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Breast Cancer Treatment: A Prospective Study

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FOREWORD

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INTRODUCTION

MENSTRUAL CYCLE MAINTENANCE AND QUALITY OF LIFE: A PROSPECTIVE STUDY

PROTOCOL SUMMARY

INTRODUCTION The frequent morbidity associated with most cancers and their treatments make the measurement of health-related quality of life a critical mechanism for determining the toll of the entire disease. Young breast cancer patients additionally may face treatment-induced menopause and with it may experience hot flashes, mood changes, sleep disturbances, vaginal dryness, and the cascading effect of anxiety and depression. In the United States, Wake Forest University has particular expertise in quality of life with naturally occurring menopause. Wake Forest is the Coordinating Center in this issue for the Women's Health Initiative, funded by the National Institute of Health, which has accrued more than 163,000 study subjects.

Very little is known about the incidence, onset, time course, and symptomatology of premature menopause induced by breast cancer therapy. No prospective study exists. The purpose of the present study is to identify determinants of treatment-related amenorrhea and its effect on quality of life in a cohort of young breast cancer patients.

SUMMARY OF EXPERIMENTAL DESIGN This multi-center study, under the direction of Jeanne Petrek, will include patients from Memorial Sloan Kettering Cancer Center, M.D. Anderson Cancer Center, and Wake Forest University, and self-referred patients.

Extensive baseline data will be collected by an in-depth review of medical reports and interview for additional data. Information will be gathered on demographic, clinical, menstrual/reproductive and treatment variables.

The study intervention consists of collecting data on bleeding through the bleeding diary and on health-related quality of life through specific questionnaires. The data collection instruments will be obtained at baseline and every six months. Follow-up will range between 24 - 42 months for participants. The follow-up contacts provide an opportunity to collect data on study parameters and monitor the status of reproductive events, disease recurrence, complications of treatment such as lymphedema, or other illnesses. Data collection instruments will be mailed to each participant at regularly scheduled 6-month intervals accompanied by a stamped, addressed envelope. If study forms are not returned within three weeks by the participant, the participant will be called. The study measurements are : 1. Bleeding Diary, 2. Rand Health Status Profile, 3. Beck Depression Inventory, 4. Sleep Disturbance Scale, 5. Watts Sexual Functioning Questionnaire, 6. Physical Symptom Check List, 7. Rand Social Support Questionnaire, 8. Spirituality Sub Scale, 9. Fact B, 10. Self Concept Scale, and 11. Interval Medical History.

OBJECTIVES

The proposed study design. The study strategy is to evaluate menstrual cycle maintenance and its effect on the quality of life. Data on menstrual cycle maintenance, quality of life and some short term data on reproductive events will be obtained during the study period but an essential follow up period for disease-free survival will be beyond the study limits. Additional funding will be obtained in order to continue the close contact established on this singular database established under the Department of Defense funding.

Study Objectives. The overall goal of the proposed research is to recruit and follow young breast cancer patients aged 45 and younger, in order to examine menstrual cycle maintenance, a surrogate of ovarian function.

Primary Study Objectives.

1. To describe the bleeding patterns of young breast cancer patients (including those without systemic therapy): frequency, duration, amount.
2. To describe the incidence, symptomatology, and time course of treatment related amenorrhea i.e., no menstrual bleeding for more than six months after the start of the treatment
3. To compare health-related quality of life (HRQL) of women who are experiencing amenorrhea to that of women who are not experiencing amenorrhea.

Secondary Objectives.

1. To examine possible predictors of treatment-related amenorrhea including age, smoking history, race, and treatment variables.

BACKGROUND AND RATIONALE

It has long been established that systemic cancer therapy can cause premature ovarian failure. While some of the rare severe consequences of cancer chemotherapy, such as leukemogenesis and cardiac damage are being confronted and evaluated ⁽¹⁾, ovarian failure seems relatively neglected. Therapy-induced menopause has been poorly characterized as to the incidence, time course and permanence, as reviewed below; it has been wholly uncharacterized as to its symptomatology and its impact on the quality of life.

Background of research in systemic therapy-induced menopause There are probably two reasons for the meager analysis of therapy-related menopause: in the past, menopause induction itself in adjuvant chemotherapy programs was thought to increase survival from breast cancer; and secondly the occurrence of menopause, a natural phenomenon in every woman's later life, was deemed not so important.

• However, a 1994 review of previous adjuvant trials concludes that the benefit of chemotherapy in the premenopausal patient is not dependent upon menopause induction ⁽²⁾ as does the even more recently published 20-year results of the Milan study. ⁽³⁾ Also at this time natural menopause is undergoing scrutiny as to quality of life and the predisposition to chronic diseases. ⁽⁴⁾ The extent of the scanty scientific data systemic therapy-induced menopause is noted in that review "Amenorrhea following chemotherapy for breast cancer: Effect of disease-free survival". ⁽²⁾ Forty key trials which included premenopausal patients on adjuvant chemotherapy (i.e., no evidence of metastatic disease) were examined. Only 15 papers reported incidence of amenorrhea.

Acknowledged factors in menopause induction The two factors consistently found are age and drug/dose. The category of drugs most likely to induce ovarian failure is that of the alkylating agents, such as cyclophosphamide -- the most common drug in breast cancer treatment, while antimetabolites have lesser effect. ⁽⁵⁾ One study found that amenorrhea in similar age women occurred in 63% treated with CMF (cyclophosphamide, methotrexate and 5-fluorouracil) versus 70% with cyclophosphamide alone. This indirectly shows little effect on ovarian function for the two antimetabolite agents. ⁽⁶⁾ In a study of 18 premenopausal patients, amenorrhea occurred after a mean cyclophosphamide total dose of 9.3 gr in women younger than 40, and after a mean dose of 5.2 gr in women older than 40. ⁽⁷⁾

Of the non-alkylating agents, doxorubicin is the most common in breast cancer therapy. In a study of 128 patients less than 35 years old treated with the drug in combination with cyclophosphamide and 5-fluorouracil, 58% had regular menstrual cycles after chemotherapy, 32% experienced temporary amenorrhea and 9% permanent amenorrhea. ⁽⁸⁾ The potential for amenorrhea with other categories of antineoplastic agents has not been extensively studied. For new drugs, such as taxol ⁽⁹⁾ or vinorelbine ⁽¹⁰⁾, no data are available: amenorrhea is not even mentioned in two recent reviews. Specific aspects of chemotherapy have not been considered such as the modern use of cytokines and role of serious intercurrent illnesses, e.g., hospitalization

for neutropenia.

There are little data regarding ovarian failure as a result of tamoxifen alone since the practice is rare. Tamoxifen may be prescribed to premenopausal patients with permanent menopause if estrogen receptors are found on their tumors. The mechanism for tamoxifen-induced amenorrhea, which has been reported⁽¹¹⁾ is not known. In premenopausal women on Tamoxifen estrogen levels are frequently elevated and the normal feedback could be lost⁽¹²⁾ causing amenorrhea.

Limitations of retrospective studies on menstrual cycle maintenance In these reports, weaknesses include variable definitions of temporary/permanent amenorrhea, variable lengths of follow up on menses or no follow up after chemotherapy administration, and retrospective data collection. It appears that one study⁽¹³⁾ collected prospective data by twelve monthly questionnaires on 95 patients but with no menses data beyond the year. Most importantly, the study design in these reports is focussed on the analysis of disease-free survival and overall survival in a typical double or triple arm therapy protocol. Therefore, data on amenorrhea, a non-life threatening complication, is understandably relegated to a secondary analysis. Such data are weaker than that obtained in a study designed and conducted for primary endpoint of amenorrhea.

Two broad categories of age are typically reported -- less than 40 years and greater than 40 years. In one study⁽¹⁴⁾ of 221 patients the category of patients over 40 years is subdivided into greater of less than 45 years. It is clear that menopause varies greatly by age regardless of the particular regimen.⁽²⁾ Nevertheless, beyond stating that 38% of women aged 39 years or less have permanent amenorrhea after 12 months of CMF,⁽¹⁵⁾ there is no characterization of who did or did not undergo permanent menopause.

Unstudied factors associated with age of natural menopause In spite of these limitations, the most important factors causing the wide range of premature menopause incidence within a particular age group and chemotherapy regimen may be factors influencing age at natural menopause. These have never been assessed in a breast cancer population or any cancer population.

In multi variate analyses of longitudinal study population, factors influencing the age of natural menopause include, smoking history,⁽¹⁶⁻¹⁷⁾ parity,^(17,18) body mass index^(16,19) history of irregular periods before age 25 or first birth,⁽¹⁸⁾ and socioeconomic class / education / income.⁽¹⁷⁻¹⁹⁾ These factors could be responsible for one 35 year old breast cancer patient becoming permanently menopausal while another 35 year old woman maintains normal menses. It is intuitive that ovarian failure is not a random phenomenon and that a comprehensive analysis as proposed will shed light on the determinants of therapy-induced menopause.

Health related quality of life in the breast cancer survivor Recent years have witnessed a growing recognition among cancer researchers of the importance of systematically measuring

health-related quality of life (HRQL) and psychosocial factors, both to characterize the health status and well-being of this patient population, as well as to assess treatment efficacy.⁽²⁰⁻²³⁾ The frequent morbidity associated with most cancer and their treatments make the measurement of HRQL and psychosocial variables a critical mechanism for determining the toll of the entire disease. Common responses of patients with breast cancer include anxiety, depression, anger, guilt and fear.⁽²⁴⁻²⁷⁾

Additionally young breast cancer survivors face the possible impact of specific chemotherapy agents on ovarian function. Those women may experience such symptoms as changes in mood, sleep disturbances, vaginal dryness, and hot flushes and the cascading effect of anxiety and depression. For those women who were desirous of becoming pregnant following breast cancer, a premature menopause may be most distressing particularly for those women who had delayed childbearing and were childless.

In the past 10 years, significant progress has been made in the reliable and valid assessment of health related quality of life (HRQL) and other psychosocial variables.⁽²⁷⁻³⁰⁾ Although there has been some debate regarding the definition of HRQL, a recent international conference co-chaired by one of the proposal's co- investigators - Dr. Sally Shumaker, reached agreement on the fundamental dimensions essential to any HRQL assessment⁽³¹⁾ These include: physical functioning, psychological functioning, social functioning and role activities, and the individual's overall life satisfaction and perception of their health. For specific populations, other commonly assessed dimensions of HRQL may be important, such as sleep disturbance, pain, symptoms, and intimacy and sexual functioning.

Data suggests that aspects of HRQL and psychosocial factors (e.g., emotions, family relations) are rated by patients as more important to their well-being than clinical factors directly related to the effects of the disease and its treatment⁽³²⁾ further underscoring the importance of measuring HRQL in clinical research in breast cancer. Thus far the potential multiple outcomes of breast cancer treatment in young women have not been investigated: morbidity and mortality, menopausal symptoms, and the psychological impact of premature menopause and the loss of childbearing potential.

Results on the health-related quality of life from the proposed study may assist the perspective on hormone replacement for breast cancer survivors.⁽³³⁾ For example, if the proposed study shows no decrease in health-related quality of life due to menopause itself, then recommendations of hormone replacement to breast cancer survivors will be considered more for prevention of the long-term sequelae of osteoporosis and heart disease and less for "making the patient feel better."

Menstrual cycle maintenance: fertility and pregnancy outcome after systemic therapy
The assisted reproductive methods for the inception and maintenance of pregnancy have been described in the literature for older women with natural menopause.⁽³⁴⁾ However, it is very unlikely that the breast cancer patient will undergo the oral and systemic high-dose

hyperstimulation required for this procedure. In those breast cancer patients who maintain menstrual cycles after systemic therapy, even general figures on fertility are unknown.⁽³⁵⁻³⁶⁾ In a retrospective cohort study of 2,283 adolescent survivors of all cancers from 1945 to 1975, relative fertility (healthy siblings were controls) was decreased and varied with cancer and whether chemotherapy and/or radiotherapy was administered.⁽³⁷⁾

Even though apparently normal menstrual cycling may be maintained after systemic therapy and the patient chooses to become pregnant, the incidence of pregnancy and successful childbearing is unknown. The above general studies on adolescent cancer populations may be indicating subtle and unmeasured defects in fertility in spite of maintained menstrual cycles.

The potential of breast cancer chemotherapy on adverse outcome of subsequent pregnancy has not been specifically evaluated. However, a study reported on 58 pregnancies occurring after treatment for various malignancies and found no excess congenital anomalies. The study noted a total of 40% abnormal pregnancies, with most of these occurring in the first year after chemotherapy. The abnormal pregnancies consisted mainly of premature termination and low birth weights both of which was attributed to dysfunction of the uterine hormonal gestational milieu.⁽³⁸⁾

POTENTIAL BENEFIT FOR SOCIETY

About 15% of the 186,000 estimated new cases of invasive breast cancer this year will occur in women of childbearing age and the majority will be long-term survivors. Most young women with invasive breast cancer will undergo adjuvant chemotherapy and almost half will suffer therapy-induced menopause. Foregoing motherhood either for iatrogenic infertility or for concern about its safety can be overwhelmingly distressing. However, even without desire for childbearing, the quality of life of these young patients may be compromised by premature menopause with symptoms such as hot flashes, sleep disturbances, decreased libido, and vagina dryness.

Very little is known about the incidence, onset, time course, and symptomatology of premature menopause induced by breast cancer therapy and virtually nothing is known about its impact on the young survivor's quality of life. No prospective study exists. Since the improved survival following chemotherapy appears independent of menopause induction in recent data, the possibility of premature menopause should be factored into the risk/benefit assessment.

A comprehensive analysis on a large prospective study cohort as proposed herein will elucidate determinants of premature menopause. Now unavailable, such an individual risk profile of premature menopause could be critical to the clinician and to the young patient in considering options and decision-making about specific therapy. Not only must the quality of life with premature menopause be considered in the young, but also the long term predisposition to osteoporosis, heart disease, and genital atrophy, particularly in those with a good prognosis in

whom a long survivorship is expected. The multiple issues involved with premature menopause due to breast cancer chemotherapy have been recently reviewed.⁽³⁹⁾

BODY

EXPERIMENTAL METHODS

See the 1997 Annual Report for the current organization of research activities. The past year has been devoted to recruitment and accrual which began January 1, 1998. As stated, a total of 800 women was planned from three clinical centers within the time allotted for accrual.

Wake Forest University	188
M.D. Anderson Cancer Center	252
Memorial Sloan-Kettering Cancer Center	360

See statement of work from 1997 Annual Report which outlines that accrual is planned to require 16 months (January 1, 1998 to April 30, 1999). We planned on enrolling the required sample size within the first sixteen months in order to permit adequate follow up time and the evaluation of temporary versus permanent amenorrhea.

Breakdown of accrual from three centers.

CLINICAL CENTER	PLANNED April 1999	PLANNED September 1998	ACTUAL September 1998
Wake Forest University	188	94	22
MD Anderson	252	126	44
Memorial Sloan-Kettering	360	180	119

This report includes the accrual of only 9 months, from January 1998 to September 1998, however even taking into account start-up time and training, the accrual has been less than anticipated.

The situation at Memorial Sloan-Kettering has been reviewed in depth and is similar to that at the other institutions. The initial figures used to estimate the original possible sample size at Memorial Sloan-Kettering in the previous annual report are correct. The billing department at Memorial Sloan-Kettering has registered 683 women between the ages of 18 and 45 for their initial visit between January 1, 1998 and July 1, 1998 with a primary diagnosis of breast cancer. The Services include Surgery, Radiation Therapy, Medical Oncology, Psychiatry, Nutrition, and General Medicine.

Even though this appears to be an abundant population to draw an adequate number of study subjects, when this large population was carefully investigated with chart review and discussion with the consulting physician, more than three quarters of these patients were

ineligible. The vast majority had locally recurrent breast cancer or breast cancer metastasis, but a surprising percentage were ineligible due to lack of regular menstrual cycles (e.g. hysterectomy, ovarian dysfunction such as polycystic ovaries). Additionally, a small percentage were listed as having breast cancer even though they had intraductal (Stage 0) cancer, and therefore were ineligible.

There were only 78 patients of the original population of 683 who were fully eligible, but were not treated at Memorial Hospital. These were usually patients who came here for a second opinion, but whose Health Maintenance Organization Insurance did not allow coverage for treatment at Memorial Hospital. Therefore, we mailed patients the attached letter (Appendix A) and standard brochure (Appendix B) – as we had been permitted by our institutional review board. (At this point, the review board had not given us permission to phone patients after the initial letter). Twenty women responded initially and eleven performed all of the necessary entry requirements and are now registered participants. Assuming some letters may have been lost in the mail, we sent a second identical letter (Appendix A) to the remaining 58 and were able to obtain an additional 3 participants.

After obtaining such a small proportion of study subjects from the eligible population of 78 women, we petitioned our IRB board (Appendix C) to send an introductory letter to the next group of registered patients and to follow up with a phone call the following week. This request was granted, and we sent out letters (Appendix D) to 8 eligible patients, of which 7 ultimately became participants. The toll free number was also listed. After noting a greater response when a follow up call was made, it was determined that the latter procedure would be utilized. According to IRB amendment, eligible patients would be called after they received the letter.

Nevertheless, since these numbers are still insufficient to meet the projected necessary sample size, we turned to self-referred patients by increasing media attention and public awareness of this important study and publishing our toll free number. An executive decision, subsequently approved by each center's IRB, was made to accrue self-referred participants who had not been treated or diagnosed at one of the three centers. The need for an in-person baseline visit was eliminated. We communicated with accrued patients through phone and mail, including the baseline survey. All such participants were mailed an informed consent, which was required before entering the participant in the study.

The three clinical centers will continue to recruit through tumor registries and physician referrals at their participating institutions. In addition, further strategies have been implemented to recruit self-referred patients. One or more of the following strategies has been utilized in recruiting participants into the study at each clinical center:

1. Patient Identification Through Tumor and Surgical Registries. A majority of patients will continue to be identified through tumor and/or surgical registries at the participating institutions. Once women with stage I - III breast cancer have been identified, the patients' oncologists/surgeons are contacted by clinic staff to obtain approval to approach the patient. If the physician approves, the patient is approached at the clinic site, (if she is scheduled for a follow-up or treatment visit), or the patient is sent a letter describing the purpose of the study,

which will be followed by a telephone call. The clinic staff person will screen the person to ensure she meets the eligibility criteria, and then will ask the patient to participate in the study if she is eligible.

2 Referral Through Physicians. Participants are also identified by the clinical center's participating investigators, oncologists, surgeons, and radiologists. In most instances, these physicians will have already explained the study to the participant, and the clinic staff contacts the patient to invite her to participate in the study. The patient is screened to ensure that she meets all eligibility criteria. If no baseline clinic visit is scheduled the patient is contacted by phone. The patient signs the informed consent and medical record release forms before being entered into the study.

3 Self-Referral. Women receiving treatment from any of the three centers may hear of the study and want to participate. These women may self-refer. Additionally, women may hear about the study through the many strategies that have been implemented to recruit participants nationally. These women do not have to be patients at one of the three clinical centers. They are screened for study eligibility, and asked to join the study if the eligibility criteria are met. The patients will sign the informed consent before beginning the study intervention, sign a medical record release, and will complete all baseline study questionnaires. Recruitment strategies that have been implemented are listed below:

A. Advertisement In MAMM Magazine

A one page advertisement was placed in the August/September issue of *MAMM* magazine, with a subsequent half-page in the October/November issue (Appendix E). *MAMM* is a bimonthly magazine targeted to those whose lives have been impacted by breast and reproductive cancers. Issues include information on the latest treatments, inspiring stories of survivors, and controversies surrounding a cancer diagnosis.

MAMM guarantees a circulation of 70,000 copies through four venues. 35,000 copies are distributed through major bookstore chains and newsstands. Currently, there are approximately 7,000 regular subscribers to the magazine, with an additional 10,000 copies that go to randomly selected persons from lists of women who have expressed an interest in cancer related issues. 15,000 copies are distributed to 274 different breast care organizations, support groups, physicians' offices, and activist organizations who have requested copies.

The following is a geographic breakdown of *MAMM*'s circulation from a subscriber profile conducted in March of 1998 by the Polk Company:

CENSUS DIVISION	%	CENSUS DIVISION	%
East North Central	23.1%	Pacific	11.2%
East South Central	2.0%	South Atlantic	15.2%
Middle Atlantic	25.0%	West North Central	4.7%
Mountain	4.9%	West South Central	7.5%
New England	5.6%	Unknown Census Division	0.7%

As of September 15, 1998, 13 people had responded to the first advertisement. Seven of these respondents were eligible for the study, and five agreed to participate. Since many physicians' offices keep these magazines in their waiting rooms for several months past the circulation date, it is our hope that additional women will respond to this first advertisement. At this point, the October/ November issue has not been circulated. The October/November issue will be placed in the first anniversary issue for *MAMM* magazine. For this reason, and because October is breast cancer awareness month, we hope to receive a larger response to this advertisement. The advertisement was paid for by philanthropic funds of Memorial Sloan-Kettering Cancer Center designated for breast cancer research.

B. Organizations Displaying Brochures

Brochures (Appendix B) were distributed to the following support group organizations for display:

The Susan G. Komen Breast Cancer Foundation - This organization is dedicated to advancing research, education, screening and treatment of breast cancer. Nancy Goodman Brinker established the foundation in 1982, in honor of her sister Susan Komen who died of the disease. It is the nation's largest private funder of research dedicated solely to breast cancer, raising more than \$90 million dollars since being founded. The Komen Foundation is best known for its sponsorship of *Race for the Cure*, an annual run/walk held in October to raise money for breast cancer.

Two hundred brochures were distributed to the foundation for display at various locations including support group meetings and at the annual *Race for the Cure*.

Y-ME - This national breast cancer organization was founded in 1978 by two breast cancer patients. It was established to provide information and support to those touched by the disease. They maintain 24 hour toll free hotlines for both English and Spanish-speaking women who need support. Y-ME has many local chapters that run open door groups, early detection workshops, survivor groups, and many other support programs. Five hundred brochures were distributed to Y-ME for display.

SHARE - Self-help for Women with Breast or Ovarian Cancer - This self-help

organization serves women, men and children affected by breast and ovarian cancer. They promote public awareness and early detection. They place special emphasis on wellness programs dedicated to reducing stress, healthy diets, imagery, and exercise.

