilk
☐ Non-dairy creamer
☐ Don't know

14. Did you drink milk? *Also include beverages made with milk such as lattes or hot chocolate.*

- ☐ Yes →

When you drank milk or beverages made with milk, was it usually... *Mark one or two*

- ☐ Whole milk
☐ 2% milk
☐ 1% milk or buttermilk
☐ Nonfat or skim milk
☐ Acidophilus milk
☐ Soymilk
☐ Don't know

15. Did you eat cold cereal?

- ☐ No
☐ Yes →

**When you ate cold cereal, what type did you usually eat? ...
*Mark one or two***

- ☐ Highly fortified cereals (100% of daily values) such as Total®, Smart Start® and Product 19®
☐ High fiber or bran cereals such as Raisin Bran® and All Bran®
☐ Regular granola (not low fat)

- ☐ All other cereals such as low fat granola, Cheerios® and Corn Flakes®

16. In your household, what kinds of fat were usually used for cooking, for example to flavor vegetables or fry meat?

Mark up to three.

- ☐ Butter
- ☐ Stick margarine
- ☐ Tub or liquid margarine
- ☐ Low fat margarine
- ☐ Olive oil
- ☐ Canola oil
- ☐ Other oils such as corn, soybean, safflower or peanut
- ☐ Lard, bacon fat or meat drippings
- ☐ Didn't use fat or used non-stick spray (Pam®)

17. What kinds of fat did you use at the table, for example on breads, vegetables or potatoes?

Mark one or two.

- ☐ Butter
- ☐ Stick margarine
- ☐ Tub or liquid margarine
- ☐ Low fat margarine
- ☐ Olive oil
- ☐ Sour cream
- ☐ Didn't use fat

18. What type of salad dressing did you usually use?

Mark one or two

- ☐ Regular, including oil and vinegar
- ☐ Low or reduced fat
- ☐ Fat free or nonfat
- ☐ Didn't use salad dressing

19. What type of mayonnaise did you usually use?

Mark one or two.

- ☐ Regular
- ☐ Low or reduced fat
- ☐ Fat free or nonfat
- ☐ Didn't use mayonnaise

20. Did you eat cookies or cakes?

☐ Yes → **When you ate cookies or cakes, how often were they fig bars SnackWells®, angel food cakes, or other types of low or nonfat cookies or cakes?**

- ☐ No
↓
- ☐ Almost always
 - ☐ Often
 - ☐ Sometimes
 - ☐ Rarely
 - ☐ Never

21. Did you drink orange, grapefruit, or other fruit juices?

☐ Yes → **Were any of these vitamins or minerals added (specially fortified) to the juices that you drank? *Mark all that apply***

- ☐ No
↓
- ☐ Extra vitamin C
 - ☐ Vitamin E
 - ☐ Calcium
 - ☐ None
 - ☐ Don't Know

22. On average, how many times a day did you eat (meals plus snacks)? *Snacks include food, milk and milk beverages such as lattes. Coffee, tea and soft drinks alone do not count as snacks.*

- ☐ 1 time per day
- ☐ 2 times per day
- ☐ 3 times per day
- ☐ 4 times per day
- ☐ 5 times per day
- ☐ 6 times per day
- ☐ 7 or more

HOT FLASHES AND SWEATS

For each of the following questions, circle the number that most closely indicates how you have been feeling during the PAST 7 DAYS.

	Not at all								A great deal			
	▼								▼			
23. To what degree have you experienced hot flashes and/or sweats?	1	2	3	4	5	6	7	8	9	10		

If you have not had any hot flashes or sweats in the past 7 days, stop here and skip to question 29 on page 13.

	Mild								Severe			
	▼								▼			
24. How severe are your hot flashes and/or sweats?	1	2	3	4	5	6	7	8	9	10		

	No distress								A great deal of distress			
	▼								▼			
25. To what degree has hot flashes and/or sweats caused you distress?	1	2	3	4	5	6	7	8	9	10		

26. Over the past 7 days, how often have you had hot flashes and/or night sweats?

- 1 ☐ Every day
- 2 ☐ Most, but not all days
- 3 ☐ Occasionally (fewer than half the days)
- 4 ☐ Hardly any days

27. To what degree has your hot flashes and/or sweats changed during the past 7 days?

- 1 ☐ Increased
- 2 ☐ Gone up and down
- 3 ☐ Stayed the same
- 4 ☐ Decreased

28. Circle the number that most closely indicates to what degree HOT FLASHES AND/OR SWEATS have interfered with your ability to do the following activities in the past 7 days. For activities you don't do, for reasons other than hot flashes (e.g. you don't work because you are retired), check the box.