SHARE-A-WALK is an annual 4 mile walk held to raise funds for breast and ovarian cancer. This year at its eighth annual walk held in Central Park in New York City, 100 brochures will be made available to the public. SHARE will also put brochures on display at meetings and workshops that were held for breast cancer patients.

Over 800 brochures were sent to these three organizations in September. The Race for Cure and SHARE-A-WALK occurred in early October in conjunction with Breast Cancer Awareness Month. There has been a small response to this at this early time with only two participants responding as of September 15, 1998. However, these brochures will remain available at these organizations, and may increase self-referral as public awareness of the study increases.

C. Web Page

A web page announcing this study has been established on the Memorial Sloan-Kettering Cancer Center web site. (Appendix F). The page was activated as of August 31, 1998 and is located in the cancer and treatment section of the web site.

Additionally, the page has been linked to the website of Cancer Care, Inc. This organization is a resource for people diagnosed with all types of cancer and offers counseling support, cancer information, referral services, and financial support to these patients. The page has been linked to their breast cancer and sexuality section.

As of September 16, 1998, only two responses were received as a result of the web page. Several future links hope to recruit additional participants. NBC's *Today Show* will link the page to their web site for one weekend in October following an appearance by Dr. Jeanne Petrek on the show. The National Association for Breast Cancer Organization (NABCO) has agreed to link the page to their site in November of this year. Breast Cancer News Daily will also provide a link in October in their newsletter online. In addition, contacts are being made to web search engines to pursue other website opportunities.

D. Physician Letters

Physician organizations were targeted as an additional recruitment resource. Merge mailings were sent to both the New York Metropolitan Breast Cancer Group, Inc. and The American Society of Breast Disease. Physicians were sent a letter, brochures, and information about the purpose of the study.

New York Metropolitan Breast Cancer Group, Inc. - This year marks the 25th anniversary for this organization. It is a tri-state society for physicians involved in the treatment of breast cancer. Each physician was sent a letter (Appendix G) explaining the study and asking

for their assistance with recruitment. At least three brochures were included with each letter.

American Society of Breast Disease - A group of physicians founded this society in 1977 for those interested in studying diseases of the breasts. It was expanded into a multi-disciplinary organization in 1980. The group has more than 600 members representing 44 states and 16 foreign countries. 21 different specialties related to the breast are represented. A similar letter (Appendix H) was sent along with five brochures to 404 physicians. Listed below is a geographic and specialty breakdown of letters sent.

SPECIALTY	TOTAL	SPECIALTY	TOTAL
Surgery	253	Administration	2
Medical Oncology	55	Genetics	1
Radiology	37	Preventive Oncology	1
Radiation Oncology	21	Emergency Medicine	1
Ob/Gyn	8	Family Practice	1
Internal Medicine	7	Public Relations	1

GEOGRAPHIC LOCATION (U.S. TIME ZONES)	TOTAL
Eastern	183
Central	138
Mountain	11
Pacific	72

Association of Women Surgeons - A third letter will be sent out to members of The Association of Women Surgeons (AWS). AWS was established in 1981 to promote the growth and advancement of female surgeons. They have over 890 regular members representing every surgical specialty. Membership includes women from every U.S. state and international members from Canada, Mexico, Europe, and Asia.

The Clinical Coordinating Center at the Wake Forest School of Medicine continues to monitor recruitment and issues monthly recruitment reports to each participating institution. The strategies listed above were developed to assist the clinical centers in meeting their recruitment goals.

Jeanne A. Petrek, M.D.

STATEMENT OF WORK

Task 1. Months 1 – 2

a. Focus groups for final questionnaire wording.

Focus groups were held at Wake Forest University under the direction of Dr. Sally Shumaker, the Principal Investigator of the clinical coordinating center. As well as the wording for the baseline data questionnaires, the proposed procedural sequences were decided with attention to the women's preferences for baseline and follow-up procedures.

See work output attached as Appendix I with the title of the research project. This Manual of Procedures, contains more than 200 pages and consists of chapters on organizational structure; protocol; recruitment prescreening and eligibility; consenting process; baseline data collection visits; collecting participant information; chart review forms; study data forms and questionnaires; instructions for menstrual diaries; follow-up contacts; data management; and quality control. This assures that the research study procedure is conducted absolutely identically among the clinical centers in accruing women throughout the country.

b. Pilot calendar and questionnaires in Texas and New York City population.

The questionnaires and menstrual bleeding calendars were tested on non-protocol patients in Texas and New York City and were found to be satisfactory. This included these follow-up forms. See Appendix J (purple cover document) for baseline data and questionnaires; Appendix K (blue cover document) for six month follow-up; and Appendix L (unbound document) for one year follow-up. Some of the wording was not able to be changed as one of the goals is the comparison of this group of women with premature menopause to the data also collected by Wake Forest University in a similar capacity for the Women's Health Intervention (WHI), a national study of more than 100,000 women undergoing menopause at the natural age. Therefore, the wording of the questionnaires in some categories remained the same.

c. Hire personnel.

Personnel were hired on schedule and within the budgeted salary amount.

- d. Keep lists of potential patients.

Patients were identified from registrations of various services within each of the hospitals: Surgery, Radiation Therapy, Medical Oncology, Psychiatry, Nutrition and General Medicine.

Task 2. Months 2 – 24

- a. Identify and enroll patients.

As noted, by September of 1998, 185 patients had been enrolled. This was considerably less than half of the targeted accrual by Month 9 after accrual began and steps were taken to increase the self-referral patients, as noted in the body of this grant. That text is unchanged.

- b. Write annual report.

Annual report completed and now hereby revised.

Task 3. Months 8 – 45

- a. Mail out and receive back study calendars and other data instruments.

Questionnaires and menstrual calendars have been received on schedule for 6 month follow-up. At the time of September 1998, less than 10 patients had been followed for the 6 month figure and, therefore, results containing follow-up will be quoted in the October 1999 Annual Report.

- b. Enter data in ongoing fashion.

Such data has been entered in an ongoing fashion and such data is presented in the tables under Results in this section and this is unchanged.

- c. Cross-check data and clean.

This is ongoing and has proceeded according to plan.

- d. Write annual report.

October 1999 Annual Report is in progress.

See
Revision
Sept
99

RESULTS - STATEMENT OF WORK

The following time line was initially determined for the completion of this protocol.

Recruitment: January 1, 1998 - April 30, 1999
Follow-up: July 1, 1998 - April 30, 2001
Data Analyses: May 1, 2001 - October 20, 2001

Since we have been unable to reach the planned recruitment numbers, we have implemented several additional recruitment strategies as noted in the body of the report. Additionally, we will have an executive meeting in January 1999 to discuss the progress of the study and any possible revisions necessary, including an additional accrual period or decreasing the sample size of the study.

The charts below list the demographics of the 185 patients collected as of September 19, 1998.

	Sloan-Kettering		MD Anderson		Wake Forest	
MARITAL STATUS	N	%	N	%	N	%
Never Married	22	18.5%	2	4.5%	3	13.6%
Presently Married	84	70.6%	34	77.3%	17	77.3%
Marriage-like relationship	6	5.0%	2	4.5%	0	0.0%
Divorced/Separated	6	5.0%	6	13.6%	1	4.5%
Widowed	0	0.0%	0	0.0%	1	4.5%
No Response	1	0.8%	0	0.0%	0	0.0%

	Sloan-Kettering		MD Anderson		Wake Forest	
RACE	N	%	N	%	N	%
White (not Hispanic)	98	82.4%	32	72.7%	18	81.8%
Black/African American	8	6.7%	5	11.4%	4	18.2%
Hispanic	4	3.4%	3	6.8%	0	0.0%
Asian/Pacific Islander	8	6.7%	4	9.1%	0	0.0%
American Indian/Alaskan	1	0.8%	0	0.0%	0	0.0%

	Sloan-Kettering		MD Anderson		Wake Forest	
EDUCATION LEVEL	N	%	N	%	N	%
Some High School	2	1.7%	1	2.3%	1	4.5%
High School Diploma, GED	11	9.2%	6	13.6%	5	22.7%
Business/Vocational Training	2	1.7%	2	4.5%	3	13.6%
Some College	14	11.8%	8	18.2%	5	22.7%
Associate's Degree	9	7.6%	1	2.3%	0	0.0%
College Graduate, B.A., B.S.	33	27.7%	10	22.7%	3	13.6%
Some College or Prof. School	10	8.4%	8	18.2%	2	9.1%
Master's Degree	31	26.1%	8	18.2%	3	13.6%
Doctoral Degree	7	5.9%	0	0.0%	0	0.0%

	Sloan-Kettering		MD Anderson		Wake Forest	
OCCUPATION	N	%	N	%	N	%
Unemployed	37	31.1%	17	38.6%	6	27.3%
Professional/Technical	41	34.5%	17	38.6%	5	22.7%
Manager, Administrator	18	15.1%	2	4.5%	2	9.1%
Clerical	7	5.9%	3	6.8%	5	22.7%
Sales	6	5.0%	2	4.5%	0	0.0%
Service	0	0.0%	2	4.5%	0	0.0%
Skilled, Service Repair	1	0.8%	0	0.0%	1	4.5%
Laborer	0	0.0%	0	0.0%	1	4.5%
Farmer	1	0.8%	0	0.0%	0	0.0%
Other	8	6.7%	1	2.3%	2	9.1%

	Sloan-Kettering		MD Anderson		Wake Forest	
RELIGION	N	%	N	%	N	%
Catholic	59	49.6%	12	27.3%	2	9.1%
Jewish	22	18.5%	1	2.3%	0	0.0%
Protestant	23	19.3%	17	38.6%	18	81.8%
Muslim	1	0.8%	0	0.0%	0	0.0%
Russian Orthodox	1	0.8%	0	0.0%	0	0.0%
Other	5	4.2%	7	15.9%	1	4.5%
None	7	5.9%	7	15.9%	1	4.5%
No Response	1	0.8%	0	0.0%	0	0.0%

CONCLUSIONS

NONE

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Menstrual Cycle Maintenance and Quality of Life After Breast Cancer Treatment: A Prospective Study

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Appendix A



Jeanne A. Petrek, MD

Jane Smith
1 Smith Lane
Smithtown, NY 10000

Dear Ms. Smith,

Young women have asked many questions about the effects of treatment on their menstrual cycles. We physicians need more specific knowledge about treatment effects on the ovary. I am working on a research study for these answers.

Dr. Borgen, whom you saw at Memorial Hospital on 5/1/98, thought that you might be interested in hearing about this study and in the opportunity to participate. Enclosed is a brochure with additional information.

If you would like to learn more about this study, please call Joanna Winawer, our research coordinator, at 877-636-7562 (toll-free line). She will be happy to speak to you about my study.

Sincerely,

Jeanne A. Petrek, MD

Enc:

Appendix B

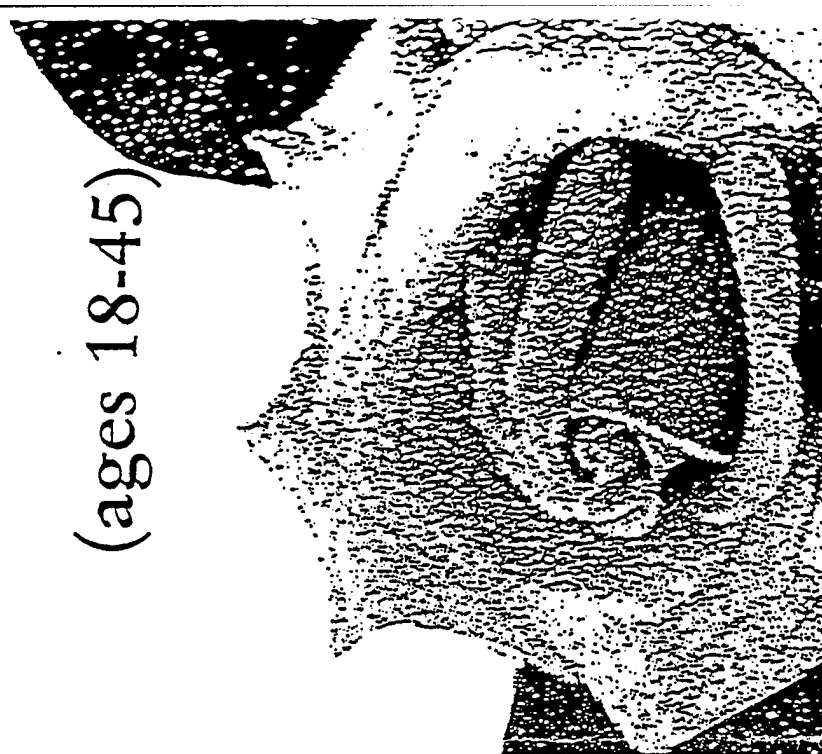
WANTED:

A

FEW GOOD

WOMEN

(ages 18-45)



The Menstrual Cycle Maintenance and
Quality of Life study is funded by the
Department of Defense.

Appendix C



Jeanne A. Petrek, MD

August 7, 1998

Roger Wilson, MD
Chairman,
Institutional Review Board
Memorial Hospital

Dear Dr. Wilson:

In order to increase patient accrual for protocol 97-127, Menstrual Cycle Maintenance and Quality of Life, we obtained a list of 683 women, from information systems, who were first seen at Memorial Hospital within the past 6 months with the diagnosis of breast cancer and are between the ages of 18 - 45. After looking over the pathology and the patient charts and excluding the patients who had recurrent breast cancer, only 78 were eligible. These 78 women were sent letters asking them if they would like to participate in this study. See attached letter which was used, as approved by the Institutional Review Board.

Only 21 out of the 78 women responded to the letter, and 11 out of these 21 wanted to participate and sent back the questionnaire, informed consent and medical release.

Therefore, we are requesting permission to send a letter which states that we will call them in a week to discuss the study in more detail. We anticipate approximately 9 - 10 women per month who will be eligible. Please see attached letter which we are requesting permission to use in the future.

Thank you.

Sincerely,

Jeanne A. Petrek, MD

Enc:
JAP/ba

29

*Memorial Sloan-Kettering Cancer Center
1275 York Avenue, New York, New York 10021
Telephone 212.639.8128 • FAX 212.794.5812
E-mail: petrekj@mskcc.org*

NCI-designated Comprehensive Cancer Center

Appendix D



Jeanne A. Petrek, MD

Jane Smith
1 Smith Lane
Smithtown, NY 10000

Dear Ms. Smith,

Young women have asked many questions about the effects of treatment on their menstrual cycles. We physicians need more specific knowledge about treatment effects on the ovary. I am working on a research study for these answers.

Dr. Borgen, whom you saw at Memorial Hospital on 5/1/98, thought you possibly might be interested in hearing about this study and in the opportunity to participate. Enclosed is a brochure with additional information.

Joanna Winawer, research coordinator, will call you the week of _____ to discuss the study with you. If there is any particular time that is most convenient for you, or phone number you would like to be called at during that week, please call toll free, (877) 636-7562 and leave a message, or e-mail: winawerj@mskcc.org. Thank you.

Sincerely,

Jeanne A. Petrek, M.D.

MENSTRUAL CYCLE MAINTENANCE & QUALITY OF LIFE

MEMORIAL SLOAN-KETTERING CANCER CENTER

WHAT IS THE PURPOSE OF THE STUDY ?

To determine how treatment for breast cancer may affect a woman's menstrual cycles and her quality of life. Questionnaires and menstrual cycle diaries are used.

IMPORTANT FACTS TO KNOW:

- Study information will be kept completely confidential.
- Informed consent will be obtained from all study participants.
- There are no medical or health risks in participating in this study.
- No blood or urine samples are collected.
- There is no cost for participation in this study.
- Participation will not affect your medical care.
- No in-person visits are necessary to participate in this study.
- Women who have participated in previous studies report their satisfaction at making a contribution to breast cancer research.

HOW DO I BECOME A PARTICIPANT ?

- Are you between the ages of 18-45?
- Have you been diagnosed with breast cancer, stage I, II, or III, in the past eight months?
- Were you having regular menstrual cycles at the time of your diagnosis?
- If you answered yes to these questions you are eligible to participate in this study.

HOW DO I PARTICIPATE?

- An initial questionnaire will be sent to all women, followed by additional questionnaires every six months.
- The initial questionnaire may take 45 minutes, and subsequent questionnaires will take 20-30 minutes.
- Every woman will be provided with menstrual cycle diaries, which they will fill out for the duration of the study.

How & When will I receive follow-up questionnaires & calendars ?

- All follow-up questionnaires will be sent to you from the Wake Forest University School of Medicine for 3 years—the duration of the study.
- Every six months, from original date of enrollment, you will be sent a new questionnaire, and every 3 months you will be sent new menstrual diaries.

Who is involved in this study ?

- Memorial Sloan-Kettering Cancer Center in New York is conducting the study. The Wake Forest University School of Medicine in Winston-Salem, North Carolina, one of the largest centers in menopause research, is analyzing the data.
- A total of 800 women will participate in this study.



Appendix F

**Cancer and Treatment
Information**

THE BEST CANCER CARE. ANYWHERE.

A Study of Breast Cancer and It's Effect on Premature Menopause and Quality of Life

Memorial Sloan-Kettering Cancer Center and the Wake Forest University School of Medicine in Winston-Salem, North Carolina, are initiating a study of how breast cancer may affect women's menstrual cycles and their quality of life. A total of 800 women are needed to participate in the study, which involves the use of questionnaires and menstrual-cycle diaries.

Participation Eligibility

To participate in this study, you must:

- Be between the ages of 18 and 45
- Have been diagnosed with stage I, II, or III breast cancer in the past 8 months
- Have had regular menstrual cycles at the time of diagnosis

How to participate

An initial questionnaire will be sent to all study participants, followed by additional questionnaires every six months. The initial questionnaire will take about 45 minutes to complete. Subsequent questionnaires will take 20 to 30 minutes. Every woman in the study will be provided with menstrual-cycle diaries, which they will fill out for the duration of the study.

The follow-up questionnaires will be sent from the Wake Forest University School of Medicine every six months for the full three-year duration of the study. Participants will receive a new menstrual-cycle diary every three months.

Other important facts about the study

- No in-person visits are necessary to participate in this study.
- Study information will be kept completely confidential.
- Informed consent will be obtained from all participants.
- There are no medical or health risks associated with participating in this study.
- No blood or urine samples will be collected.
- There is no cost for participation in this study.
- Participation will not affect your medical care.
- Women who have participated in previous studies report their satisfaction at having made a contribution to breast-cancer research

If you would like to learn more about this study, please contact Joanna Winawer, research study coordinator at Memorial Sloan-Kettering Cancer Center, by e-mail at winawerj@mskcc.org, or call toll free: (877) 636-7562.

Appendix G



Jeanne A. Petrek, MD

Jane Smith, M.D.
1 Smith Lane
Smithtown, NY 10000

Dear Dr. Smith;

Enclosed is a brochure made for accruing young breast cancer patients to a study on the relationship between breast cancer treatment and premature menopause.

Thus far there has not been a prospective study of the determinants of ovarian failure as a result of breast cancer treatment and the effect of menopausal symptoms on the quality of life. Wake Forest University is the coordinating center since they fulfill the same role in the Women's Health Intervention (WHI) research project with 100,000 study subjects of normal women going through menopause at the natural age.

The study is conducted entirely by phone and mail and consists only of menstrual cycle bleeding diaries and questionnaires on the quality of life.

I invite you to give this brochure to any patients you wish. Women less than 45 years old with Stage I, II, or III breast cancer diagnosed within the last eight months are eligible.

Sincerely,

Jeanne A. Petrek, M.D.

Appendix H



Jeanne A. Petrek, MD

Jane Smith, M.D.
1 Smith Lane
Smithtown, NY 10000

Dear Dr. Smith;

Enclosed is a brochure which offers a research study to young breast cancer patients. The brochure was made to introduce this study on the relationship between breast cancer treatment and premature menopause.

The study is conducted entirely by phone and mail and consists only of menstrual cycle bleeding diaries and questionnaires on the quality of life.

Thus far there has not been a prospective study of the determinants of ovarian failure as a result of breast cancer treatment and the effect of menopausal symptoms on the quality of life. Wake Forest University is the coordinating center for this project since they fulfill the same role in the Women's Health Intervention (WHI) research project with 100,000 study subjects of normal women going through menopause at the natural age.

I invite you to give this brochure to any patients you wish. Women less than 45 years old with Stage I, II, or III breast cancer diagnosed within the last eight months are eligible.

Sincerely,

Jeanne A. Petrek, M.D.

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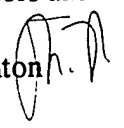
Appendix I
Revised October 1998 Annual Report
DAMD 17-96-1-6292
J. Petrek

Memorial Sloan-Kettering Cancer Center
1275 York Avenue, New York, New York 10021

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The Bowman Gray
School of Medicine

Department of Public Health Sciences
Section on Social Sciences and Health Policy

Date: December 18, 1997
To: DOD Investigators and Staff
From: Michelle Naughton 
Re: Revisions to the MOP and Questionnaires

Enclosed are copies of the revised chapters of the MOP and study forms. I have also enclosed summary sheets that highlight the major changes that were made to these items. You may find it helpful to refer to these summaries when reviewing these materials. Please place these new chapters and forms in your binders, and discard the older versions.

In general, we tried to accommodate all the suggestions for additions and deletions that were discussed at the training session. Some of the questionnaires we are using, however, are standard forms, and we are not able to change specific items. Please look through the questionnaires and let us know immediately if you notice any problems with them.

Clinic coordinators (Susanne Binkley, Janet Stough, and Kathy Tran) were also sent "non-hole punched" copies of the questionnaires and other study forms that are to be used to make copies until the questionnaire booklets are available for use. Copies of the bleeding diaries will also be sent to these individuals before December 23rd. The diaries will not need to be copied. Julia is going to laser print enough forms for each clinic to get you all started.

If the clinical centers could please identify the specific clinics and/or hospitals from which patients will be recruited, it would be helpful. We would like to begin assigning clinic codes to each of the three sites. (Remember, you need to enter the clinic code as part of the participant ID number.) This information should be given to Judy Bahnson.

I will be out of the office until December 30th. If you have any questions in the interim, please call either Judy Bahnson or Kathy Dotson.

We enjoyed meeting you all last week. I hope you all have a happy holiday season!

SUMMARY OF CHANGES TO MANUAL OF PROCEDURES

December 15, 1997

Chapter 1:

Added sections: 1.5 Funding Source
 1. 7 Paper Proposals

Updated section: 1.6 Phone numbers and addresses, etc., have been updated

Chapter 2:

Minor editing.

Inclusion criteria: Have been updated to include:

5. Receiving one form of treatment (i.e., medical, surgical, and/or radiation)
6. Must have had regular menstrual cycles (i.e., every 4-5 weeks) at the time of their breast cancer diagnosis.
7. Must not be pregnant.

Chapter 3:

* Section 3.3: Inclusion criteria have been revised to include:

5. Receiving one form of treatment (i.e., medical, surgical, and/or radiation)
6. Must have had regular menstrual cycles (i.e., every 4-5 weeks) at the time of their breast cancer diagnosis.
7. Must not be pregnant.

* An example of the recruitment report to be mailed monthly to each clinical center has been included.

Chapter 4:

Minor editing.

Chapter 5:

Deletion: Section on measuring height and weight.

Section 5.3.2: Listing of the baseline questionnaires has been revised to reflect each separate form. (Previously, the quality of life forms/scales were listed under health-related quality of life regardless of whether they were “officially” in the quality of life questionnaire.)

Revised: Checklist for Clinical Center Staff
Checklist of what participants take home.
Participant Information Sheet
Schedule of 6 Month Follow-up Contacts

Chapter 6:

Minor editing.

Chapter 7:

This chapter has been revised to reflect the division of the chart review form into the baseline chart review assessment and the 1 year chart review assessment. Instructions are only included for the revised baseline chart review form.

Chapter 8:

Minor editing.

- Revisions: 1) The order of the questions on the Quality of Life Form has been changed. The sleep items now appear before the spirituality and depression questions.
- 2) Medications have been included under Part IV of the Medical and Reproductive History Form.

Chapter 9:

This chapter has been revised to exclude the use of check marks as an option for the completion of the diaries/calendars.

Also, the instruction sheet for the participants now excludes the instructions for how to fill in the top boxes with their ID numbers and acrostics, because the clinic staff will be completing these fields. The instructions for the correct way to write numbers and letters, however, has been left in the manual for the clinic staff persons.

Chapter 10:

Minor editing.

Section 10.1: Listing of the follow-up questionnaires has been revised to reflect each separate form. (Previously, the quality of life forms/scales were listed under health-related quality of life regardless of whether they were “officially” in the quality of life questionnaire.)

Chapter 11:

Minor editing.

Chapter 12:

Minor editing.

CHAPTER 1

ORGANIZATIONAL STRUCTURE

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1.1 INTRODUCTION

This manual will serve as your guide to the conduct of the study entitled: Menstrual Cycle Maintenance and Quality of Life After Breast Cancer Treatment: A Prospective Study. The following chapters will provide crucial information regarding study procedures and follow-up.

1.2 CHANGES IN THE MANUAL OF PROCEDURES

The DOD Manual of Procedures (MOP) will be updated throughout the study to reflect suggestions from clinical center staff and investigators, changes in the protocol or procedures, changes in the study organization or administration, and omissions in earlier versions. The clinical coordinating center will keep copies of all sequential MOPs. The clinical centers are expected to keep copies of the current version of the MOP.

When changes are made to the MOP, the clinical coordinating center will circulate copies of all pages affected by the changes. The clinical centers will be required to insert these updated pages in their MOPs, and may discard earlier versions of these pages. Each page of the MOP will include a version date. Only the most recent version should be included in the clinical center MOP.

1.3 STUDY ORGANIZATION

The organizational structure of this study includes the following components: the Clinical Centers (CC) and the Clinical Coordinating Center (CCC).

1.3.1 Clinical Centers. Three clinical centers are participating in the current protocol:

Memorial Sloan-Kettering Cancer Center, (Jeanne Petrek, M.D., Principal Investigator)
M.D. Anderson Cancer Center, (Eva Singletary, M.D., Principal Investigator)
Wake Forest University School of Medicine, (Electra Paskett, Ph.D., Principal Investigator)

Each clinical center is composed of an inter-disciplinary team of clinical investigators and staff who provide the areas of expertise necessary for the successful completion of the study. The responsibilities of the clinical center staff and investigators include:

1. Identifying and recruiting eligible participants for the study.
2. Completing medical record chart reviews regarding breast cancer diagnosis and treatment, and comorbidities.
3. Collecting high quality data in accordance with the study protocol.
4. Collaborating in the analysis and dissemination of study results.

1.3.2 Clinical Coordinating Center. The clinical coordinating center for the current study will be located at the Wake Forest University School of Medicine, Department of Public Health Sciences, (Michelle Naughton, Ph.D., Principal Investigator).

The clinical coordinating center has the primary responsibility for collecting the follow-up data, monitoring the quality of all data collected, managing the study data, and analyzing data generated by the clinical centers. Additional responsibilities of the CCC include:

1. Preparing (with the aid of the clinical center investigators and staff) the protocol, forms, and Manual of Operations.
2. Working with the investigators in the development and pre-testing of forms and procedures, and assuming responsibility for the reproduction and distribution of forms.
3. Training study coordinators, data coordinators and other clinical center personnel.
4. Managing quality control aspects associated with the collection and management of the study data.
5. Monitoring clinical center performance through the use of summary data reports generated by the CCC (i.e., participant recruitment reports; quality control checks of collected data).
6. Developing the statistical analysis plan for the study data.
7. Monitoring follow-up activities, and monitoring quality control of follow-up data collected by the CCC staff.
8. Preparing, in collaboration with the clinical investigators, various manuscripts of the study results.

1.4 ORGANIZATION OF THE CLINICAL COORDINATING CENTER

The Clinical Coordinating Center (CCC) is organized to coordinate the tasks of the multicenter study. The Principal Investigator is directly responsible for all facets of the study, and works closely with coordinating center staff to complete study tasks. The Project Manager oversees the day-to-day management of the research project, and serves as the point of contact for staff within the coordinating center and staff at each of the clinical centers. Data programming, management and analyses are completed under the direction of Dr. Claudine Legault.

Study Leadership:	Michelle Naughton, Ph.D., Principal Investigator Sally Shumaker, Ph.D., Co-Principal Investigator
Study Coordination:	Judy Bahnson, M.S., Project Manager Kathy Dotson, Assistant Project Manager
Data Management/ Analysis:	Claudine Legault, Ph.D., Co-Investigator, (Data Core Leader) Julia Robertson, Programmer Stacey Slone, M.S., Statistician TBN, Data Entry

Regular meetings of all investigators and staff are held routinely at the Clinical Coordinating Center. The agenda for each meeting includes progress reports of study tasks, as well as discussions of current problems and solutions.

1.5 FUNDING SOURCE

This study is funded by a U.S. Army Medical Research and Material Command (Breast Cancer Research Program A) Grant awarded to Dr. Jeanne Petrek at the Memorial Sloan-Kettering Cancer Center in New York City, New York. The clinical coordinating center at the WFUSM, the clinical center at the WFUSM, and the clinical center at the M.D. Anderson Cancer Center are funded through subcontracts from the Memorial Sloan-Kettering Cancer Center.

1.6 STUDY-WIDE MEETINGS AND DISTRIBUTION OF MINUTES

Conference calls will be held periodically between staff and investigators at all three clinical centers and the coordinating center. In those instances, it will be the responsibility of the coordinating center to compile and distribute the minutes of these calls to all participating individuals. Minutes will be circulated no later than one month after the date of the call. The coordinating center will maintain a master archive of minutes from all conference calls and meetings.

Currently, quarterly study-wide conference calls are held between the Principal Investigators of the three clinical centers and their key staff, and the investigators and staff at the clinical coordinating center. In addition, one face-to-face meeting is planned per year of all investigators and key staff.

1.7 PAPER PROPOSALS

On the quarterly conference calls, proposals for papers to be written from the study data will be discussed. Investigators/staff are requested to submit a brief, written abstract of the proposed paper to the coordinating center at least one week prior to each conference call. Each abstract must contain: the research questions and/or primary hypotheses to be examined, a brief review of previous literature indicating the importance of the topic, and the methodology and analyses to be used. The abstracts will be distributed by the coordinating center to all study investigators and key staff prior to the conference calls. Staff persons interested in submitting an abstract using the study data must consult with their principal investigator prior to submitting an abstract to the coordinating center.

1.8 STUDY PERSONNEL

Names, addresses, and telephone numbers of study personnel at all three clinical centers and the coordinating center are listed on the following pages. These lists will be updated periodically by the clinical coordinating center.

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CHAPTER 2

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MENSTRUAL CYCLE MAINTENANCE AND QUALITY OF LIFE AFTER BREAST CANCER TREATMENT: A PROSPECTIVE STUDY

PROTOCOL

1. Background of the Study

About 15% of the 200,000 estimated new cases of intraductal and invasive breast cancer this year will occur in women of childbearing age and the majority will be long-term survivors. Most young women with invasive breast cancer will undergo adjuvant chemotherapy and almost half will suffer chemotherapy-related amenorrhea (TRA). Foregoing motherhood either for iatrogenic infertility or for concern about its safety can be very distressing. However, even without desires for childbearing, the health-related quality of life of these young patients may be compromised by premature menopause with symptoms such as hot flashes, sleep disturbances, decreased libido, and vaginal dryness.

Very little is known about the incidence, onset, time course, and symptomatology of premature menopause induced by breast cancer therapy, or the impact on the young survivor's quality of life. No prospective studies exist. Since improved survival following chemotherapy in recent years appears to be independent of menopausal status, TRA should be evaluated in a risk/benefit assessment.

To date, the prevalence of TRA has been derived from adverse event reports of patient survival following various adjuvant therapy regimens. Age and dose of chemotherapy agent, particularly cyclophosphamide, are clearly important risk factors to investigate, as well as other factors known or suspected to be associated with iatrogenic menopause or natural menopause. These factors include other chemohormonal agents, the duration of treatment, agent combination, intercurrent illness episodes, smoking history, familial age at menopause, parity, socioeconomic class, and body mass index.

For those women who maintain their ovarian function, subsequent pregnancy is often desired. All reports to date find that pregnancy after breast cancer treatment does not decrease patient survival. However, there are no prospective studies. Data from small retrospective studies contain multiple biases and report on less than a total of 1,000 patients over the past 50 years. When compared to other issues dealing with disease-free survival, such as adjuvant chemotherapy for patients with negative nodes, the effect of subsequent pregnancy is a neglected issue.

The purpose of this study is to identify determinants of TRA in a prospective cohort of premenopausal women diagnosed and treated for breast cancer. Data, such as an individual risk profile of premature menopause, could be critical to the clinician and the young patient in decision-making about specific therapies. A parallel goal of the proposed study is the creation of a database to track patients' disease-free and overall survival in relation to subsequent pregnancy.

following treatment for breast cancer, for which additional funding will be obtained. Nevertheless, survivor follow up will continue without funding through the tumor registry and other standard procedures at the participating institutions.

1.a. Background of research in systemic chemotherapy-related amenorrhea. There are two likely reasons for the meager analysis of TRA. In the past, menopause induction itself in adjuvant chemotherapy programs was thought to increase survival from breast cancer; and secondly, the occurrence of menopause, a natural phenomenon in every woman's later life, was deemed not so important. However, a 1994 review of previous adjuvant trials concluded that the benefit of chemotherapy in the premenopausal patient is not dependent upon menopause induction.⁽²⁾ This was confirmed by the 20-year results of a Milan study.⁽³⁾ The extent of the scanty scientific data on systemic therapy-induced menopause is noted in that review entitled "Amenorrhea following chemotherapy for breast cancer: Effect of disease-free survival".⁽²⁾ Forty key trials which included premenopausal patients on adjuvant chemotherapy (i.e., no evidence of metastatic disease) were examined. Only 15 papers reported incidence of amenorrhea.

The examination of TRA is also compelling due to the extensive research being conducted currently on natural menopause and its impact on chronic diseases and health-related quality of life.⁽⁴⁾

1.a.1. Acknowledged factors in menopause induction. Two factors consistently found in menopause induction are age and drug/dose. The category of drugs most likely to induce ovarian failure is alkylating agents, such as cyclophosphamide, the most common drug in breast cancer treatment, while antimetabolites have a lesser effect.⁽⁵⁾ One study found that amenorrhea in similar age women occurred in 63% treated with CMF (cyclophosphamide, methotrexate and 5-fluorouracil) versus 70% with cyclophosphamide alone. Indirectly, this result showed little effect on ovarian function for the two antimetabolite agents.⁽⁶⁾ In a study of 18 premenopausal patients, amenorrhea occurred after a mean cyclophosphamide total dose of 9.3 gr in women younger than 40, and after a mean dose of 5.2 gr in women older than 40.⁽⁷⁾

Of the non-alkylating agents, doxorubicin is the most common in breast cancer therapy. In a study of 128 patients less than 35 years old treated with the drug in combination with cyclophosphamide and 5-fluorouracil, 58% had regular menstrual cycles after chemotherapy, 32% experienced temporary amenorrhea and 9% permanent amenorrhea.⁽⁸⁾ The potential for amenorrhea with other categories of antineoplastic agents has not been studied extensively. For new drugs, such as taxol⁽⁹⁾ or vinorelbine⁽¹⁰⁾, no data are available; amenorrhea is not even mentioned in two recent reviews. In addition, specific aspects of chemotherapy have not been considered such as the modern use of cytokines and the role of serious intercurrent illnesses, e.g., hospitalization for neutropenia.

There are little data regarding ovarian failure as a result of tamoxifen alone since the practice is rare. Tamoxifen may be prescribed to premenopausal patients if estrogen receptors are found on their tumors. The mechanism for tamoxifen-induced amenorrhea, which has been reported, is not known.⁽¹¹⁾ In premenopausal women on Tamoxifen, estrogen levels are frequently elevated and the normal feedback could be lost,⁽¹²⁾ causing amenorrhea.

1.a.2. Limitations of retrospective studies on menstrual cycle maintenance. Limitations of retrospective studies include various definitions of temporary/permanent amenorrhea, variable lengths of follow up on menses or no follow up after chemotherapy administration, and retrospective data collection. Most importantly, the study designs in these reports are focused on the analysis of disease-free survival and overall survival in a typical double or triple arm therapy protocol. Therefore, data on amenorrhea, a non-life threatening complication, are understandably relegated to a secondary analysis. Such data are weaker than those obtained in a study designed and conducted to assess amenorrhea as a primary endpoint.

Two broad categories of age are also reported typically -- less than 40 years and greater than 40 years. In one study⁽¹⁴⁾ of 221 patients, the category of patients over 40 years is subdivided into greater or less than 45 years. It is clear that menopause varies greatly by age regardless of the particular regimen.⁽²⁾ Nevertheless, beyond stating that 38% of women aged 39 years or less have permanent amenorrhea after 12 months of CMF,⁽¹⁵⁾ there is no characterization of who did or did not undergo permanent menopause.

1.a.3. Unstudied factors associated with age of natural menopause. In spite of these limitations, the most important factors causing the wide range of TRA within a particular age group and chemotherapy regimen, may be factors that influence age at natural menopause. These have never been assessed in a breast cancer population or any cancer population.

In multivariate analyses of longitudinal study population,⁽⁵⁾ factors influencing the age of natural menopause include smoking history,^(16, 17) parity,^(17, 18) body mass index,^(16, 17, 18, 19) history of irregular periods before age 25 or first birth,⁽¹⁸⁾ and socioeconomic status, education, and income.^(17, 18, 19) These factors could be responsible for one 35 year old breast cancer patient becoming permanently menopausal, while another woman of the same age maintains normal menses. It suggests that ovarian failure is not a random phenomenon and that a comprehensive analysis, as is proposed, will shed light on the determinants of therapy-induced menopause.

1.b. Health related quality of life in the breast cancer survivor. Recent years have witnessed a growing recognition among cancer researchers of the importance of systematically measuring health-related quality of life (HRQL) and psychosocial factors, both to characterize the health status and well-being of this patient population, as well as to assess treatment efficacy.^(20, 21, 22, 23) The frequent morbidity associated with most cancers and their treatments make the measurement of HRQL and psychosocial variables critical components in determining health outcomes.

Common psychological responses of patients with breast cancer include anxiety, depression, anger, guilt and fear.^(24, 25, 26, 27) Additionally, young breast cancer patients face the possible impact of specific chemotherapy agents on ovarian function. Those women may experience such symptoms as changes in mood and emotional affect, hot flushes, vaginal dryness, and sleep disturbances. For those women who were desirous of becoming pregnant following treatment, TRA may be most distressing, especially for those childless women who had delayed childbearing.

In the past 10 years, significant progress has been made in the reliable and valid assessment

of health related quality of life (HRQL) and other psychosocial variables.^(27, 28, 29, 30) Although there has been some debate regarding the definition of HRQL, a recent international conference reached agreement on the fundamental dimensions essential to any HRQL assessment.⁽³¹⁾ These include physical functioning, psychological functioning, social functioning and role activities, and the individual's overall life satisfaction and perception of their health. For specific interventions, other dimensions of HRQL may be important to assess, such as sleep disturbance, pain, symptoms, and intimacy and sexual functioning.

Data suggest that quality of life and psychosocial factors (e.g., emotions, family relations) are rated by patients as more important to their well-being than clinical factors directly related to the effects of the disease and its treatment, further underscoring the importance of measuring HRQL in clinical research in breast cancer.⁽³²⁾ To date, the potential multiple outcomes of breast cancer treatment in young women have not been investigated. These include morbidity and mortality, menopausal symptoms, and the psychological impact of premature menopause and the loss of childbearing potential.

Results from this study regarding the impact of TRA on women's health-related quality of life may assist with treatment decisions regarding hormone replacement therapy for breast cancer survivors.⁽³³⁾ For example, if the proposed study shows no decrease in health-related quality of life due to TRA itself, then recommendations of hormone replacement for breast cancer survivors will be considered more for prevention of the long-term sequelae of osteoporosis and heart disease and less for "making the patient feel better."

1.c. Menstrual cycle maintenance: Fertility and pregnancy outcome after systemic therapy. The assisted reproductive methods for the inception and maintenance of pregnancy have been described in the literature for older women with natural menopause.⁽³⁴⁾ However, it is very unlikely that the breast cancer patient will undergo the oral and systemic high-dose hyperstimulation required for this procedure. In those breast cancer patients who maintain menstrual cycles after systemic therapy, general figures on fertility are unknown.^(35, 36) In a retrospective cohort study of 2,283 adolescent survivors of all cancers from 1945 to 1975, relative fertility (healthy siblings were controls) was decreased and varied with the type of cancer and treatment administered (e.g., chemotherapy and/or radiotherapy).⁽³⁷⁾

Even though apparently normal menstrual cycling may be maintained after systemic therapy and the patient chooses to become pregnant, the incidence of pregnancy and successful childbearing is unknown. The above studies on adolescent cancer populations may indicate subtle and unmeasured defects in fertility in spite of maintained menstrual cycles.

The potential of breast cancer chemotherapy to impact adversely on subsequent pregnancies has not been evaluated specifically. However, one study reported on 58 pregnancies occurring after treatment for various malignancies and found no excess of congenital anomalies. The study noted a total of 40% abnormal pregnancies, with most of these occurring in the first year after chemotherapy. The abnormal pregnancies consisted mainly of premature termination and low birth weight, both of which were attributed to dysfunction of the uterine hormonal gestational milieu.⁽³⁸⁾

1.c.1. Subsequent pregnancy after breast cancer treatment has not been reported to adversely effect survival. The limited data on survival after subsequent pregnancy in breast cancer patients is derived from retrospective studies, some of which employ case-control methodology in the attempt to eliminate the obvious bias of pregnancy occurring in those with better prognosis. It has been consistently observed, as noted in recent reviews, that breast cancer patients who subsequently become pregnant have a good survival rate, often the same or better than patients with no subsequent pregnancy.^(39,40) The results of several studies led their authors to suggest that subsequent pregnancy may be beneficial to overall prognosis.^(41, 42, 43) Several investigators believed these findings could be due either to careful self-selection of women with less aggressive tumors becoming pregnant or pregnancy potentially providing a tumor-suppressing effect.^(42, 43, 44)

The importance of the endogenous hormonal milieu as a determinant of patient survival has been recognized for the past century after Beatson published the results of bilateral oophorectomy for metastatic breast cancer in the Lancet.⁽⁴⁵⁾ One might surmise that the effect of such a profound hormonal event as pregnancy would have been studied carefully.

1.c.2. Limitations on the reporting of subsequent pregnancy. An extensive review⁽⁴⁰⁾ published in 1991, found only 565 patients across 10 studies since 1940 where the patients' disease stage was known. Among these women, the mean survival at 5 years after pregnancy was 71.5% with a range from 52% to 78.5%. These estimates are similar to published overall breast cancer survival data. Seven of these ten studies occurred in the past fifteen years. The Memorial Sloan Kettering Cancer Center reported an 80% five year survival rate for 41 Stage I and II patients⁽⁴⁶⁾ after subsequent pregnancy. In a 1986 nationwide French study, the 10-year survival rate of 68 patients of any stage with subsequent pregnancy was 71%. The survival of the negative-node patients was 90% at 10 years with no difference between cases and controls.⁽⁴⁷⁾ In addition, a 1989 study reported that subsequent pregnancies did not affect overall prognosis in a large private practice experience.⁽⁴⁸⁾ In the largest study, 136 Canadian patients⁽⁴¹⁾ with Stages I-III were reported to have a 71% 5-year survival rate.

The major drawback of these studies is the retrospective and unsystematic method of obtaining patients with subsequent pregnancy. For example, in the series from Memorial Sloan-Kettering Cancer Center, 41 Stage I and II patients were found over 30 years who had become pregnant after breast cancer treatment.⁽⁴⁶⁾ The patients were compiled by asking clinicians to name the patients in their practices with subsequent pregnancies. However, 6,000 patients younger than age 40 without initial oophorectomy were found in those 30 years in the Memorial Hospital Tumor Registry, and assuming even a small percentage became pregnant, this study could have reported on a much larger number of patients with subsequent pregnancy.⁽³⁹⁾ These same methodological problems occurred in several of the other retrospective studies as well.