IN THE PAST 7 DAYS, to what degree has HOT FLASHES AND/OR SWEATS interfered with your ability to:

	Don't do	Not at all ▼	1	2	3	4	5	6	7	8	9	A great deal ▼	10
Do household chores	☐		1	2	3	4	5	6	7	8	9		10
Cook	☐		1	2	3	4	5	6	7	8	9		10
Sleep	☐		1	2	3	4	5	6	7	8	9		10
Work	☐		1	2	3	4	5	6	7	8	9		10
Visit or socialize with friends or family	☐		1	2	3	4	5	6	7	8	9		10
Engage in sexual activity	☐		1	2	3	4	5	6	7	8	9		10
Engage in leisure and recreational activities	☐		1	2	3	4	5	6	7	8	9		10
Shop and do errands	☐		1	2	3	4	5	6	7	8	9		10
Walk	☐		1	2	3	4	5	6	7	8	9		10
Exercise, other than walking	☐		1	2	3	4	5	6	7	8	9		10

29. Did you experience hot flashes and/or sweats in the last 6 months?

0 ☐ No, I didn't experience hot flashes and/or sweats —————→ **Go to question 37 on page 16**
 1 ☐ Yes

→ **How long did you experience having hot flashes and/or sweats?**

- 1 ☐ Less than 6 weeks
 2 ☐ Between 6 weeks and 3 months
 3 ☐ Between 3 months and 6 months
 77 ☐ Don't know

30. In the last 6 months, were hot flashes and/or sweats one of your top health problems?

- ¹ ☐ Yes
⁰ ☐ No

31. To what degree has hot flashes and/or sweats changed during the past 6 months?

- ¹ ☐ Markedly increased (at least 75% more)
² ☐ Moderately increased (about 50% more)
³ ☐ Slightly increased (about 25% more)
⁴ ☐ The same
⁵ ☐ Slightly reduced (about 25% less)
⁶ ☐ Moderately reduced (about 50% less)
⁷ ☐ Markedly reduced (at least 75% less)

32. Compared to before you were diagnosed with breast cancer, how severe are your hot flashes and/or sweats?

- ¹ ☐ I did not experience any hot flashes or sweats before my breast cancer diagnosis
² ☐ Markedly increased (at least 75% more)
³ ☐ Moderately increased (about 50% more)
⁴ ☐ Slightly increased (about 25% more)
⁵ ☐ The same
⁶ ☐ Slightly reduced (about 25% less)
⁷ ☐ Moderately reduced (about 50% less)
⁸ ☐ Markedly reduced (at least 75% less)

**33. When do your hot flashes and/or sweats typically begin during the day?
(choose one)**

- ¹ ☐ I awaken with a hot flash
² ☐ In the morning (before 12 noon)
³ ☐ In the early afternoon (between 12 and 3 pm)
⁴ ☐ In the late afternoon (between 3 and 5 pm)
⁵ ☐ In the evening (after 6 pm)
⁸⁸ ☐ Don't know

**34. How many hot flashes and/or sweats do you typically have in a usual day?
(choose one)**

- ¹ ☐ 0 to 1
² ☐ 2 to 4
³ ☐ 5 to 7
⁴ ☐ 8 to 10
⁵ ☐ 11 or more
⁸⁸ ☐ Don't know

35. What do you think is the reason for your hot flashes and/or sweats? (*check all that apply*)

- ☐ Cancer treatment(s)
 - ☐ A recent or recurrent infection (i.e. a cold, bronchitis, urinary tract).
 - ☐ Hot or humid weather
 - ☐ Physical activity at home or work
 - ☐ Problems or stress at home or at work
 - ☐ Depression
 - ☐ Difficulty sleeping or frequent awakening
 - ☐ Eating hot foods and/or drinks
 - ☐ Eating too much
 - ☐ Other Please Specify _____
-

36. In the past month, have you tried any of the treatments listed below for your hot flashes and/or sweats? (*check all that apply*)

- ☐ Napping or resting during the day
- ☐ Wearing less clothing
- ☐ Using less bedding (blankets)
- ☐ Taking cool baths/showers
- ☐ Turning down the heat at home or work
- ☐ Using a fan or turning up the air conditioner
- ☐ Exercising less
- ☐ Changing your diet
- ☐ Taking vitamin supplements Please list _____
- ☐ Changing your level of activity at home or at work or changing jobs
- ☐ Eating less
- ☐ Drinking cold beverages
- ☐ Other treatments or medications not listed above _____

FEELING COLD OR CHILLED

For each of the following questions, circle the number that most closely indicates how you have been feeling during the PAST 7 DAYS.

	Not at all ▼												A great deal ▼
37. To what degree have you experienced feeling inappropriately cold or chilled when others feel fine or hot?	1	2	3	4	5	6	7	8	9	10			

If you have not felt cold or chilled in the last 7 days, stop here and skip to question 43 on page 17.

	Mild ▼												Severe ▼
38. How severe is your feelings of being cold or chilled?	1	2	3	4	5	6	7	8	9	10			

	No distress ▼												A great deal of distress ▼
39. To what degree has feeling cold or chilled caused you distress?	1	2	3	4	5	6	7	8	9	10			

40. Over the past 7 days, how often have you felt cold or chilled?

- 1 ☐ Every day
- 2 ☐ Most, but not all days
- 3 ☐ Occasionally (fewer than half the days)
- 4 ☐ Hardly any days

41. To what degree has your feeling cold or chilled changed during the past 7 days?

- 1 ☐ Increased
- 2 ☐ Feeling cold or chilled has gone up and down
- 3 ☐ Stayed the same
- 4 ☐ Decreased

42. Circle the number that most closely indicates to what degree FEELING COLD OR CHILLED has interfered with your ability to do the following activities in the past 7 days. For activities you don't do, for reasons other than feeling cold or chilled (e.g. you don't work because you are retired), check the box.