In the past year Swedish⁽⁴⁹⁾ and Finnish population-based studies⁽⁵⁰⁾ have been published. A 1995 Swedish study⁽⁴⁹⁾ found excellent survival in 50 women with subsequent pregnancies (30 normal deliveries) from a cohort of 2,119 breast cancer patients less than age 50 followed from 1 to 19 years. The Finnish study⁽⁵⁰⁾ linked the computer records of the tumor registry and birth certificates. Cases with subsequent pregnancy(ies) survived better than controls with no subsequent pregnancies,

although the Finnish authors subtitle their study "a healthy mother effect," since the tumor registry matching may have introduced bias.

1.c.3. The theoretical concern of subsequent pregnancy is the breast cancer survivor. The safety of subsequent pregnancy after breast cancer treatment is now accepted as dogma on the basis of this limited reporting. In recent textbooks of obstetrics and gynecology, and breast cancer, subsequent pregnancy is designated as safe.^(51,52, 53, 54)

Does a good survival rate in these studies indicate the safety of subsequent pregnancy after breast cancer? Ongoing concern is justified, considering the long-term exposure to intense gestational hormones in the presence of established breast cancer with possible micro metastases. In the production of hormone-sensitive mammary tumors following dimethylbenzanthracene (DMBA), pregnancy enhances both the induction and growth of such tumors.⁽⁵⁵⁾ Whether the disproportionately high rise of estriol during pregnancy, a relatively weak estrogen, and possibly an antagonist of estrone and estradiol, confers some measure of protection has been questioned.^(56, 57) The effect (beneficial, detrimental, or indeterminate) of subsequent pregnancy on breast cancer prognosis is uncertain due to the lack of prospective data.

2. Study Objectives

The DOD Breast Cancer Study is a prospective study which will enroll and follow 800 female breast cancer patients aged 45 years and younger. Participants will be enrolled at three clinical centers: Memorial Sloan-Kettering Cancer Center(MSK), M.D. Anderson Cancer Center (MDA), and the Bowman Gray School of Medicine (WFUSM).

The study will examine the effect of treatment for breast cancer on menstrual cycle maintenance and health-related quality of life. This study will also include the creation of a database to track subsequent pregnancies and their effect on patients' morbidity and mortality. Data on menstrual cycle maintenance, health-related quality of life and some short term data on the effects of post-treatment pregnancies will be obtained during the study period. Extensive follow-up to examine pregnancy and disease-free survival, however, will be beyond the limits of this study. Additional funding will be sought to continue to follow this cohort of women. However, even without additional funding, survival data will continue to be collected though the interest of the participating investigators and their tumor registries.

The following primary and secondary study objectives have been formulated.

2.a. Primary Study Objectives.

1) To describe the menstrual bleeding patterns of female breast cancer patients aged 45 years and younger, including those without systemic therapy, in terms of frequency of bleeding, duration of each bleeding episode, and amount (i.e., light, medium, heavy).

2) To compare the incidence of chemotherapy related amenorrhea (TRA) (i.e., no menstrual bleeding for $\geq$ six months within three months of stopping treatment), in breast cancer patients by treatment group (i.e., cyclophosphamide versus tamoxifen, cyclophosphamide alone versus cyclophosphamide and tamoxifen, or tamoxifen alone versus cyclophosphamide and tamoxifen).

3) To compare the health-related quality of life of women undergoing chemotherapy who experience amenorrhea with those who do not have amenorrhea. We hypothesize that the HRQL of women who experience amenorrhea will be lower than for women who retain menstrual cycling, regardless of the type of chemotherapy regimen completed. Specifically, women with amenorrhea will have lower overall health-related quality of life, as measured by the total score on the FACT-B, the primary HRQL assessment instrument.

2.b. Secondary Objectives

1) To examine possible predictors of TRA, including smoking, age, race, stage of cancer, and treatment modality.

2) To describe comprehensively the quality of life and psychosocial status of young women with breast cancer receiving any form of therapy (chemotherapy, radiation, surgery or a combination). Specifically, we will examine the participants' overall health-related quality of life, their physical symptoms and sleep quality, their depressive symptomatology, sexual functioning (i.e., arousability and satisfaction), their self-concept, and levels of social support and spirituality.

2.c. Operational Objectives

1) To recruit, and follow for a minimum of 24 months and a maximum of 3 years a total of 800 participants, across three clinical centers, who meet a specific set of inclusion/exclusion criteria.

2) To maintain levels of adherence and retention at 80% or greater in order to attain study goals.

3) To ensure the collection of high quality data through careful monitoring of all data collection procedures.

3. Methods

3.a. Study Population. A total of 800 breast cancer patients will be enrolled in the study from three clinical centers: Memorial Sloan Kettering, M.D. Anderson Cancer Center, and the Wake Forest University Gray School of Medicine. The study population is defined by the following inclusion and exclusion criteria:

3.a.1. Inclusion Criteria:

1. Must be female.
2. Between the ages of 18 and 45 years at the baseline visit.
3. Community dwelling as opposed to living in a residential care or a correctional facility.
4. Be diagnosed with invasive breast cancer Stage I, II, III within the previous **eight months**.
5. Receiving one form of treatment (i.e., medical, surgical, and/or radiation) at the clinical center or one of its affiliates..
6. Must have had regular menstrual cycles (i.e., every 4-5 weeks) at the time of the breast cancer diagnosis. Women who have had a hysterectomy will be excluded from participation.
7. Must not be pregnant.
8. Have physician agreement for patient participation.
9. Provide informed consent.

3.a.2. Exclusion Criteria:

Any of the following will exclude the participant:

1. No menstrual cycles. The presence of regular menstrual cycles will be considered as the surrogate of ovarian function. Therefore all participants must be pre-menopausal at time of diagnosis. Women who have been rendered sterile such as by tubal ligation or women with any previous pelvic surgery, other than a hysterectomy, will be eligible as long as regular menstrual cycling is present at breast cancer diagnosis.
2. Psychiatric or psychologic abnormality precluding the informed consent process or which would impact on compliance.
3. Previous or another concurrent malignancy (excepting basal and squamous skin cancer and stage 0 cervical cancer).
4. Stage IV breast malignancy.
5. Inability to read and understand English.
6. No telephone in the home.
7. Resident outside of the United States.

3.a.1. Inclusion Criteria:

1. Must be female.
2. Between the ages of 18 and 45 years at the baseline visit.
3. Community dwelling as opposed to living in a residential care or a correctional facility.
4. Be diagnosed with invasive breast cancer Stage I, II, III within the previous six months.
5. Receiving one form of treatment (i.e., medical, surgical, and/or radiation) at the clinical center or one of its affiliates..
6. Must have had regular menstrual cycles (i.e., every 4-5 weeks) at the time of the breast cancer diagnosis. Women who have had a hysterectomy will be excluded from participation.
7. Must not be pregnant.
8. Have physician agreement for patient participation.
9. Provide informed consent.

3.a.2. Exclusion Criteria:

Any of the following will exclude the participant:

1. No menstrual cycles. The presence of regular menstrual cycles will be considered as the surrogate of ovarian function. Therefore all participants must be pre-menopausal at time of diagnosis. Women who have been rendered sterile such as by tubal ligation or women with any previous pelvic surgery, other than a hysterectomy, will be eligible as long as regular menstrual cycling is present at breast cancer diagnosis.
2. Psychiatric or psychologic abnormality precluding the informed consent process or which would impact on compliance.
3. Previous or another concurrent malignancy (excepting basal and squamous skin cancer and stage 0 cervical cancer).
4. Stage IV breast malignancy.
5. Inability to read and understand English.
6. No telephone in the home.
7. Resident outside of the United States.

3.b. Recruitment

A total of 800 women will be recruited from three clinical centers:

Wake Forest University School of Medicine	188
M.D. Anderson Cancer Center	252
Sloan-Kettering Cancer Center	360

Local sources of patients have been identified by the participating investigators. One or more of the following strategies will be utilized in recruiting participants into the study at each clinical center:

1. Patient Identification Through Tumor and Surgical Registries. The majority of patients will be identified through tumor and/or surgical registries at the participating institutions. Once women with stage 1-3 breast cancer have been identified, the patients' oncologists/surgeons will be contacted by clinic staff to obtain approval to approach the patient. If the physician approves, the patient will be approached at the clinic site, (if she is scheduled for a follow-up or treatment visit), or the patient will be sent a letter describing the purpose of the study, which will be followed by a telephone call. The clinic staff person will screen the person to ensure she meets the eligibility criteria, and then will ask the patient to participate in the study if she is eligible. The patient will be scheduled for the baseline study clinic visit at which time she will sign the informed consent form, a medical record release, and will complete all baseline study questionnaires. The patients' physicians will be notified as to whether the patient has enrolled in the study.

2. Referral Through Physicians. Participants will also be identified by the clinical center's participating investigators, oncologists, surgeons, and radiologists. In most instances, these physicians will have already explained the study to the participant, and the clinic staff will contact the patient to invite her to participate in the study. The patient will be screened to ensure that she meets all eligibility criteria. If the patient is eligible and willing to participate, she will be scheduled for a baseline clinic visit. At this visit, the patient will sign the informed consent and medical record release forms, and will complete all baseline questionnaires. Her physician will be notified as to her decision to participate.

3. Self-Referral. Women receiving treatment from any of the three centers may hear of the study and want to participate. These women may self-refer with physician approval. They will be screened for study eligibility, and will be asked to join the study if the eligibility criteria are met. The patients will be scheduled for the baseline study clinic visit at which time they will sign the informed consent form, a medical record release, and will complete all baseline study questionnaires. The patients' physicians will be notified as to their decision to enroll in the study.

The Clinical Coordinating Center at the Wake Forest University Gray School of Medicine will monitor recruitment and issue monthly recruitment reports to each participating institution. Strategies will be developed to assist the clinical centers in meeting their recruitment goals, if necessary.

3.c. Informed Consent

In accordance with local institutional review board guidelines, informed consent procedures and consent forms will vary somewhat by clinical center. All consent forms will stress the voluntary and confidential nature of participation in this research investigation. Patients will be told that a decision not to participate in this study will in no way influence their treatment or medical care. Study staff will inform the participants about the purpose of the study and their requirements for participation in this research protocol. Patients will be told that they may drop out of the study at any time without penalty.

If the patient agrees to participate in the study, she will sign the informed consent form at the baseline clinic visit, prior to the completion of any study questionnaires.

3.d. Primary Physician Contact

Upon entering the study, each participant will be asked to name her primary care physician, as well as her oncologist, radiologist and/or surgeon. The participants will be asked to indicate which of these physicians has primary responsibility for their treatment (i.e., the physician they see most often for follow-up care). Once this physician has been named, a letter will be sent from the Principal Investigator of each of the clinical centers requesting the patients' medical records. Once the records are received, a clinic staff person at each clinical center will abstract the medical chart using the Medical Chart Review Form.

It should be noted that all three of the Principal Investigators of the clinical centers have close working relationships with the oncologists, radiologists, and breast surgeons at their respective institutions. Many have collaborated on research projects in the past, and already have procedures in place to ensure the process of identifying participants and accessing clinical data and charts for research investigations.

3.e. Measures

3.e.1. Baseline Clinic Visit. The following study forms will be completed at the enrollment/baseline clinic visit, which will be approximately 1 hour and 15 minutes in length. The baseline administration time for all study questionnaires is approximately 35-45 minutes. These estimates are based on the pre-testing of these forms at the Wake Forest University School of Medicine with young breast cancer patients currently undergoing treatment. Participants will be provided with opportunities to rest during the completion of the study forms at baseline, if necessary. The study coordinators will also be able to assist the patients as needed.

The following information will be obtained at baseline:

1) Demographics. Basic demographic information will be obtained on all participants including: age, marital status, educational background, employment status, occupation, and income. (This questionnaire takes approximately 3 minutes to complete.)

2) Medical and Reproductive History. Information will be collected regarding the patients' comorbid conditions; family history of breast and ovarian cancer; and reproductive history, including parity, pelvic surgery, menstrual cycling, contraceptive use, and plans for future childbearing. (This instrument is completed in approximately 5-7 minutes.)

3) Arm and Hand Swelling. Treatment-related swelling of the arm and hand will be assessed to document the occurrence, duration, and circumstances surrounding arm and hand swelling. (This instrument takes approximately 1-3 minutes to complete.)

4) Personal Habits Questionnaire. Information will be obtained regarding the patients' smoking and alcohol use, height and weight, weight cycling, and exercise habits. (This instrument takes approximately 3-5 minutes to complete.)

5) Health-Related Quality of Life. The following instruments and subscales will compose the quality of life questionnaire. All of these measures are standardized instruments, with excellent psychometric properties. All instruments were developed using a combination of focus groups, patient interviewing, and adaption from other established scales in the area of interest. Thus, both qualitative and quantitative methodologies were used to develop each scale.

a) SF-12 Health Survey. The SF-12 is a general health status measure to assess physical and mental health dimensions of health-related quality of life.⁵⁸ This questionnaire contains 12 items that were selected from the SF-36, a widely used general quality of life instrument. This scale has excellent psychometric properties, and has two subscale scores. (This instrument takes approximately 1-2 minutes to complete.)

b) Functional Assessment of Cancer Therapy - Breast (FACT-B). This 44 item questionnaire is a multidimensional HRQL scale. This instrument was developed after extensive interviewing and testing with cancer patients, and has excellent psychometric properties.⁵⁹ This scale assesses the patients' physical well-being, social/family well-being, relationship with doctor, emotional well-being, fulfillment/contentment, and concerns specific to breast cancer patients. Scores can be calculated for each of the 6 subscales, and a total HRQL score composed of all 6 subscales can be calculated as well. (This scale takes approximately 5-10 minutes to complete.)

c) Beck Depression Inventory. This is a 21-item scale that will be used to assess the depressive symptomatology/general distress of the participants in the study.⁶⁰ This instrument has been used with a variety of clinical and non-clinical populations, and has been validated as a reliable screening tool for depression. A total score is calculated from this instrument. In general, scores above 15 are considered to indicate persons who need further evaluation to determine if clinical depression exists. (This inventory takes approximately 5-7 minutes to complete.)

d) Physical Symptoms Checklist. Physical symptoms associated with breast cancer treatment and menopause will be assessed. A total score is calculated from this scale to

indicate both the occurrence and bothersomeness of physical symptoms. (This checklist takes approximately 3-5 minutes to complete.)

e) Sleep Disturbance Scale. Sleep patterns and sleep quality may be disrupted by treatment regimens and physical and emotional symptoms. Lack of restful sleep has been related to greater emotional distress and depressive symptomatology, as well as to general fatigue, in both clinical and non-clinical populations. To measure these effects, a 6 item sleep disturbance scale will be used to assess the overall quality of the participants' sleep. This scale was developed for an international study evaluating the effect of hormone replacement on peri-menopausal women. This scale was recently validated on 70,000 women from the baseline data of the Women's Health Initiative, which is examining the impact of hormone replacement therapy, diet, and calcium/vitamin D on the long-term morbidity and mortality of post-menopausal women. A total score is calculated from this scale. (Completion time for this scale is approximately 1 minute.)

f) Watts Sexual Functioning Questionnaire. The arousability and satisfaction subscales of the Watts Sexual Functioning Questionnaire will be used to assess the impact of treatment and/or amenorrhea on sexual functioning.⁶¹ Two subscale scores are calculated from these items, one for arousability and one for satisfaction with sexual activity. (These subscales take approximately 2-3 minutes to complete.)

g) MOS Social Support Questionnaire. The social support questionnaire developed in conjunction with the Medical Outcomes Study, completed by the RAND Corporation, will be used to assess the amount of instrumental and emotional support available to the participants.⁶² Social support has been found to be an important predictor of adherence to treatment regimens, one's emotional health, and overall health-related quality of life. This 20-item measure produces a total score, as well as 4 subscale scores: tangible support, affectionate support, positive social interactions, emotional-informational support. (This scale takes approximately 5 minutes to complete.)

h) Self-Concept Scale. This 10-item scale assesses the participants' satisfaction with different areas of their body and their overall weight. Persons undergoing surgery for breast cancer may experience an alteration in their perception of their body image, which may affect their psychosocial status and intimate relationships. This scale is being assessed as a secondary HRQL endpoint, and was developed by Dr. David Cella, (Director, Center on Outcomes Research and Education at Northwestern University), through his work with breast cancer patients. (Administration time for this instrument is approximately 1-2 minutes.)

I) Spirituality Subscale. Spiritual beliefs have been identified recently as an important predictor of patients' coping and hopefulness for the future when dealing with a serious illness. To measure this construct, we will be using a 7-item scale developed by Dr. David Cella. (Administration time is approximately 1 minute.)

6) Monthly Menstrual Bleeding Diary. At the baseline visit, patients will be instructed as to how to complete the menstrual bleeding diary. The participants will be asked to indicate on the diary each day whether they experienced either "no bleeding," "spotting," or "bleeding" (i.e., mild, moderate, or heavy). From this form, the frequency, duration, and amount of menstrual flow can be calculated for every participant each month.

7) Medical Chart Review. Medical chart reviews will be performed by clinical staff on all patients following the baseline clinic visit. The information to be obtained includes the: date of breast cancer diagnosis, stage and grade, size and number of positive lymph nodes, estrogen and progesterone receptors (positive and negative), treatment prescribed (e.g., surgery, radiation, and/or chemotherapy; adjuvant therapy), dose and duration of treatment, whether reconstructive surgery was performed, current medications, comorbid conditions, and patients' height and weight.

All data forms completed at the baseline visit will be checked for completeness by the study coordinators before the patient has left the clinic. Any missing items will be double-checked with the participants to inquire as to whether they intended to leave items blank or chose not to answer the questions. Staff will also be asked to check the participants' response to question #9 on the Beck Depression Inventory to see if the patient is strongly considering suicide. Patients who make a response of "3" on question 9 will be referred to the Principal Investigator of the respective clinical center for immediate physician follow-up. (See Section 3.g. Alert Values below.)

3.e.2. Follow-Up of Study Participants. Participants will be followed at six month intervals from the date they enroll in the study. Follow-up will range between 24 and 36 months for all participants. Data collection during the follow-up period will be centralized in that all follow-up forms will be mailed to participants, along with a self-addressed stamped envelope, at 6 month intervals by the Clinical Coordinating Center staff at the Bowman Gray School of Medicine. If the study forms are not returned to the coordinating center in a timely manner (i.e., within 15 days of the date the forms were mailed), a member of the coordinating center staff will complete a reminder call to the participants and complete a phone interview, if necessary. Because only updates of several of the forms will be required at the 6 month assessment points, the questionnaire completion time will be shorter at follow-up (i.e., approximately 25-35 minutes).

Once the follow-up questionnaires have been received by the clinical center, the project managers will examine each returned follow-up questionnaire for completeness. Participants with greater than 10% missing data on any of the study forms will be telephoned in order to reduce the occurrence of missing data.

The project managers will also score the Beck Depression Inventory, and check whether response "3" was marked on question #9 of this instrument. If the total score is 16 or greater and/or if the participant marked response "3" to question 9, the principal investigator of the participants' institution will be notified immediately. (See section 3.g. below.)

3.e.2.a. Follow-up Measures

The measures described below will be mailed to the participants during the follow-up period:

1. Demographic and Contact Information: Updates
2. Medical and Reproductive History: Updates will be completed on the patients' co-morbid status, menstrual cycling, contraceptive use, pregnancies and outcomes, and plans for future childbearing.
3. Arm and Hand Swelling Form
4. Personal Habits: Updates on patients' smoking and alcohol use status, height and weight, and exercise habits.
5. Health-Related Quality of Life Form
6. Menstrual Bleeding Diaries. The monthly menstrual bleeding diaries will be completed each month from the patients' time of enrollment to the end of the study data collection period (i.e., April, 2001). Patients will be instructed to return the diaries to the clinical coordinating center every three months. The coordinating center will, in turn, mail the participants the next consecutive, three months of diaries each quarter. Unusual bleeding patterns will be determined, and the principal investigators of the participating institutions will be notified, if necessary. (See section 3.g. below.)
7. Medical Chart Review. Medical chart reviews will be performed on patients who have serious complications resulting from treatment, undergo additional treatment(s) and/or have a cancer recurrence during the study period. Information to be obtained on these individuals includes the stage and grade of cancer, size and number of positive lymph nodes, estrogen and progesterone receptors, prescribed treatment, medications, and comorbidities.

3.f. Follow-up Alert Values Safety Monitoring.

During the course of the study certain safety monitoring procedures will be maintained to detect unusual bleeding patterns and higher than average rates of depressive symptomatology. The operational definitions of these two alert values are described below:

3.f.1. Unusual Bleeding Patterns. Participants' bleeding patterns will be recorded on the monthly bleeding diaries. Alert values for bleeding and spotting have been defined as follows:

1. Any episode of bleeding lasting longer than eight days. (A bleeding episode is defined as two or more consecutive days of bleeding or spotting bounded by at least two bleeding-free days.)
2. An interval between bleeding episodes of less than twenty-four days.

3. "On and off" bleeding within a 15 day period (e.g., 3 days bleeding, 2 days no bleeding, 4 days of bleeding).

A notice has also been placed on the bottom of the bleeding diary form asking the women to call their physician if they experience any unusual bleeding in terms of frequency, duration, or amount.

3.f.2. Depressive Symptomatology. The Beck Depression Inventory will be used, in part, as a screen for clinical depression. A cutoff score of 16 or greater is indicative of individuals who are experiencing higher than average depressive symptomatology, which could indicate the presence of clinical depression.

Item 9, response choices #3 on the Beck Depression Inventory also concerns whether the person is considering suicide. Persons who mark either response #3 ("I would kill myself if I had the chance.") will be referred for immediate consultation.

3.f.3. Process of Referral for Alert Values. For both unusual bleeding patterns, and the detection of higher than average depressive symptomatology and/or the consideration of suicide, the Principal Investigators of the Clinical Centers will be notified using the following procedures:

At baseline, the clinic staff persons will be asked to examine question #9 of the Beck Depression Inventory to see if the participant marked response category "3." If the person marked this category, the PI of the clinical center will be notified. The PI, in turn, will notify the participants' designated physician for further evaluation for clinical depression.

At the follow-up assessments, the Principal Investigators of the clinical centers will be contacted should any of their participants have an unusual bleeding pattern (as described above), a Beck Depression Inventory score of 16 or greater and/or if the participant marked response "3" on question 9 of this form. The Principal Investigators will then be responsible for contacting the patients' designated physician for further follow-up.

4. Data Analyses and Management

4.a. Sample Size Determinations. A total of 800 women will be followed in this study. This sample size will provide a statistical power $\geq 80\%$ to detect a difference of 14%-22% in the proportions of women with treatment related amenorrhea (TRA) between two groups. The following group comparisons are of interest: 1) cyclophosphamide but no tamoxifen versus tamoxifen but no cyclophosphamide (C vs T); 2) cyclophosphamide but no tamoxifen versus cyclophosphamide and tamoxifen (C vs CT); and 3) tamoxifen but no cyclophosphamide versus cyclophosphamide and tamoxifen (T vs CT).

Assuming that losses to follow-up will be about 20%, 640 (800×0.80) women will complete at least 24 months of follow-up. We expect that 10% ($n=64$) will have received a treatment that did not include cyclophosphamide nor tamoxifen, 10% ($n=64$) will have had a treatment that includes

tamoxifen but no cyclophosphamide, 35% (n=224) cyclophosphamide but no tamoxifen, and 45% (n=288) will have received both cyclophosphamide and tamoxifen as part of their treatment.

The following table shows the detectable differences that were obtained using a two-sided chi-square test with the above sample sizes, 80% power and a significance level of .0167 to control for the 3 group comparisons.

<u>Comparisons</u>	n_0	n_1	p_0 ¹	m ²	p_1 ³	Δ ⁴
C vs T	224	64	.7	3.5	<.48 or >.89	.22
C vs CT	224	288	.7	.78	<.56 or >.82	.14
T vs CT	64	288	.8	4.5	<.60 or >.95	.15

¹ Proportion of women with TRA in group 0, based on published studies

² n_0/n_1

³ Detectable proportion of women with TRA in Group 2

⁴ Detectable difference in proportions of women with TRA

4.b. Data Analyses: Chemotherapy-Related Amenorrhea. Descriptive statistics will be presented regarding the frequency, duration and amount of bleeding experienced by all participants. The duration and amount of bleeding will be analyzed with longitudinal mixed models. Transformation of the dependent variables will be explored to satisfy assumptions of linearity, homogeneity and normality. Variables believed to be related to bleeding will be included in the models. Maximum likelihood techniques will be used to estimate parameters.

Treatment related amenorrhea will be defined as six months of amenorrhea occurring within three months of stopping treatment. Multivariate logistic regression analysis will be employed to identify the major predictive factors for developing amenorrhea. The binary outcome will be the presence or absence of amenorrhea. Multivariate models including characteristics possibly related to amenorrhea, such as age and treatment modality, will be fitted. Logistic regression diagnostics will be used to summarize the agreement of observed and fitted values.

In secondary analyses, survival modeling will be used to investigate the time to amenorrhea from the start of chemotherapy treatment. In most instances, amenorrhea will occur during the first year after diagnosis, but survival analyses will allow us to take into account the different follow-up times for each participant and the possibility that amenorrhea may occur later for some participants. With these models, we will explore the factors that might influence amenorrhea, using all the data available.

4.c. Health Related Quality of Life

4.c.1. Primary and Secondary Endpoints. Various statistical analyses, as described below, will be used to compare patient's HRQL and psychosocial outcomes with respect to their treatments and the maintenance of ovarian function (i.e., those amenorrheic and those not rendered amenorrheic), and

to estimate the association between these variables. The following primary and secondary HRQL endpoints have been defined.

Primary Endpoints:

1) FACT-B	(Total Score: Continuous Variable)

Secondary Endpoints:

1) SF-12	(Physical Subscale: Continuous Variable) (Mental Health Subscale: Continuous Variable)
2) Beck Depression Inventory	(Total Score: Continuous Variable)
3) Physical Symptoms Checklist	(Total Score: Continuous Variable)
4) Sleep Disturbance Scale	(Total Score: Continuous Variable)
5) Watts Sexual Functioning:	(Arousal Subscore: Continuous Variable) (Satisfaction Subscore: Continuous Variable)
6) MOS Social Support Questionnaire	(Total Score: Continuous Variable)
7) Self-Concept Scale	(Total Score: Continuous Variables)
8) Spirituality Scale	(Total Score: Continuous Variable)

4.c.2. Power Calculation for the Primary HRQL Quality of Life Endpoint. A higher number of women will be recruited at the beginning of the study recruitment period through reviews of cancer registers and other sources available at each institution. Assuming a uniform drop-out rate of 20%, after recruiting 75 women each month during the first 6 months, and 35 women monthly for months 7- 16, 640 women will be followed for 24 months, and 240 will be followed for 36 months. Based on previous studies on breast cancer patients, estimates of the mean and standard deviations for the primary quality of life endpoint is as follows:

Endpoint	Mean	Standard Deviation
FACT-B	117.2	24.7

Assuming that at least 50% of the participants will experience treatment related amenorrhea (TRA), the following differences can be detected with 80% power at the .05 two-sided significance level.

Endpoint	Mean	Std. Dev. TRA	% with	Follow-up	N	Δ^*	(Δ /Mean) * 100
FACT-B	117.2	24.7 .5	36 months	240	8.9	7.6 %	
				24 months	640	5.5	4.7%

* Δ : Detectable difference

A total sample size of 800 patients will ensure 80% power for detecting 36-month relative effects of 7.6% or more for the FACT-B at the .05 two-sided significance level in a t-test analysis, assuming that 20% of the patients will be lost to follow-up. Both detectable relative effects are less than 20%, which represents a clinically meaningful cutpoint.

4.c.3. Data Analyses: Health-Related Quality of Life. Descriptive statistics consisting of frequency tables and percents will be tabulated for categorical variables, and means, medians, standard deviations, ranges, etc., will be calculated for all continuous variables at the baseline and follow-up assessment points. Logistic regression will be used to assess differences in the categorical outcomes, and analysis of covariance will be used to assess treatment differences in the continuous variables. These analyses adjust for pre-study values of the outcome measures and other factors, such as age and stage of disease, to correct for chance imbalances in the covariates between groups and to reduce the variance of the estimate of the group effect, thus increasing the statistical power. All test hypotheses and reported p-values will be two-sided. Regression diagnostics and residual plots will be used to find appropriate transformations, if needed, to satisfy the assumptions of the various analyses, including linearity for both, and homogeneity of variances and normality for the covariance analyses.

Spearman rank correlations will also be used to estimate the association between the various factors at each measurement time. In addition, these associations will be examined by studying bivariate scatterplots. Regression analyses will be completed to assess multivariate relationships and to see if the relationships differ over the course of the study.

All significance tests will be two-sided. Clinical center will be included in all models. Secondary analyses will explore the presence of amenorrhea in subgroups of patients according to the specific drug they were prescribed. We will also perform subgroup analyses for the different treatment modalities that did not involve chemotherapy. Interim analyses will be performed by the Coordinating Center to provide information for reviewing the conduct and progress of the study. A description of the characteristics of the dropouts will be provided and comparisons with the participants will be presented.

4.d. Pregnancy Data Base. As the number of pregnancies is expected to be small, the analyses will be exploratory. The pregnancies reported during the study will be described and important factors like treatment modality, and age of the mother will also be reported in association with pregnancy data. Short term survival of the patients will be analyzed if the number of pregnancies

allows it. The main focus will be maintaining a high quality database for further follow-up and analysis.

4.e. Data Management in the DOD Breast Cancer Study. The goal of data management is to ensure the accuracy and completeness of study data, and to make the data available for analysis and reporting. To that end, data entry, editing and reporting systems will be utilized at the clinical coordinating center (CCC) at WFUSM. Because the protocol requires only minimum contact between the participant and the clinical center after the baseline visit, all data management operations will take place centrally, at the CCC.

4.f. Data Flow. Completed paper forms will be mailed to the CCC by staff at the clinical centers (baseline) or by the participants themselves (follow-up). After an initial review by the project manager, data forms will be entered electronically. Logical consistency checks will be run on the full data set. Errors will be identified and corrected, and the correct data will be re-entered and re-edited. Finally, the entire study database will be "frozen" periodically to provide a stable data set for interim analyses. The freeze process involves resolving outstanding discrepancies and copying all data into permanent SAS data sets. Only data that have passed all quality assurance checks will be frozen for analysis.

4.g. Quality Assurance. Quality assurance will be a major activity of the CCC throughout the study. Initial screening of the data will be done by the project manager when the forms are received. She will verify that the forms are legible, and that they are filled out correctly and completely. Any problems identified will be resolved before the data entry step. If necessary, the clinic or participant will be contacted to provide missing information or to correct items where there are obvious inconsistencies. Participant ID and visit verification will be incorporated into the data entry system, as will gross range checking. More refined range checking, logical consistency, and longitudinal edits will be done in a separate step after data entry. Initially, a random 10% sample of study forms will be selected for duplicate data entry. Data from the first and second entry will be compared, and error rates calculated. The results will be used to determine the need for future double keying of all data or of key study variables.

In addition to the main study data, an inventory will be maintained, containing participant contact information, follow-up status information, and form status and completion date information. This inventory will form the core of the data and participant tracking system. Most study management reports, including recruitment reports, missed visit reports, and missing form reports will be generated from this inventory.

4.h. Hardware and Software. The data management system will be implemented on a Sun SparcServer 1000E in the Department of Public Health Sciences at the Wake Forest University School of Medicine. The data entry application will be developed using FoxPro software, which will have built in validation and range checking. Quality assurance checks and routine study reports will also be done in SAS. Statistical analysis will be done using SAS and Splus.

All study data will reside on the SparcServer's disk drives. Full file system backups to tape are made each weekday night. In general, in the event of a hard disk failure no more than a day's worth of work will need to be repeated.

5. Study Organization

The organizational structure for this study includes the following key components: the Clinical Centers (CC) and the Clinical Coordinating Center (CCC).

5.a. Clinical Centers. Three clinical centers are participating in the current protocol:

Memorial Sloan-Kettering Cancer Center, (Jeanne Petrek, M.D., Principal Investigator)
M.D. Anderson Cancer Center, (Eva Singletary, M.D., Principal Investigator)
Wake Forest University School of Medicine, (Electra Paskett, Ph.D., Principal Investigator)

Each clinical center is composed of an inter-disciplinary team of clinical investigators and staff who provide the areas of expertise necessary for the successful completion of the study. The responsibilities of the clinical center staff and investigators include:

1. Identifying and recruiting eligible participants for the study.
2. Completing medical record chart reviews regarding breast cancer diagnosis and treatment, and comorbidities.
3. Collecting high quality data in accordance with the study protocol.
4. Collaborating in the analysis and dissemination of study results.

5.b. Clinical Coordinating Center. The clinical coordinating center for the current study will be located at the Wake Forest University School of Medicine, Department of Public Health Sciences, (Michelle Naughton, Ph.D., Principal Investigator).

The clinical coordinating center has the primary responsibility for collecting the follow-up data, monitoring the quality of data collected, and analyzing data generated by the clinical centers. Additional responsibilities of the CCC include:

1. Preparing (with the aid of the clinical center investigators and staff) the protocol, forms, and Manual of Operations.
2. Developing the statistical design of the trial.

3. Working with the investigators in the development and pre-testing of forms and procedures, and assuming responsibility for the reproduction and distribution of forms.
4. Training study coordinators, data coordinators and other clinical center personnel.
5. Managing quality control aspects associated with the collection and management of the study data.
6. Monitoring clinical center performance through the use of summary data reports generated by the CCC (i.e., participant recruitment reports; quality control checks of collected data).
7. Monitoring follow-up activities, and monitoring quality control of follow-up data collected by the CCC staff.
8. Preparing, in collaboration with the clinical investigators, various manuscripts of the study results.

6. Study Time Line

The following time line has been determined for the completion of this protocol.

Recruitment:	January 1, 1998 - April 30, 1999
Follow-up:	January 1, 1998 - April 30, 2001
Data Analyses:	May 1, 2001 - October 20, 2001

A 16 month recruitment period is planned for all three clinical centers (January 1, 1998 - April 30, 1999). All participants will be reassessed at 6 month intervals from their time of entry into the study through April 30, 2001. (The study recruitment period will overlap with the follow-up period from January 1, 1998 - April 30, 1999.) At least 24 months of follow-up data will be obtained on all study participants. The final six months of the study will be devoted to the completion of data analyses and manuscript preparation.

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PURPOSE

The study will examine the effect of treatment for breast cancer on menstrual cycle maintenance and health-related quality of life in young female patients (18-45 years).

This study will also develop a database to track subsequent pregnancies and their effect on patients' morbidity and mortality.

PRIMARY STUDY OBJECTIVES

1) To describe the menstrual bleeding patterns of female breast cancer patients aged 45 years and younger, including those without systemic therapy, in terms of frequency of bleeding, duration of each bleeding episode, and amount (i.e., light, medium, heavy).

2) To compare the incidence of chemotherapy related amenorrhea (TRA) (i.e., no menstrual bleeding for $\geq$ six months within three months of stopping treatment), in breast cancer patients by treatment group (i.e., cyclophosphamide versus tamoxifen, cyclophosphamide alone versus cyclophosphamide and tamoxifen, or tamoxifen alone versus cyclophosphamide and tamoxifen).

PRIMARY STUDY OBJECTIVES

3) To compare the health-related quality of life of women undergoing chemotherapy who experience amenorrhea with those who do not have amenorrhea.

We hypothesize that the HRQL of women who experience amenorrhea will be lower than for women who retain menstrual cycling, regardless of the type of chemotherapy regimen completed. Specifically, women with amenorrhea will have lower overall health-related quality of life, as measured by the total score on the FACT-B, the primary HRQL assessment instrument.

SECONDARY OBJECTIVES

1) To examine possible predictors of TRA, including smoking, age, race, stage of cancer, and treatment modality.

2) To describe comprehensively the quality of life and psychosocial status of young women with breast cancer receiving any form of therapy (chemotherapy, radiation, surgery or a combination).

Specifically, we will examine the participants' overall health-related quality of life, their physical symptoms and sleep quality, their depressive symptomatology, sexual functioning (i.e., arousability and satisfaction), their self-concept, and levels of social support and spirituality.

OPERATIONAL OBJECTIVES

- 1) To recruit, and follow for a minimum of 24 months and a maximum of 36 months a total of 800 participants, across three clinical centers, who meet a specific set of inclusion/exclusion criteria.
- 2) To maintain levels of adherence and retention at 80% or greater in order to attain study goals.
- 3) To ensure the collection of high quality data through careful monitoring of all data collection procedures.

STUDY POPULATION

A total of 800 women will be recruited from three clinical centers:

Wake Forest University School of Medicine	188
M.D. Anderson Cancer Center	252
Sloan-Kettering Cancer Center	360

INCLUSION CRITERIA

1. Must be female.
2. Between the ages of 18 and 45 years at the time of diagnosis.
3. Community dwelling
4. Be diagnosed with intraductal ~~or invasive~~ breast cancer Stage I, II, III within the previous six months.
5. Must have had ^{self-defined} regular menstrual cycles at the time of the breast cancer diagnosis. *cycling at all*
6. Must have received at least one form of treatment: surgical, radiation, and/or chemotherapy.
7. Have physician agreement for patient participation.
8. Provide informed consent.

EXCLUSION CRITERIA

1. No menstrual cycles.
2. Psychiatric or psychologic abnormality precluding the informed consent process or which would impact on compliance.
3. Previous or another concurrent malignancy (excepting basal and squamous skin cancer and stage 0 cervical cancer). *one ovary, still cycling OK*
4. Stage IV breast malignancy
5. Inability to read and understand English.
6. No telephone in the home.
7. Resident outside of the United States.
not currently pregnant
breast feeding - OK

RECRUITMENT

		<u>Mos. 1-6*</u>	<u>Mos. 7-16</u>
WFU	188	9/wk	4/wk
M.D. Anderson	252	6/wk	3/wk
<u>Sloan-Kettering</u>	<u>360</u>	<u>4/wk</u>	<u>2/wk</u>
Total	800	19/wk	9/wk
		76/mos	36/mos
		456/6 mos	360/10 mos

* January 1, 1998 - June 30, 1998
 July 1, 1998 - April 30, 1999

TOTAL RECRUITMENT

Assuming 80% of the participants will complete the study:

240 will have 36 months of follow-up

640 will have 24 months of follow-up

RECRUITMENT

A total of 800 women will be recruited from three clinical centers:

Wake Forest University School of Medicine	188
M.D. Anderson Cancer Center	252
Sloan-Kettering Cancer Center	360

Recruitment Period:

January 1, 1998 - April 30, 1999

RECRUITMENT SOURCES

1. Patient Identification Through Tumor and Surgical Registries.
2. Referral Through Physicians.
3. Self-Referral

MEASURES

Demographics

Medical and Reproductive History

Arm and Hand Swelling

Personal Habits Questionnaire

Health-Related Quality of Life:

● SF-12 Health Survey

Functional Assessment of Cancer Therapy -
Breast (FACT-B) *David Gella SW*

Beck Depression Inventory

Sleep Disturbance Scale

Watts Sexual Functioning Questionnaire:
(arousability and satisfaction subscales)

MOS Social Support Questionnaire

Self-Concept Scale

Spirituality Subscale

MEASURES

Monthly Menstrual Bleeding Diary/Calendar

Medical Chart Review

Follow-Up of Study Participants

Participants will be followed at six month intervals from their date of enrollment.

Follow-up will range between 24 and 36 months for all participants.

Data collection during the follow-up period will be centralized and completed by the coordinating center.

Questionnaires: mailed every 6 months

Diaries: mailed every 3 months

SAFETY MONITORING

Beck Depression Inventory:

- 1) Response "3" is marked on question #9 of this instrument.
- 2) If the total score is 16 or greater.

*Look for these on
baseline data.*

Call P.I.

Poss. do not enroll

CCC will score at baseline

SAFETY MONITORING

● Unusual Bleeding Patterns:

1. Any episode of bleeding lasting longer than eight days. (A bleeding episode is defined as two or more consecutive days of bleeding or spotting bounded by at least two bleeding-free days.)
2. An interval between bleeding episodes of less than twenty-four days.
3. "On and off" bleeding within a 15 day period (e.g., 3 days bleeding, 2 days no bleeding, 4 days of bleeding).

A notice has also been placed on the bottom of the bleeding diary form asking the women to call their physician if they experience any unusual bleeding in terms of frequency, duration, or amount.

SAMPLE SIZE DETERMINATIONS

A total of 800 women will be followed in this study. This sample size will provide a statistical power $\geq 80\%$ to detect a difference of 14%-22% in the proportions of women with treatment related amenorrhea (TRA) between two groups:

- 1) cyclophosphamide but no tamoxifen versus tamoxifen but no cyclophosphamide (C vs T);
- 2) cyclophosphamide but no tamoxifen versus cyclophosphamide and tamoxifen (C vs CT);
- 3) tamoxifen but no cyclophosphamide versus cyclophosphamide and tamoxifen (T vs CT).

SAMPLE SIZE DETERMINATIONS

Assuming that losses to follow-up will be about 20%, 640 (800×0.80) women will complete at least 24 months of follow-up.

We expect that 10% ($n=64$) will have received a treatment that did not include cyclophosphamide nor tamoxifen, 10% ($n=64$) will have had a treatment that includes tamoxifen but no cyclophosphamide, 35% ($n=224$) cyclophosphamide but no tamoxifen, and 45% ($n=288$) will have received both cyclophosphamide and tamoxifen as part of their treatment.

SAMPLE SIZE DETERMINATIONS

The following table shows the detectable differences that were obtained using a two-sided chi-square test with the above sample sizes, 80% power and a significance level of .0167 to control for the 3 group comparisons.

<u>Comparisons</u>	<u>n</u> ₀	<u>n</u> ₁	<u>p</u> ₀ ¹	<u>m</u> ²	<u>p</u> ₁₋ ³	<u>Δ</u> ⁴
C vs T	224	64	.7	3.5	<.48 or >.89	.22
C vs CT	224	288	.7	.78	<.56 or >.82	.14
T vs CT	64	288	.8	4.5	<.60 or >.95	.15

¹ Proportion of women with TRA in group 0, based on published studies

² n_0/n_1

³ Detectable proportion of women with TRA in Group 2

⁴ Detectable difference in proportions of women with TRA

PREGNANCY DATA BASE

● Plans to collect information on the patients' desire: to become pregnant in the future, use of contraception, number of months spent trying to get pregnant, number of pregnancies and the outcome of each pregnancy, and the morbidity and mortality of both the mother and child during birth and beyond.

1 cycle within 6 mos of diagnosis

CHAPTER 3

RECRUITMENT, PRE-SCREENING AND ELIGIBILITY OVERVIEW

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3.1 RECRUITMENT GOALS

Timely and successful recruitment of participants is important in order to obtain sufficient numbers of patients to perform meaningful, follow-up analyses. A 16 month recruitment period is planned for all three clinical centers which will begin January 1, 1998 and continue through April 30, 1999. All participants will be reassessed at 6 month intervals from their time of entry into the study through April 30, 2001. Thus, between 24 and 36 months of follow-up data will be obtained on all study participants. The final six months of the study (i.e., May 1 - October 21, 2001) will be devoted to the completion of data analyses and manuscript preparation.

A total of 800 women will be recruited from the three clinical centers:

Sloan-Kettering Cancer Center	360
M.D. Anderson Cancer Center	252
Wake Forest University School of Medicine	188

In order to achieve recruitment goals, each clinical center will need to enroll between 4 to 9 participants per week from January 1, 1998 to June 30, 1998, and 2 to 4 participants per week from July 1, 1998 through April 30, 1999. The number of participants to be recruited each week will vary by clinical center as indicated below:

	Months (1-6) <u>Jan. - June, 1998</u>	Months (7-16) <u>July, 1998 - April, 1999</u>
Sloan-Kettering Cancer Center	9/week	4/week
M.D. Anderson Cancer Center	6/week	3/week
Wake Forest University Medical School	4/week	2/week

The clinical coordinating center will monitor recruitment, and issue monthly recruitment

reports to each participating institution. (See attached pages for an example of the study recruitment report.) Strategies will be developed to assist the clinical centers in meeting their recruitment goals, if necessary.