IN THE PAST 7 DAYS, to what degree has FEELING COLD OR CHILLED interfered with your ability to:

	Don't do	Not at all ▼	1	2	3	4	5	6	7	8	9	A great deal ▼	10
Do household chores	☐		1	2	3	4	5	6	7	8	9		10
Cook	☐		1	2	3	4	5	6	7	8	9		10
Sleep	☐		1	2	3	4	5	6	7	8	9		10
Work	☐		1	2	3	4	5	6	7	8	9		10
Visit or socialize with friends or family	☐		1	2	3	4	5	6	7	8	9		10
Engage in sexual activity	☐		1	2	3	4	5	6	7	8	9		10
Engage in leisure and recreational activities	☐		1	2	3	4	5	6	7	8	9		10
Shop and do errands	☐		1	2	3	4	5	6	7	8	9		10
Walk	☐		1	2	3	4	5	6	7	8	9		10
Exercise, other than walking	☐		1	2	3	4	5	6	7	8	9		10

43. Did you experience feeling cold or chilled in the last 6 months?

0 ☐ No, I didn't experience feeling cold or chilled at all → **Stop here, you are now finished with this questionnaire.**
 1 ☐ Yes

→ **How long did you experience feeling cold or chilled?**

- 1 ☐ Less than 6 weeks
 2 ☐ Between 6 weeks and 3 months
 3 ☐ Between 3 months and 6 months
 88 ☐ Don't know

44. In the last 6 months, was feeling cold or chilled one of your top health problems?

- ¹ ☐ Yes
⁰ ☐ No

45. To what degree has feeling cold or chilled changed during the past 6 months?

- ¹ ☐ Markedly increased (at least 75% more)
² ☐ Moderately increased (about 50% more)
³ ☐ Slightly increased (about 25% more)
⁴ ☐ The same
⁵ ☐ Slightly reduced (about 25% less)
⁶ ☐ Moderately reduced (about 50% less)
⁷ ☐ Markedly reduced (at least 75% less)

46. Compared to before you were diagnosed with breast cancer, how severe is your feelings of being cold of chilled?

- ¹ ☐ I did not experience feeling cold or chilled before my breast cancer diagnosis
² ☐ Markedly increased (at least 75% more)
³ ☐ Moderately increased (about 50% more)
⁴ ☐ Slightly increased (about 25% more)
⁵ ☐ The same
⁶ ☐ Slightly reduced (about 25% less)
⁷ ☐ Moderately reduced (about 50% less)
⁸ ☐ Markedly reduced (at least 75% less)

47. When does your feeling of being cold or chilled typically begin during the day? (*choose one*)

- ¹ ☐ I awaken feeling cold or chilled
² ☐ Feeling cold or chilled begins in the morning (before 12 noon)
³ ☐ Feeling cold or chilled begins in the early afternoon (between 12 and 3 pm)
⁴ ☐ Feeling cold or chilled begins in the late afternoon (between 3 and 5 pm)
⁵ ☐ Feeling cold or chilled begins in the evening (after 6 pm)
⁶ ☐ I usually only feel cold or chilled AFTER getting a hot flash
⁸⁸ ☐ Don't know

48. How long do you typically feel cold or chilled during a usual day? (choose one)

- 1 ☐ Less than 3 hours
 2 ☐ 3 to 6 hours
 3 ☐ 7 to 12 hours
 4 ☐ 13 to 24 hours
 88 ☐ Don't know

49. What do you think is the reason for this feeling of being cold or chilled? (check all that apply)

- ☐ Cancer treatment(s)
☐ A recent or recurrent infection (i.e. a cold, bronchitis, urinary tract).
☐ Cold and/or damp weather
☐ Lack of physical activity at home or work
☐ Problems or stress at home or at work
☐ Depression
☐ Difficulty sleeping or frequent awakening
☐ Eating cold foods and/or drinks
☐ Not eating enough
☐ Other Please Specify _____
-

50. In the past month, have you tried any of the treatments listed below for your feelings of being cold or chilled? (check all that apply)

- 1 ☐ Napping or resting during the day
 2 ☐ Wearing more clothes
 2 ☐ Using more bedding (blankets)
 2 ☐ Using an electric blanket
 2 ☐ Taking hot baths/showers
 2 ☐ Turning up the heat at home or work, or using a space heater
 2 ☐ Exercise
 3 ☐ Changing your diet
 4 ☐ Taking vitamin supplements Please list _____
 5 ☐ Changing your level of activity at home or at work or changing jobs
 2 ☐ Eating more, especially high calorie foods
 8 ☐ Drinking hot beverages
 10 ☐ Other treatments or medications not listed above _____