3.2. RECRUITMENT STRATEGIES

Local sources of patients have been identified at each participating institution. A variety of strategies will be utilized in recruiting participants to the study, and will include:

- a) identification through tumor and surgical registries
- b) physician referrals
- c) self-referral

3.2.1 Patient Identification Through Tumor and Surgical Registries

The majority of patients will be identified through tumor and/or surgical registries at the participating institutions. Once women meeting the minimum eligibility criteria have been identified, the patients' oncologists/surgeons will be contacted by clinic staff to obtain approval to approach the patient. If the physician approves, the patient will be approached at the clinic site, (if she is scheduled for a follow-up or treatment visit), or the patient will be sent a letter describing the purpose of the study, which will be followed by a telephone call. The clinic staff person will screen the person using the Participant Eligibility Form to ensure she meets the eligibility criteria, and then will ask the patient to participate in the study if she is eligible. If the patient is interested in participating, the staff person will schedule her for the baseline clinic visit at which time she will sign the informed consent form, a medical record release form, and will complete all baseline study questionnaires. The patients' physicians will be notified as to whether the patient has enrolled in the study.

3.2.2 Referral Through Physicians

Participants will also be identified by the clinical center's participating investigators, oncologists, surgeons, and radiologists. In most instances, these physicians will have already explained the study to the participant, and the clinic staff will contact the patient to invite her to participate in the study. The patient will be screened to ensure that she meets all eligibility criteria. If the patient is eligible and willing to participate, she will be scheduled for a baseline clinic visit. At this visit, the patient will sign the informed consent and medical record release forms, and will complete all baseline questionnaires. Her physician will be notified as to her decision to participate.

3.2.3 Self-Referral

Women receiving treatment from any of the three centers may hear of the study and want to participate. These women may self-refer with physician approval. They will be screened for study eligibility, and will be asked to join the study if the eligibility criteria are met. The participants will be scheduled for the baseline clinic visit, at which time they will sign the informed consent form, a medical record release, and will complete all baseline study questionnaires. The patients' physicians will be notified as to their decision to enroll in the study.

3.3 PRESCREENING AND ELIGIBILITY

The first contact between clinical staff and participants will be recorded using the Participant Eligibility Form. The eligibility form consists of questions designed to determine whether the participant is eligible to participate in the current protocol. Eligibility for the current study is based on the following inclusion and exclusion criteria.

Inclusion Criteria

1. Must be female.
2. Between the ages of 18 and 45 years at the baseline visit.
3. Community dwelling as opposed to living in a residential care or correctional facility.
4. Be diagnosed with invasive breast cancer Stage I, II, III within the previous six months.
5. Receiving one form of treatment (i.e., medical, surgical, and/or radiation) at the clinical center or one of its affiliates.
6. Must have had regular menstrual cycles (i.e., every 4-5 weeks) at the time of their breast cancer diagnosis.
(Women who have had a hysterectomy will be excluded from participation.)
7. Must not be pregnant.
8. Have physician agreement for patient participation.
9. Provide informed consent.

Exclusion Criteria

Any of the following will exclude the participant:

1. No regular menstrual cycles.
2. Psychiatric or psychologic abnormality precluding the informed consent process or which would impact on compliance.
3. Previous or another concurrent malignancy (excepting basal and squamous skin cancer and stage 0 cervical cancer).
4. Stage IV breast malignancy
5. Inability to read and understand English.
6. No telephone in the home.
7. Resident outside of the United States.

Women will be pre-screened in clinic or by telephone to determine if they are eligible to participate in the study. The Participant Eligibility Form has been designed to assist the clinic staff in determining eligibility. Interested women meeting the pre-screening eligibility criteria are scheduled for a baseline clinic visit as soon as is convenient. In some situations, the pre-screening and baseline visit may occur during the same contact.

3.4 DESIGNATED PHYSICIAN CONTACT

Upon entering the study, each participant will be asked to name the physician who has primary responsibility for her treatment. Once this physician has been named, a letter will be sent informing the physician that his/her patient is participating in the study. Health care issues will be referred to the designated physician in all cases.

Example of Study Recruitment Report

Recruitment Tracking All Clinics

	Dec 97	Jan 98	Feb 98	Mar 98	Apr 98	May 98	Jun 98	Jul 98	Aug 98	Sep 98	Oct 98	Nov 98
Baseline	5	73	73	73	73	73	73	38	37	36	36	35
6 mo							5	73	73	73	73	73
Total	5	73	73	73	73	73	78	111	110	109	109	108

Year
One

	Dec 98	Jan 99	Feb 99	Mar 99	Apr 99	May 99	Jun 99	Jul 99	Aug 99	Sep 99	Oct 99	Nov 99
Baseline	35	35	35	35	35	35	35	35	35	35	35	
6 mo	73	38	37	36	36	36	36	38	37	36	36	35
1 year	5	73	73	73	73	73	73	73	73	73	73	73
18 mo							5					
Total	113	146	145	144	144	108	113	146	145	144	144	108

Year
Two

	Dec 99	Jan 00	Feb 00	Mar 00	Apr 00	May 00	Jun 00	Jul 00	Aug 00	Sep 00	Oct 00	Nov 00
Baseline												
6 mo												
1 year	35	35	35	35	35	35	35	35	35	35	35	35
18 mo	73	38	37	36	36	73	73	38	37	36	36	35
24 mo	5	73	73	73	73	73	5	73	73	73	73	73
30 mo												
Total	113	146	145	144	144	108	108	73	72	71	71	35

Year
Three

	Dec 00	Jan 01	Feb 01	Mar 01	Apr 01	May 01	Jun 01	Total
Baseline								800
6 mo								800
1 year								800
18 mo								800
24 mo	35	35	35	35	35			800
30 mo	73	38	37	36	36			590
36 mo	5	73	73	73	73			297
Total	108	73	72	71	71	0	0	4000

Year
Four

Goal Mo 1-6 443
 Mo 7-16 357
 800

CHAPTER 4
INFORMED CONSENT GUIDELINES

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4.2	BASIC ELEMENTS OF INFORMED CONSENT	1
4.3	THE PROCESS OF OBTAINING CONSENT	4

4.1 INTRODUCTION

The success of every study depends on the cooperation of its participants. For this study to succeed, the participants must agree to complete questionnaires regarding their cancer diagnosis and treatments, menstrual cycles, medical history, demographics, and health-related quality of life. In addition, they will be asked to complete study questionnaires that will be mailed to them every six months. To aid in meeting these objectives, it is important to obtain truly informed and voluntary consent. If the consent process is simply a mechanical ritual, the study could be jeopardized by a large number of early drop outs, poor adherence, and confusion about the study protocol.

4.2 BASIC ELEMENTS OF INFORMED CONSENT

The Department of Health and Human Services' (DHHS) guidelines for informed consent include eight essential elements:

- (1) **Participants must be advised that the study involves research. An explanation must be given regarding the purposes of the research, the expected duration of the subject's participation and a description of the procedures to be followed.**

With respect to routine procedures, participants should be told that they are expected to attend a baseline clinic visit. During the baseline visit, the participants will be asked to complete a variety of questionnaires about their health status, medical history, and health-related quality of life. The participants' eligibility to participate in the study will also be re-checked at this time.

All participants enrolled in the study will be followed at 6 month intervals. Follow-up questionnaires will be mailed to the participants' homes for them to complete and return to the clinical coordinating center. Women not returning the forms in a timely manner will be telephoned by coordinating center staff, and a telephone interview will be conducted, if necessary. Participants

should have a thorough idea of the demands of the study to avoid misunderstandings. It should be made clear that the study is expected to last for approximately two to three years for each participant, depending on when they begin the study.

(2) Anticipated benefits of the trial must be explained to patients.

Many participants appreciate the opportunity to be involved in relevant research and to contribute to medical knowledge. In this study, the knowledge we gain may not apply specifically to the participants in the study, but may inform the treatment options of future, young cancer patients.

(3) Attendant discomforts and risks must be described.

In this study, there is little likelihood that the subjects will be harmed by participating. Some participants, however, may experience temporary psychological discomfort due to the nature of some of the questions. Other studies using similar questionnaire items, though, have not found this to be a major problem among their participants.

(4) Appropriate alternative procedures that might be advantageous for the subject must be disclosed.

Not applicable to the current study.

(5) The extent to which confidentiality of records identifying the participant will be maintained must be described.

Confidentiality of all participant information is assured in all collaborating centers. No unauthorized personnel should have access to participant records or completed questionnaires. Additionally, all record storage rooms should be secured appropriately, and should contain necessary locked file cabinets or other storage equipment.

It may be useful to explain that in studies of this nature, numerical and alphabetic codes are assigned to each participant. Although participants' names are kept in a central file, it is the numerical and alphabetic ID codes that are used in patient records and data files. Participants are not identified by name in any reports or publications.

- (7) **Persons responsible for the study must offer an explanation of who to contact for answers to pertinent questions about the research and the participant's rights, and who to contact in the event of a research related question.**

We suggest that one or more people associated with the study be available to answer relevant questions during the baseline visit. If the study coordinator is unable to answer a participants' questions, arrangements should be made to find out the answer(s) to the participants' question(s) and/or schedule a telephone interview with the clinical center PI.

Once they are enrolled in the study, we recommend that participants receive written information regarding who to contact at any time concerning questions they may have about the study or their rights as a participant in the protocol.

- (8) **Participants must be told that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which he or she is otherwise entitled.**

Obviously we would like each of our participants to remain in the study until the end, if possible, but each woman has the right to withdraw at any time. We must communicate this option to participants without luring them into the study on a probationary "look and see" basis. Hesitant participants should be evaluated very carefully to screen out those who are likely to withdraw early.

The right to withdraw from a trial is meaningless if such behavior invokes penalties. This is the reason for the phrase, "without penalty or loss of benefits," and the idea should be explained to

participants. If they drop out of the trial, the act of dropping out will not jeopardize their regular care.

The eight requirements of informed consent in the above guidelines refer primarily to categories of information that enable participants to make rational decisions regarding participation in research investigations. Except for the stipulation that participants' inquiries should be answered, these basic elements do not refer to the process of obtaining informed consent.

4.3 THE PROCESS OF OBTAINING CONSENT

Various studies indicate that the circumstances under which consent is obtained can have a profound influence on the participant's understanding of the study protocol and requirements, and on the participants' ability to make a "non-coerced" and unbiased decision about whether to participate.

Given the data at hand, we are recommending the following guidelines to ensure that the consent we obtain will be as informed and voluntary as possible:

- (1) Participants should be fully informed about the study and have adequate time to evaluate the pros and cons of participation.**

The Informed Consent Form may be sent to the participants for review at home prior to the baseline visit, so that they may review it carefully. During the baseline visit the consent form will be reviewed, at which time the pros and cons of participation will be discussed, and a signature will be obtained if the patient is agreeable.

- (2) **Participants should be encouraged to discuss the study with anyone they wish, particularly family and friends.**

Close associates of the participant may raise questions and considerations that the participant has overlooked. These questions are better answered sooner than later. Furthermore, there is evidence to suggest that family support increases the probability of participant cooperation during the course of the research. The participant is also free to discuss participation with her personal physician.

- (3) **To be eligible for participation in this study, participants must have the capacity to give their own informed consent.**

If a participant is incapable of understanding what is expected of her as a participant in the study, it is not permissible to enroll this participant or obtain informed consent from a guardian. The study requires daily responsibilities that cannot be assumed by other persons.

- (4) **The setting in which consent is obtained should be as private as possible so participants can freely ask questions without embarrassment.**

If extraneous parties can hear the conversation, participants may be reluctant to ask appropriate questions. The consenting process should be conducted in as private an area as possible.

- (5) **To avoid pressuring the participant, only one person associated with the study should be present when the participant reviews the consent forms.**

If a second witness is required, he or she should be as unobtrusive and non-committal as the situation permits.

- (6) **The participant should be given a copy of the informed consent form after it is signed and witnessed.**

Even though participants are free to withdraw from the study at anytime, the consent form

spells out our obligations to the participant and the participant's responsibilities in enrolling in the study protocol. The consent forms also contain useful information about the study which participants may want to review from time to time. After the participant has signed the consent form, forward the consent form to the principal investigator of the clinical center for her signature.

See Appendix B for a copy of the consent forms being used at Memorial Sloan Kettering, the Wake Forest University School of Medicine, and the M.D. Anderson Cancer Center.

CHAPTER 5

BASELINE DATA COLLECTION VISIT

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5.1 OVERVIEW

Those women who are eligible and willing to participate in the study will be invited to attend a baseline clinic visit. During this visit, a clinical center staff person will meet with the prospective participants and explain the purpose of the research project and the study requirements in detail. If the participant decides to join the study officially, she will sign the Informed Consent Form and the Medical Release Form, and complete the baseline questionnaires. This chapter outlines the tasks to be performed during the baseline clinic visit.

5.2 INFORMED CONSENT

When the participant arrives at the clinical center, the staff person charged with explaining the study will describe: the purpose of the study, the study requirements, the schedule for follow-up contacts, the various measurements to be obtained, and the forms to be completed by the participant. The participant and staff person will then review the Informed Consent Form approved by their institution's Internal Review Board.

In accordance with local institutional review board guidelines, informed consent procedures and consent forms will vary somewhat by clinical center. All consent forms will stress the voluntary and confidential nature of participation in this research investigation. The participant should be told that a decision not to participate in the study will in no way influence their treatment or medical care. The participant must also be informed that they may drop out of the study at any time without penalty.

The staff person should answer any questions that the prospective participant may have. When all information has been provided and all questions have been answered satisfactorily, the participant should sign the Informed Consent Form and the Medical Release Form, if she agrees to join the study. The staff person should also witness, sign and date the consent and medical release forms. These forms should then be sent to the Clinical Principal Investigator for her signature. A copy of the Informed Consent Form and the Medical Release Form should be given to the participant to take home with her, and the originals should be filed in the participant's study file. After obtaining informed consent and the medical record release, the participant will be given the packet of baseline forms to be completed.

5.3 INSTRUCTIONS FOR COMPLETION

The following study forms will be completed at the enrollment/baseline clinic visit, which will be approximately 1 hour and 30 minutes in length. The baseline administration time for all study questionnaires is approximately 35-45 minutes. These estimates are based on the pre-testing of these forms at the Wake Forest University School of Medicine with young breast cancer patients currently undergoing treatment. Participants can be provided with opportunities to rest during the completion of the study forms, if necessary. The study coordinators should also be available to assist the patients as needed.

5.3.1 Standard Items:

Prior to giving the forms to the participants, the clinical center staff should write the following identifying information on the top of each of the study forms:

1. Patient ID Number
Clearly enter the six-digit patient ID Number that has been previously assigned and check carefully to make sure that it is copied correctly. The patient ID should be written on every page of the study forms.
2. Acrostic
Clearly enter the six-digit Acrostic and check carefully to make sure that it is copied correctly. This should appear on every page of the study forms.
3. Visit Type/Number Appropriate
Clearly check the Visit Type marked "BV" or "Baseline" on all study form.

Chapter 11 of this manual outlines the proper form for the patient ID number, acrostic, and visit type. Please refer to this chapter as necessary.

5.3.2 Baseline Questionnaires

The following information will be obtained at baseline:

- 1) Demographics.
- 2) Medical and Reproductive History.
- 3) Arm and Hand Swelling.
- 4) Personal Habits Questionnaire.
- 5) Health-Related Quality of Life
 - a) SF-12 Health Status Profile
 - b) Functional Assessment of Cancer Therapy - Breast (FACT-B).
 - c) Beck Depression Inventory.
 - d) Sleep Disturbance Scale.
 - e) Watts Sexual Functioning Questionnaire.
 - f) Self-Concept Scale.
 - g) Spirituality Subscale.

- 6) Physical Symptoms Checklist.
- 7) MOS Social Support Questionnaire.

5.3.3 Instructions for Questionnaire Administration

Detailed instructions for how to administer the surveys are provided in Chapter 6 of this manual.

5.4 REVIEW OF QUESTIONNAIRES

5.4.1 General Instructions

All data forms filled out at the baseline visit must be checked by the study coordinators before the patient leaves the clinic. The clinical center staff person should review each form for completeness and consistency, check any skip patterns, and read any written responses to assure that the answers are complete and understandable. Any missing items should be double-checked with the participants to inquire as to whether they intended to leave items blank or chose not to answer the questions. It is easier to ask questions and get clarification prior to the participant leaving the clinic.

5.4.2 Alert Values *add instr. for marking forms*

Staff will also be asked to check the participants' responses to question #9, (which is question 101 on the Quality of Life Form), on the Beck Depression Inventory to see if the patient is strongly considering suicide. Patients who make a response of "3" on this question must be referred to the Principal Investigator of the respective clinical center for immediate physician follow-up.

5.5 INSTRUCTIONS FOR COMPLETING THE MENSTRUAL DIARIES

All participants will need to be instructed in how to complete the menstrual diaries/calendars. This instruction is to be completed after the participants have filled out the baseline questionnaires.

Each day, participants will be asked to record whether they had no bleeding, spotting, or bleeding (Light, medium, heavy). The diaries are optical recognition forms, known as Teleforms, and will be scanned using a machine. There are specific instructions for the completing these forms, which are provided in Chapter 9. Clinical center staff must familiarize themselves with these instructions prior to training participants in the correct completion of the calendars.

At the end of the baseline visit, participants are to be given menstrual diaries for the current month (e.g., February), and then for the next 3 consecutive months (e.g., March, April, May). Participants should also be given the instruction sheet outlining the correct completion of the diaries. Participants should fill out all of these diaries before returning them to the coordinating center. (All participants will be reminded by coordinating center staff when it is time for them to return their completed diaries.) Participants will automatically be sent the next 3 months of dairies every quarter.

5.7 PARTICIPANT FOLLOW-UP

At the close of the follow-up visit, the follow-up schedule of data collection must be reviewed with the participants. Participants need to be informed that:

- All follow-up questionnaires and diaries will be mailed to the participants' homes by staff persons from the clinical facilitating center at the Wake Forest University School of Medicine, (formerly the Bowman Gray School of Medicine of Wake Forest University), in Winston-Salem, North Carolina. Participants should expect to receive a letter from the coordinating center welcoming them to the study within a week to 10 days of the baseline visit.
- Menstrual bleeding diaries will be automatically mailed to the participants' homes every 3 months by staff from the clinical coordinating center. Self-addressed, stamped envelopes will be enclosed in which the diaries are to be returned. Participants will be asked to complete all 3 months of the diaries before returning them to the coordinating center.
- Every 6 months, staff from the clinical coordinating center will mail participants a packet of follow-up questionnaires. These forms are to be completed and returned to the coordinating center in an enclosed self-addressed, stamped envelope. Participants should be given their Schedule of Follow-Up Visits prior to leaving the clinic, so that they will know when these forms are to be mailed to them.

An information sheet has also been developed for the participants which covers: the purpose of the study, the study procedures, and the conduct of follow-up data collection. This sheet should be given to the participants at the end of the visit.

5.7 ENDING THE BASELINE VISIT

5.7.1 Checklist for the Clinical Center Staff Persons:

Before the patient leaves the baseline visit, make sure that all the baseline activities have been completed. These include:

- Study requirements have been reviewed in detail.
- Informed Consent Form has been signed
- Medical Release Form has been signed
- All baseline forms/questionnaires have been completed
- All baseline forms have been checked for completeness, clarity, etc.
- Menstrual Bleeding Diary instruction has been provided
- Participant has been informed about follow-up data collection.
- Participants have been given their schedule for the 6 month follow-up contacts.

5.7.2 What the Participants Take Home:

The following items need to be provided to the participants to take home with them after the baseline visit has been completed. These are:

- Copy of the Informed Consent Form
- Copy of the Medical Release Form
- 4 months of Menstrual Bleeding Diaries and Instructions for Completion (i.e., current calendar month, plus the next 3 consecutive months of diaries)
- Information sheet about the study purpose, procedures, and follow-up.
- Schedule of 6 Month Follow-Up Contacts

5.8 PARTICIPANT REGISTRATION FORM

Immediately following the baseline clinic visit, the Participant Registration Form needs to be completed by clinical center staff. This form will serve to register the participants in the study, and contains information about the participants' name, address and phone number, designated physician, age, race/ethnicity, stage of cancer, date of birth, date of baseline visit, and participant identification number.

The Participant Registration Form is to be filled out if the participants have completed all the requirements of the baseline clinic visit (described above). **The registration form is then to be faxed to Ms. Judy Bahnson at the clinical coordinating center the same day that the participant completes the baseline visit.** The receipt of this form at the coordinating center will officially enroll the person in the study. It is very important that the registration forms are received in a timely manner, so that

the participants can be entered into the data base and the follow-up procedures can be implemented.

5.9 SHIPMENTS TO CLINICAL COORDINATING CENTER

All data forms and questionnaires completed by clinical center staff and/or the participants are to be mailed to the clinical coordinating center on roughly **the 15th and the 30th of each month**. This includes the packet of questionnaires completed by the participants, and a hard copy of the participant registration and eligibility forms. Questionnaires received at the clinical coordinating center will be re-checked for clarity, completeness, etc., and clinical center staff may be contacted if questions arise regarding particular items and/or participants. Adherence to this mailing schedule is requested, so that study forms are received and entered into the centralized data bases efficiently.

5.10 MEDICAL CHART REVIEWS

A review of the participants' medical records will be completed following the baseline visit, using the Chart Review Form. **The baseline chart review form should be returned to the coordinating center no later than 6 weeks following the participants' baseline clinic visit.** Instructions for the completion of this form are included in Chapter 7 of this manual.

CHECKLIST FOR COMPLETION OF THE BASELINE VISIT TASKS

Checklist for the Clinical Center Staff Persons:

- ☐ Study requirements have been reviewed in detail
- ☐ Informed Consent Form has been signed
- ☐ Medical Release Form has been signed
- ☐ All baseline forms/questionnaires have been completed
- ☐ All baseline forms have been checked for completeness, clarity, etc.
- ☐ Menstrual Bleeding Diary instruction has been provided
- ☐ Participant has been informed about follow-up data collection.
- ☐ Participants have been given their schedule for the 6 month follow-up contacts.

Participants Have Been Given the Following to Take Home:

- ☐ Copy of the Informed Consent Form
- ☐ Copy of the Medical Release Form
- ☐ 4 months of Menstrual Bleeding Diaries and Instructions for Completion
(i.e., current calendar month, plus the next 3 consecutive months of diaries)
- ☐ Information sheet about the study purpose, procedures, and follow-up.
- ☐ Schedule of 6 Month Follow-up Contacts

PARTICIPANT INFORMATION SHEET

What is the name of the study?

The name of the study is: Menstrual Cycle Maintenance and Quality of Life After Breast Cancer Treatment: A Prospective Study.

What is the purpose of the study?

The purpose of this study is to determine how treatment for breast cancer may affect a woman's menstrual cycles and her quality of life.

How long will the study last?

The study will begin January 1, 1998 and will end in April of 2001.

How many women will participate in the study?

800 women will participate in this research study.

How many hospitals are involved in the study?

Patients are being asked to participate in the study from three cancer centers in the United States. These centers are the Memorial Sloan-Kettering Cancer Center in New York, New York; the M.D. Anderson Cancer Center in Houston, Texas; and the Wake Forest University School of Medicine in Winston-Salem, North Carolina.

Who is being asked to participate in the study?

To be asked to participate in the study, a woman must have been diagnosed with breast cancer for the first time within the past 6 months, be 45 years of age or younger, and be having regular menstrual cycles at the time her breast cancer was diagnosed. Women whose breast cancer has metastasized to another part of the body, or who currently have or have had another form of cancer in the past, (other than non-melanoma skin cancer or stage 0 cervical cancer), are ineligible for the study.

What will I be asked to do in this study?

If you agree to participate in this study, you will be asked to attend a baseline clinic visit, which will be about one and a half hours long. At this visit, more detailed information will be provided to you regarding the purpose of the study, and you will be asked to participate. If you decide to join the study, you will be asked to sign an Informed Consent Form and a Medical Release

Form. You will then be asked to fill out questionnaires regarding your health status, family medical history, and quality of life. You will also be given a monthly calendar for you to mark when you have your period each month.

You do not have to return to the medical center in-person after the baseline clinic visit. You will simply be sent questions and calendars to complete and return to us through the mail.

How will I receive the follow-up questionnaires and calendars?

In order to help reduce costs, all follow-up questionnaires will be mailed to you from the Wake Forest University School of Medicine. That means that even if you enrolled in the study at the M.D. Anderson Cancer Center or Memorial Sloan-Kettering, you will still receive all of your follow-up questionnaires from the Wake Forest University School of Medicine.

When will I receive the follow-up questionnaires and calendars?

Every six months, from the time of your baseline clinic visit, you will be sent a set of questionnaires to complete and mail back to staff at the Wake Forest University School of Medicine in self-addressed, stamped envelopes. For example, if you had your baseline visit in April, 1998, you would receive questionnaires in: October, 1998; April, 1999; October, 1999; April, 2000; October, 2000; and April, 2001. These questionnaires will take approximately 30 minutes to complete.

Every three months you will also receive 3 monthly calendars for you to mark when you have your period. For example, if you are enrolled in the study in April, 1998, you will be given calendars for the months of April - July, 1998, (the month you joined the study plus the next three consecutive months). At the end of July, 1998, you will be sent calendars for August - October of 1998, and so on. The calendars are to be returned to the Wake Forest University School of Medicine in self-addressed stamped envelopes every 3 months.

Does my doctor know about the study?

All physicians at each of the three hospitals involved in the study have been told about this research project. In fact, in order to ask you to join the study, we had to get permission from your primary doctor before we could talk with you about the study.

Who do I contact with questions after the baseline clinic visit?

Any questions you have about the study, the questionnaires, or the calendars can be referred to: Ms. Judy Bahnson, Wake Forest University School of Medicine, Department of Public Health Sciences, Medical Center Boulevard, Winston-Salem, NC 27157-1063. Her telephone number is (910) 716-2116.

Questions should not be directed to the specific person at the clinical center who enrolled you in the study.

CHAPTER 6

COLLECTING PARTICIPANT INFORMATION

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6.1. INTRODUCTION

At baseline, the questionnaires will be completed by the participants (i.e., self-administered). However, there may be particular circumstances when interviewer administration in the clinic or by telephone is required. Although it is not anticipated that these special situations will arise often, there may be instances in which factors such as poor eyesight, ill health, weather, or conflicting time commitments will necessitate a change in how the questionnaires are administered. Therefore, instructions for both self-administered and interviewer-administered questionnaires are provided.

6.2. THE ROLE OF THE CLINICAL CENTER STAFF

The clinical center staff persons play a critical role in the collection of baseline information. The staff person's ability to develop and maintain a positive rapport with the participants will influence initial recruitment, the quality of the data obtained, and the willingness of the participant to remain in the study for its duration. The first contact with a participant will set the tone for the entire study. It is important that the staff maintain a professional and friendly manner at every contact with the participants.

In the ideal situation, the staff person's presence should not influence a participant's decision to join the study or her answers on the questionnaires. There is the potential for the quality of the participant's responses to be affected by the general attitudes and actions of the interviewer. Different staff members should obtain the same information from the same participants. In order to enhance the neutrality of the staff, the essential elements of the study protocol should be followed in the same manner for every participant. The staff members should convey a sense of impartiality. They should be gracious and adaptable to all participants regardless of whether their dress, appearance, style of speech, or personal preferences are consistent with the staff person's values and preferences.

Clean, neat and professional dress are also important. The staff person's dress and demeanor should convey that he or she is an appropriate representative of the medical community, that the research is important, and that the participant is a respected member of the study. In addition, the demeanor of the staff member should be friendly, yet professional. A major objective is to put the participant at ease. If the participant is not relaxed it will be more difficult to accomplish the tasks of the baseline visit.

6.3 THE SETTING

The interviewer or other clinic staff person should be available to greet the participants as they arrive. If you are situated in an office that is difficult to locate, or if you know that a participant has physical limitations, arrange to meet the participant ahead of time and escort her to the place where the survey will be administered.

Optimally, the baseline clinic visit should be conducted in a comfortable and private place, free from interruptions or distractions. This will enable the participant to concentrate on the forms more completely and become less fatigued during the questionnaire administration.

Family members or friends of the participant should not be present during the baseline interview, particularly when the patient is completing the questionnaires. Oftentimes, family members will offer to help participants complete the questionnaires, but this may bias the participants' responses to the questionnaire items. If family members/friends offer to help respondents, politely decline their offer of help, and indicate that you would prefer to have the patient complete the questionnaires alone. The interviewer should explain the necessity of providing privacy and confidentiality to research participants, and should be prepared to suggest a place where the family member(s) or friend(s) can wait comfortably while the participant completes the baseline visit and questionnaires. Be polite, but firm.

6.4 PREPARING FOR THE BASELINE VISIT

In preparing for the baseline visit and questionnaire administration, the staff should:

- a) Review the MOP and training materials.
- b) Re-familiarize themselves with the consent forms and questionnaires.
- c) Organize all the necessary materials, such as pens, extra paper, etc.
- d) Be certain the interview room(s) is neat and organized.
- e) Review any information available on the participant, and information needed for the visit (e.g., name of participant, time of appointment, whether she is currently receiving treatment).
- f) Complete the standard items on the top of all study forms: Participant Identification Number, Participant Acrostic, and Visit Type.
- f) Be certain their appearance is appropriate to conduct the visit.

All data forms should be completed in ink, not pencil. For best results, black ink should be used. Other colors, especially light blue, are not picked up by many fax machines, and will cause interpretation errors. Dark colors always work better than light colors.

6.5 ASSESSING THE LITERACY AND/OR PHYSICAL STATUS OF THE PARTICIPANTS

It is possible that the clinic staff will encounter a participant with vision problems or physical conditions which will make it difficult for her to complete the questionnaire on her own. Other participants may have problems with literacy/reading. Approximately 6% of the American population (with a range from 2-13% across individual states) are considered functionally illiterate, having completed fewer than four years of formal education. This rate may also be an underestimate of the number of individuals who are likely to have difficulty completing a self-

administered questionnaire because of problems with concentration, reading fluency, or comprehension.

It is the task of the clinic staff person to determine whether the participant is able to complete the questionnaire without assistance. In many cases, the participant's "fitness" will be readily apparent. For example, some patients may appear extremely fatigued or may tell you that they are unable to read the questionnaire due to vision problems.

It may be harder to recognize participants with low literacy skills, unless the participants verbalize that they are unable to read at a level sufficient to complete the questionnaires. Cues to low reading skills may include participants asking many questions, completing the measures very slowly, glancing up and around, appearing confused, or checking off responses without clearly reading the items. In these instances, data will be poor. Therefore, *while avoiding any embarrassment to the participants*, it is in the best interest of the study and the participants to determine if they are able to complete the questionnaire on their own. If you suspect a participant is unable to read, you may say to him/her: "Many individuals prefer to have the questionnaires read to them. Would you like me to read the questionnaires to you?" If the answer is yes, read the questionnaires to the participant following the guidelines for interviewer administration which are reviewed later in this chapter.

6.6 ANSWERING QUESTIONS

Regardless of whether the questionnaires are self- or interviewer administered, participants will have questions that need to be addressed. In order to be able to anticipate participants' questions and respond to them appropriately, clinical center staff should be thoroughly familiar with the forms before they are used with the participants. Staff will be unable to give assistance to participants if they do not have a working knowledge of the structure and content of the questionnaires.

In answering questions, survey administrators must be careful not to bias the participants' responses. The data collector may read a question to a respondent, define terms, indicate where the answer is to be marked, etc., but they should not paraphrase questions unless it is absolutely necessary. It is easy to alter the meaning of a question in this way. Therefore, the data collector should not suggest an answer for the participant.

In general, most of the participants' questions can be handled by reminding them to follow the directions on the questionnaire, or simply by rereading the statement to the respondents. The interviewer should read the statement exactly as it is written. The administrator should remind the participants that they should answer the question with the response that they believe is more true for them at the present time.

If a respondent tells the data collector which answer she has selected, the staff person should refrain from reacting to that answer or conveying either approval or disapproval of the

population (with a range from 2-13% across individual states) are considered functionally illiterate, having completed fewer than four years of formal education. This rate may also be an underestimate of the number of individuals who are likely to have difficulty completing a self-administered questionnaire because of problems with concentration, reading fluency, or comprehension.

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participant's choice. The administrator may indicate to the participant that there are no right or wrong answers to these questions, and that it is her choice as to how to respond to the statement. **Under no circumstances should the survey administrator help the participant decide how to mark a questionnaire item.**

6.7 SELF-ADMINISTRATION OF THE QUESTIONNAIRES

If it has been determined that the participant is able to complete the questionnaires on her own, introduce the questionnaires to the study participant by telling her that the questionnaires contains questions about her health history, symptoms, and quality of life. The interviewer should indicate that as a participant in the study, we are asking her to complete this questionnaire because we are interested in knowing how treatment for breast cancer influences a young woman's menstrual cycles and quality of life.

It is sometimes useful to tell participants that there are no right or wrong answers on the questionnaires. It is often helpful to tell this to the respondent if any uncertainty or hesitation is observed. It is important to put the participants at ease.

In addition, the respondents should be reminded that their responses to the measures will be kept completely confidential. That is, the respondent's identity will be protected. No one but the research staff will have access to the patients' names, and data will be entered into the computer by identification number rather than a name. Results will be calculated using large groups of patients, and not individuals. If results are published, no patients' names or other identifying characteristics will ever be used.

The clinic staff person should read over the directions to the questionnaires with the participant and then leave her to complete the forms in privacy. The staff person should remain in the general area, however, in case the participant has a question or needs some other form of assistance.

Some participants in this study may need to take a break midway through the collection of the data forms. We are suggesting that the participants complete at least half of the study forms before a rest is provided, if at all possible.

6.8 INTERVIEWER ADMINISTRATION OF THE QUESTIONNAIRES

6.8.1 The Interviewer

The interviewer plays a critical role in the process of data collection. It is important that the interviewer does not influence the participant's response to any question. Since more than one interviewer may be administering the questionnaires, the following guidelines should be used to standardize the administration so that each interviewer administers the questionnaires in the same way. Variability in administration of the questionnaires introduces bias in data collection and

reduces the quality of the data.

In the ideal situation, the interviewer's presence should not influence the participant's perceptions or responses to questionnaire items, and different interviewers should be able to obtain the same responses from the same participant. Recognizing the limitations inherent in this ideal, however, there are methods that can enhance the neutrality of the interviewer. Interviewers should not provide either verbal or non-verbal responses that could influence the participant's responses. For example, an interviewer should not convey surprise, pleasure, or disapproval to any answer. The interviewer's role is to obtain honest, uninfluenced responses to the questions.

The interviewer should be thoroughly familiar with the questionnaire before interviewing the first participant. This will ensure that the interviewer can easily address the participants' questions or concerns. Inexperienced interviewers should also practice completing an interview by practicing with someone who is pretending to be a participant. This will help to reduce the mechanical style that sometimes results from reading unfamiliar material.

6.8.2 Introducing the Study Questionnaires

Introduce the questionnaires to the study participants by telling them that the questionnaires contains questions about their health history, symptoms, and quality of life. The interviewer should indicate that as a participant in the study, we are asking them to complete this questionnaire because we are interested in knowing how treatment for breast cancer influences a young woman's menstrual cycles and quality of life.

It is useful to tell participants that there are no right or wrong answers on the questionnaires. It is often helpful to tell this to the respondent if any uncertainty or hesitation is observed. It is important to put the participants at ease.

In addition, the participants should also be reminded that their responses to the measures will be kept completely confidential. That is, the participant's identity will be protected. No one but the research staff will have access to the patients' names, and data will be entered into the computer by identification number rather than a name. Results will be calculated using large groups of patients, and not individuals. If results are published, no patients' names or other identifying characteristics will ever be used.

6.8.3 Administering the Questionnaires

Read through the directions for each form with the participants and ask them if they clearly understand how the questions are to be answered. If the participants have no questions, proceed to read the statements to the participants, using the following guidelines:

Read each statement to the respondents verbatim. The wording has been carefully selected and tested in order to ensure the validity of the participant's responses. Do not paraphrase or simplify the statements. Even minor changes in wording can affect the validity of

the results.

Read the questions to the respondent in the order in which they were written. Do not skip over statements and then come back to them later.

Record the participants' responses on the questionnaires as they are given. Never depend on memory to mark the participants' choices.

6.8.4 Answering Questions

The interviewer should be thoroughly familiar with the questionnaire before interviewing the first participant. This will ensure that the interviewer can easily address the participants' questions or concerns. Here are some points to remember in answering questions:

a) The interviewer may repeat questions if the participant does not understand them. The interviewer should also assume responsibility for faulty communication by saying that perhaps they didn't read the questions clearly enough, etc.

b) If the respondent complains about particular questions, wording or redundancy of items, respond that you do not know why it the questionnaires were designed the way they were, but that it is important for them to answer the questions as best they can.

c) Keep explanations to a minimum. Don't interpret questions. The interviewer may, for example, define a word, but not say "I think they mean...." It is easy to alter the meaning of a question in this way. In some rare instances, it may be necessary to paraphrase or simplify a statement for a respondent, but paraphrasing a question should only be done if absolutely necessary.

d) The majority of questionnaire items have fixed response categories. All items must be answered using one of the existing response choices or the participants' answers cannot be entered into the computer. In an interview format, if a participant replies that none of the choices is correct, suggest that the choice that comes closest be selected. If the respondent still refuses, note this on the questionnaire.

e) If the participants' answer, "I don't know," to a particular question, give them a little more time to think. Sometimes this response is given to cover momentary confusion, and a meaningful answer will be forthcoming if a few moments are allowed for thought. The interviewer may say something like: "Take a moment to think about your answer."

f) In the event a respondent gives an inappropriate response, repeat the question and the response categories. For example, if the question asks the respondents to indicate how much they agree with a statement, and a participant says, "that's true," the interviewer could say, "Would you say you strongly agree, agree, etc.?"

g) If the respondent refuses to respond to a question for any reason, accept the refusal without reaction and move on to the next question.

General Reminders:

Be patient and polite. Convey a sense that the respondent's answers are important. Allow plenty of time for the respondent to understand the questions.

Never suggest an answer or disagree with a response. The interviewer's role is to obtain and record *the participants'* answers.

Always ask the questions and give the response categories verbatim and in the order they appear in the questionnaire.

The interviewer may, at any point in the interview, reassure the respondent that her answers will be kept confidential, that there are no right or wrong answers, and that the interview is going well.

6.9 TELEPHONE INTERVIEWING

Although it is not anticipated that a telephone interview will be required very often at baseline, there may be situations in which the participant cannot for reasons of ill health, weather conditions, other time commitments, etc., finish completing questionnaires which was initiated at the baseline visit. Additionally, there may be rare situations in which circumstances demand the completion of an entire questionnaire by telephone.

Telephone interviewers should follow the same guidelines as for the interviewer administration of the questionnaires. Adequate time should be allowed, so the interview can be completed in one call.

6.10 EDITING THE QUESTIONNAIRES

An important role of the clinical center staff is to examine the completed surveys immediately after the participants have completed them and/or an interview has been completed. If the participant has skipped questions and/or filled the questionnaires out incorrectly, the staff person needs to discuss this with the participant before she leaves the office. Persons who have filled out the forms incorrectly should be asked to complete the questionnaires in the appropriate manner. If an item is missing or incomplete, the interviewer should ask the participants if they noticed the item and meant to leave it blank or simply overlooked it. If the participants decline to provide the information when it is brought to their attention, the interviewer should accept the participant's refusal without comment. It is important to respect the participant's right to refuse to answer any questions.

If a question is left blank intentionally (i.e., the participant declined to answer it), the clinic staff person should write "PM" (Permanently Missing) next to the question on the form. This marking will serve as a visual cue to the coordinating center staff that the information was left blank intentionally, and that the data will be missing.

6.11 STORING THE QUESTIONNAIRES

Once the questionnaires have been completed and edited by the clinic staff person, a copy of the questionnaires should be made. The original questionnaires are to be mailed to the coordinating center bi-weekly (i.e., the 15th and 30th of each month), and the copies should be kept at the clinical centers permanently. All questions should be stored in a secure place within the clinic. The questionnaires should not be left unattended where non-research staff can review the participants' responses. Information collected for research purposes can only be shared with other members of the research team, and the participants' privacy must be protected at all times. Staff persons should never discuss any of the responses with anyone who is not directly involved in the study.

THE ROLE OF THE CLINICAL CENTER STAFF

● The clinical center staff persons play a critical role in the collection of baseline information. The staff person's ability will influence:

- initial recruitment,
- the quality of the data obtained
- willingness of the participant to remain in the study for its duration.

The first contact with the participant will set the tone for all future interactions.

At each contact with the participants, the staff must maintain:

- a professional and friendly manner
- a sense of neutrality
- sense of impartiality (gracious and adaptable)
- clean, neat and professional dress

THE SETTING

The interviewer or other clinic staff person should be available to greet the participants as they arrive.

Optimally, the baseline clinic visit should be conducted in a comfortable and private place, free from interruptions or distractions. This will enable the participant to concentrate on the forms more completely and become less fatigued during the questionnaire administration.

Family members or friends of the participant should not be present during the baseline interview, particularly when the patient is completing the questionnaires.

PREPARING FOR THE BASELINE VISIT

● In preparing for the baseline visit and questionnaire administration, the staff should:

- a) Review the MOP and training materials.
- b) Re-familiarize themselves with the consent forms and questionnaires.
- c) Organize all the necessary materials, such as pens, extra paper, etc.
- d) Be certain the interview room(s) is neat and organized.
- e) Review any information available on the participant, and information needed for the visit (e.g., name of participant, time of appointment, whether she is currently receiving treatment).
- f) Complete the standard items on the top of all study forms: Participant Identification Number, Participant Acrostic, and Visit Type.
- f) Be certain their appearance is appropriate to conduct the visit.

STANDARD ITEMS

All data forms should be completed in ink, not pencil. For best results, black ink should be used. Other colors, especially light blue, are not picked up by many fax machines, and will cause interpretation errors. Dark colors always work better than light colors.

ASSESSING THE STATUS OF THE PARTICIPANTS

In many cases, physical limitations will be readily apparent. For example, some patients may appear extremely fatigued or may tell you that they are unable to read the questionnaire due to vision problems.

Cues to low reading skills may include:

- participants asking many questions
- completing the measures very slowly
- glancing up and around
- appearing confused
- checking off responses without clearly reading the items.

ANSWERING QUESTIONS

● Clinical center staff should be thoroughly familiar with the forms before they are used with the participants. Staff will be unable to give assistance to participants if they do not have a working knowledge of the structure and content of the questionnaires.

In answering questions, survey administrators must be careful not to bias the participants' responses.

The data collector may read a question to a respondent, define terms, indicate where the answer is to be marked, etc., but they should not paraphrase questions unless it is absolutely necessary.

The data collector should never suggest an answer for the participant.

In general, most of the participants' questions can be handled by reminding them to follow the directions on the questionnaire, or simply by rereading the statement to the respondents. The interviewer should read the statement exactly as it is written.

The administrator should remind the participants that they should answer the question with the response that they believe is more true for them at the present time.

SELF-ADMINISTRATION OF THE QUESTIONNAIRES

● Introduce the questionnaires to the study participants by telling her that the questionnaires contains questions about their health history, symptoms, and quality of life.

The interviewer should indicate that we are asking her to complete this questionnaire because we are interested in knowing how treatment for breast cancer influences a young woman's menstrual cycles and quality of life.

Respondents should be reminded that their responses to the measures will be kept completely confidential. That is, the respondent's identity will be protected. No one but the research staff will have access to the patients' names, and data will be entered into the computer by identification number rather than a name. Results will be calculated using large groups of patients, and not individuals. If results are published, no patients' names or other identifying characteristics will ever be used.

The clinic staff person should read over the directions to the questionnaires with the participant and then leave her to complete the forms in privacy. The staff person should remain in the general area, however, in case the participant has a question or needs some other form of assistance.

Some participants in this study may need to take a break midway through the collection of the data forms.

We are suggesting that the participants complete at least the quality of life, social support, symptoms, and swelling forms before a rest is provided, if at all possible.

INTERVIEWER ADMINISTRATION

● The Interviewer

Important that the interviewer does not influence the participant's response to any question.

Guidelines should be used to standardize the administration so that each interviewer administers the questionnaires in the same way.

There are methods that can enhance the neutrality of the interviewer. Interviewers should not provide either verbal or non-verbal responses that could influence the participant's responses. For example, an interviewer should not convey surprise, pleasure, or disapproval to any answer. The interviewer role is to obtain honest, uninfluenced responses to the questions.

The interviewer should be thoroughly familiar with the questionnaire before interviewing the first participant.

Inexperienced interviewers should also practice completing an interview by practicing with someone who is pretending to be a participant. This will help to reduce the mechanical style that sometimes results from reading unfamiliar material.

Introducing the Study Questionnaires

● Introduce the questionnaires to the study participants by telling her that the questionnaires contains questions about their health history, symptoms, and quality of life.

The interviewer should indicate that we are asking her to complete this questionnaire because we are interested in knowing how treatment for breast cancer influences a young woman's menstrual cycles and quality of life.

Respondents should be reminded that their responses to the measures will be kept completely confidential. That is, the respondent's identity will be protected. No one but the research staff will have access to the patients' names, and data will be entered into the computer by identification number rather than a name. Results will be calculated using large groups of patients, and not individuals. If results are published, no patients' names or other identifying characteristics will ever be used.

Conducting the Interview

Read through the directions for each form with the participants.

Read each statement to the respondents verbatim. The wording has been carefully selected and tested in order to ensure the validity of the participant's responses. Do not paraphrase or simplify the statements. Even minor changes in wording can affect the validity of the results.

Read the questions to the respondent in the order in which they were written. Do not skip over statements and then come back to them later.

Record the participants' responses on the questionnaires as they are given. Never depend on memory to mark the participants' choices.

Answering Questions

The interviewer should be thoroughly familiar with the questionnaire before interviewing the first participant.

Points to remember in answering questions:

a) The interviewer may repeat questions if the participant does not understand them. The interviewer should also assume responsibility for faulty communication by saying that perhaps they didn't read the questions clearly enough, etc.

b) If the respondent complains about particular questions, wording or redundancy of items, respond that you do not know why it the questionnaires were designed the way they were, but that it is important for them to answer the questions as best they can.

c) Keep explanations to a minimum. Don't interpret questions. The interviewer may, for example, define a word, but not say "I think they mean...." It is easy to alter the meaning of a question in this way. In some rare instances, it may be necessary to paraphrase or simplify a statement for a respondent, but paraphrasing a question should only be done if absolutely necessary.

● d) The majority of questionnaire items have fixed response categories. All items must be answered using one of the existing response choices or the participants' answers cannot be entered into the computer. In an interview format, if a participant replies that none of the choices is correct, suggest that the choice that comes closest be selected. If the respondent still refuses, note this on the questionnaire.

e) If the participants' answer, "I don't know," to a particular question, give them a little more time to think. Sometimes this response is given to cover momentary confusion, and a meaningful answer will be forthcoming if a few moments are allowed for thought. The interviewer may say something like: "Take a moment to think about your answer."

f) In the event a respondent gives an inappropriate response, repeat the question and the response categories. For example, if the question asks the respondents to indicate how much they agree with a statement, and a participant says, "that's true," the interviewer could say, "Would you say you strongly agree, agree, etc.?"

g) If the respondent refuses to respond to a question for any reason, accept the refusal without reaction and move on to the next question.

General Reminders:

- Be patient and polite. Convey a sense that the respondent's answers are important. Allow plenty of time for the respondent to understand the questions.

Never suggest an answer or disagree with a response. The interviewer's role is to obtain and record *the participants'* answers.

Always ask the questions and give the response categories verbatim and in the order they appear in the questionnaire.

The interviewer may, at any point in the interview, reassure the respondent that her answers will be kept confidential, that there are no right or wrong answers, and that the interview is going well.

EDITING THE QUESTIONNAIRES

● An important role of the clinical center staff is to examine the completed surveys immediately after the participants have completed them and/or an interview has been completed.

If the participant has skipped questions and/or filled the questionnaires out incorrectly, the staff person needs to discuss this with the participant before she leaves the office.

Persons who have filled out the forms incorrectly should be asked to complete the questionnaires in the appropriate manner.

If an item is missing or incomplete, the interviewer should ask the participants if they noticed the item and meant to leave it blank or simply overlooked it.

If the participants decline to provide the information when it is brought to their attention, the interviewer should accept the participant's refusal without comment. It is important to respect the participant's right to refuse to answer any questions.

● If a question is left blank intentionally (i.e., the participant declined to answer it), the clinic staff person should write "PM" (Permanently Missing) next to the question on the form. This marking will serve as a visual cue to the coordinating center staff that the information was left blank intentionally, and that the data will be missing.

Recheck to ensure that the Participant Identification Number, Acrostic, and visit type have been listed on each page of the forms.

*each questionnaire has a date completed at
end - Be sure filled in blocks.*

STORING THE QUESTIONNAIRES

● Once the questionnaires have been completed and edited by the clinic staff person, a copy of the questionnaires should be made.

The original questionnaires are to be mailed to the coordinating center bi-weekly (i.e., the **15th and 30th** of each month), and the copies should be kept at the clinical centers permanently.

All questions should be stored in a secure place within the clinic. The questionnaires should not be left unattended where non-research staff can review the participants' responses.

Staff persons should never discuss any of the responses with anyone who is not directly involved in the study.

CHAPTER 7

CHART REVIEW FORMS

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7.1 OVERVIEW

The Chart Review Form will provide valuable clinical information which will be used to determine eligibility for the study and describe some of the disease and treatment characteristics of young women who have been diagnosed with breast cancer.

During the first four to six months of the study, chart reviews may need to be completed in order to identify eligible participants in the study. After the initial six months of the study, (as patients are recruited for current clinic rosters or registries), the patient chart reviews will be completed after the baseline visit has been completed.

The answers to the questions on the chart review form will be abstracted from the patients' hospital records, including physician notes and pathology reports. What follows is a description of what is needed for each question.

7.2 CHART REVIEW QUESTIONS

Question 1. Date of Breast Cancer Diagnosis

Please enter the month, day, and year of breast cancer diagnosis. This date should be based on the day the Fine Needle Aspiration (FNA), Stereotactic core biopsy or excisional biopsy was done, not the mammogram.

Question 2. Date of Cancer Definitive Surgery

Please enter the month, day, and year that the patient had final definitive surgery for breast cancer. In some cases, for example, when an individual had a excisional biopsy, the date of surgery and date of breast cancer diagnosis will be the same.

Question 3. Type of definitive surgery:

A. Lumpectomy/excisional biopsy or quadrantectomy. (Check: No or Yes)

The above terms refer to the removal of the tumor only, the removal of the tumor and some surrounding tissue, (to ensure a tumor-free margin) and/or removal of the tumor and the tissue of the involved quadrant. Other terms that may appear in the chart include tylectomy, partial mastectomy and segmental mastectomy.

B. Mastectomy. (Check: No or Yes)

Mastectomy is the removal of the breast. Other terms which may appear in the chart include total mastectomy, which involves removal of the entire breast, the pectoral muscle and a portion of the axillary nodes. This procedure is also referred to as a simple mastectomy. Radical and extended radical mastectomy involve removal of the breast, the major and minor

pectoral muscles, the entire axillary contents and possibly the internal mammary lymph nodes.

Question 4. Margins

The margins refer to the edges of the surgical specimen or, in other words, the periphery of the resection from the final pathology report of the definitive surgery. It indicates if cancer is still left in the patient. The pathology report will state: "The margins (of resection) do not contain cancer." or "The margins contain intraductal cancer at ... (whichever location)."

Question 5. Did patient have reconstructive surgery? (Please check either No or Yes. If you check 'yes,' enter what type of reconstructive surgery the patient had.)

This question deals with reconstructive surgery of the breast. Many times, the loss of a breast has a negative impact on a woman's body-image, self esteem and general emotional well-being. Reconstructive surgery to restore the natural look and feel of the breast and too establish symmetry can lessen the psychological trauma of mastectomy. Reconstructive surgery may be done at the same time as the mastectomy, or months and even years later. Several descriptions of breast reconstruction follow.

Expander: With this type of reconstructive surgery an incision is made through the previous mastectomy scar, the skin is raised and the pectoralis major muscle is split to form a pocket. If the individual has an abundance of skin on the chest wall then an implant is inserted. If the individual has taut skin on the chest wall, an expander will be inserted and over a period of weeks or months a saline solution will be inserted to stretch the skin tissue. When adequate expansion has occurred the expander is replaced with a standard implant.

Tram: Transposition rectus abdominous myocutaneous flap. With this type of reconstructive surgery an incision is made above the pubic area, a portion of the abdominal muscle with a portion of attached skin is then brought through the upper portion of the abdomen in a skin tunnel and repositioned at the breast area. The shape of the breast is created with the patient's own tissue instead of an implant.

Gluteus/Latissimus/Other: This surgical reconstruction uses a portion of the buttock muscle. Fat and skin are detached and the artery/vein are sewn (anastomosed) into the axilla vessels. The breast shape is then surgically imitated. This reconstruction can also be performed as a free flap in which the tissue is detached and sewn (anastomosed) into the axillary vessels.

Question 6. Breast affected:

Enter which breast is affected: left, right or both.

It is unlikely that a women will present with cancer in both breasts. If she later develops cancer in the other breast, this is recorded as a medical event, but we will only follow the participant for her first cancer.

Question 7. Invasive cancer:

Enter absent or present. If invasive, enter the greatest diameter. The preferred first choice answer is the actual tumor size if it is available.

Question 8. How was invasive tumor size determined?

In most cases, the size of the invasive tumor will come from the pathology report. It is possible, but unlikely, that the size could be estimated by a mammogram or ultrasound, or could be assessed clinically.

In the event that both intraductal and invasive size are listed, please note the size of the invasive tumor.

Question 9. Histologic tumor type:

This information will come from the pathology report. Check the appropriate box. If you mark "other," list the tumor type.

Question 10. Prognostic Features:

This information will also be part of the pathology report. Please check the appropriate box for Nuclear or Histologic Grade. It is possible that the information may appear as a number. For example, the pathology report might say, "Grade: Bloom & Richardson (Elston modification) 3." This is the same as Grade III, or Blacks Nuclear Grade II.

A. Histologic Grade (invasive only)

<u>Grade</u>	<u>Key Descriptive Words</u>
Grade I	Low Grade, with differentiation
Grade II	Moderate
Grade III	High Grade, Poor
Grade IV	Anaplastic or un-differentiation

Nuclear Grade (invasive only)

<u>Grade</u>	<u>Key Descriptive Words</u>
Grade I	Mild differentiation
Grade II	Medium differentiation
Grade III	Poor differentiation

Information for B - F should appear as part of the Prognostic Features and Histologic Grade on the pathology report. Check the appropriate answer for each.

Questions 11/12. Refer to the lymph nodes located in the breast area of the chest wall.

The breast has three major pathways of lymphatic drainage. The internal mammary pathway, the interpectoral pathway and the axillary pathway. The axillary pathway is the major lymphatic drainage for the mammary gland, and regional metastatic disease from breast cancer is most usually found in the axilla. Lymph node axillary involvement is one of the most important prognostic factors for distant metastases and survival, and plays a role in developing treatment plans for each individual woman.

Question 11. Axillary Node Dissection

This refers to the surgical procedure where a sample of lymph nodes are removed from the axilla (the area under the arm and nearest the breast where the tumor is located). Check the appropriate answer.

Question 12. Was Sentinel lymph node mapping technology used?

This refers to a new procedure called lymph node mapping. It involves finding the "sentinel" lymph node or the initial lymph node that is at risk for metastatic disease. Just prior to the scheduled operation, radioisotope technetium is injected around the tumor or biopsy cavity. After anesthesia has been administered, but prior to the surgical procedure, technetium and/or blue dye is injected around the cancerous tumor. These dyes take the pathway that cancer cells would take. Therefore the sentinel lymph node is the first node that would be affected by cancer if any of the lymph nodes were affected. The node is removed and examined by pathologists. If it does not contain cancer, then the rest of the lymph nodes do not contain cancer. This method may provide a less invasive surgical procedure for women and fewer complications than the standard axillary dissection.

Question 13. Number of nodes examined?

Enter the number from the pathology report.

Question 14. Number of nodes positive?

Enter the number of positive nodes from the pathology report.

Question 15. Extra-nodal invasion/regional invasion.

This refers to the spread of cancer cells outside the axillary lymph node. Please check the appropriate box.

Question 16. Receptors.

This question deals with samples of the cancer tumor which are examined for the presence of hormone receptors. These receptors are small proteins within the cancer cell. Measurement of hormone receptors provides important information for treatment planning and predicts response to hormonal therapies. Patients whose cancer cells have receptors for the female hormones estrogen and progesterone generally have slower growing tumors and perhaps a better prognosis. Adjuvant therapy with anti-estrogen drugs is a promising area of research and treatment. These tests are often done prior to surgery, and may appear in a separate report.

Please check the appropriate box for BOTH estrogen and progesterone.

Adjuvant Therapy

This section refers to additional therapies women may have beyond the surgical procedure. This may include radiation therapy, chemotherapy, and/or hormonal therapy.

Question 17. Did the patient have radiation therapy?

Please check the correct response. If no, skip to question 22. If yes, enter the date the patient started radiation and answer questions 18-21.

Question 18. Radiation after breast reconstructive surgery?

Check the appropriate box. If yes, fill in the additional information on the type of radiation the patient received. In most cases, the women will receive "irradiation" by a beam. In some cases, a woman may have radioactive implants placed internally in the breast, which is known as interstitial radiation.

Question 19. Radiation to chest wall after lumpectomy or mastectomy.

Please check the appropriate response.

Question 20. Number of treatments.

Please enter the number of treatments the patient received.

Question 21. Total dose received.

Enter the total dose in rads and boosts the patient received.

Question 22. Did patient have chemotherapy?

Check No or Yes. If no, go to question 24. If yes, enter the date the patient started chemotherapy and answer question 23.

Question 23. Type of chemotherapy.

Please list type dose and duration of all chemotherapy agents the patient received. For example, if a patient received cyclophosphamide, methotrexate, and S-Fluorouracil, (which is sometimes abbreviated CMF), list each drug and dosing information separately.

Question 24 Did patient have hormonal therapy?

Please check either No or Yes. If no, go to question 26. If yes, answer question 25.

Question 25. Type of hormone therapy.

Please list the type of hormone the patient received, the dose and duration.

Questions 26 and 27 ask for the participant's height and weight.

Please list the participant's height and weight obtained at the clinic visit.

Question 28. Is the patient in a treatment trial?

Some patients may be on a particular treatment trial, if so, please list the name of the treatment trial.

Question 29. Date form completed.

Enter the date you completed the chart review form.

Question 30. Staff ID

Enter your 3 digit staff identification number in the space provided.

CHAPTER 8

STUDY DATA FORMS AND QUESTIONNAIRES

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8.1 OVERVIEW

This chapter briefly describes the questionnaires and forms to be used in this study. For organizational purposes, the forms have been divided into those completed prior to the baseline visit, those completed at baseline, and those which are filled out after the participants have completed the baseline clinic visit.

8.2. FORMS COMPLETED BEFORE THE BASELINE VISIT

8.2.1 Participant Eligibility Form

The Participant Eligibility Form is composed of two parts: 1) patient identification/physician approval, and 2) the prescreen. This form is completed by clinical center staff, and has been designed to assist in the identification of participants who meet the basic eligibility requirements. It also provides a script to be used in prescreening the patients. Eligibility at each step in the process is discussed. **All participants must be prescreened for eligibility before they are scheduled for a baseline clinic visit.**

8.3 FORMS COMPLETED AT THE BASELINE VISIT

The following forms are to be self-administered by the participants at the baseline clinic visit.

8.3.1 Contact Form

As a part of the study group, the participant will complete this form and provide her mailing address and telephone number, and the names of her physicians (i.e., primary care, surgeon and/or oncologist and/or radiologist). In addition, the names and addresses of three friends or relatives who will always know how to reach the participant will also be obtained.

8.3.2 Demographic Form

Questions about the participants' background are very important. This information will help describe, in general terms, the women who participate in the study. This form will collect data on age, marital status, racial/ethnic identity, education completed, household income, number of persons in household, employment status, and occupation. This information will be used to describe the group of women in study reports and publications.

8.3.3 Swelling Form

This study form asks questions concerning problems with lymphedema or swelling in the arm and/or hand. Swelling will be assessed to document the occurrence, duration, severity, and circumstances surrounding arm and hand swelling. Little is known about lymphedema. This data will provide much needed information about the condition.

8.3.4 Symptoms Questionnaire

The occurrence and bothersomeness of symptoms associated with breast cancer treatment and/or menopause are assessed in this questionnaire. Participants are asked to indicate whether they had a particular symptom, and if yes, whether the symptom was mild, moderate, or severe. This information will provide information about the symptoms experienced by young women with breast cancer, and may also provide data that can be used to compare the menopausal symptoms of older women undergoing natural menopause with the symptoms of young breast cancer patients who may be experiencing chemotherapy induced menopause.

8.3.5 Medical and Reproductive History

This form is composed of four parts: medical history, family history, and reproductive history. In part I (medical history), the participants will be asked to indicate whether they have had certain medical conditions or procedures, such as heart disease or diabetes. In part II (family history), participants will identify female family members who have had breast cancer or ovarian cancer. A positive family history of breast cancer confers a somewhat increased risk. The risk is particularly high if both the mother and sister have been affected at a young age. Family history is also very important to collect as it may support the belief that some families have a genetic susceptibility to develop breast and/or ovarian cancers at a young age. In part three (Reproductive History), participants will be asked questions about their menstrual cycles prior to breast cancer diagnosis and treatment, as well as their current menstrual cycles. Questions are also asked about all pregnancies and outcomes; past, current, and future desires to have children; and past and current methods of birth control. Most young women with invasive breast cancer will undergo adjuvant chemotherapy and almost half will suffer chemotherapy-related amenorrhea (TRA). Very little is known about the incidence, onset, time course, and symptomatology of premature menopause induced by breast cancer therapy. In part four (medications), participants are asked to list the prescription and non-prescription medications and supplements they are taking currently, in addition to their cancer treatment-related drugs.

8.3.6 Personal Habits Form

Information will be obtained regarding the patients' smoking and alcohol use, height and weight, weight cycling, and exercise habits. This information will be used to investigate how the participants' lifestyles influence their comorbid status. There is also some indication that women who exercise during treatment for breast cancer have less depression and fatigue.

8.3.7 Quality of Life Form

The health-related quality of life (HRQL) questionnaire is composed of a group of scales and instruments that will be used to measure the participants' physical, emotional, and social well-being. Each of these scales is described below.

A) SF-12 Health Survey. The SF-12 is a general health-related quality of life instrument that measures an individual's physical and mental health. This form is a shorter version of the SF-36, which is a widely used generic measure of health-related quality of life. This instrument has 12 questionnaire items, and strong psychometric properties. (Questions 1-12)

B) Functional Assessment of Cancer Therapy - Breast (FACT-B). This 44 item questionnaire is a multidimensional HRQL scale. This instrument was developed after extensive interviewing and testing with cancer patients, and has excellent psychometric properties. This scale assesses the patients' physical well-being, social/family well-being, relationship with doctor, emotional well-being, fulfillment/contentment, and concerns specific to breast cancer patients. Scores can be calculated for each of the 6 subscales, and a total HRQL score composed of all 6 subscales can be calculated as well. (Questions 13-54)

C) Self-Concept Scale. This 10-item scale assesses the participants' satisfaction with different areas of their body and their overall weight. Persons undergoing surgery for breast cancer may experience an alteration in their perception of their body image, which may affect their psychosocial status and intimate relationships. This scale was developed by David Cella, through his work with breast cancer patients. (Questions 55-64)

D) Watts Sexual Functioning Questionnaire. The arousability and satisfaction subscales of the Watts Sexual Functioning Questionnaire will be used to assess the impact of treatment and/or amenorrhea on sexual functioning. Two subscale scores are calculated from these items, one for arousability and one for satisfaction with sexual activity. (Questions 65-77)

F) Sleep Disturbance Scale. Sleep patterns and sleep quality may be disrupted by treatment regimens and physical and emotional symptoms. Lack of restful sleep has been related to greater emotional distress and depressive symptomatology, as well as to general fatigue, in both clinical and non-clinical populations. To measure these effects, a 6 item sleep disturbance scale will be used to assess the overall quality of the participants' sleep. This scale was developed for an international study evaluating the effect of hormone replacement on peri-menopausal women. This scale was recently validated on 70,000 women from the baseline data of the Women's Health Initiative, which is examining the impact of hormone replacement therapy, diet, and calcium/vitamin D on the long-term morbidity and mortality of post-menopausal women. A total score is calculated from this scale. (Questions 78-83)

E) Spirituality Subscale. Spiritual beliefs have been identified recently as an important predictor of patients' coping and hopefulness for the future when dealing with a serious illness. To measure this construct, we will be using a 7-item scale developed by David Cella. (Questions 84-91)

G) Beck Depression Inventory. This is a 21-item scale that is used to assess the depressive symptomatology/general distress of the participants in the study. This instrument has been used with a variety of clinical and non-clinical populations, and has been validated as a reliable screening tool for depression. A total score is calculated from this instrument. In general, scores above 15 are considered to indicate persons who need further evaluation to determine if clinical depression exists. (Questions 92-113)

8.3.8 MOS Social Support Questionnaire

The social support questionnaire developed in conjunction with the Medical Outcomes Study (MOS), completed by the RAND Corporation, will be used to assess the amount of instrumental and emotional support available to the participants. Social support has been found to be an important predictor of adherence to treatment regimens, one's emotional health, and overall health-related quality of life. This 20-item measure produces a total score, as well as 4 subscale scores: tangible support, affectionate support, positive social interactions, emotional-informational support.

8.4 FORMS COMPLETED FOLLOWING THE BASELINE VISIT

The following group of forms are those which are completed following the baseline visit.

8.4.1 Menstrual Bleeding Diary/Calendar

The participants' menstrual bleeding will be recorded on the Menstrual Bleeding Diary. The diary is designed in a calendar format for ease of use. Each day, participants will be asked to record whether they had no bleeding, spotting, or bleeding (light, medium, heavy). A **bleeding day** is defined as a day when a woman's blood loss is sufficient to require the use of sanitary protection. A **spotting day** is a day on which a woman's blood loss is not sufficient to require sanitary protection. From this form, the frequency, duration, and amount of menstrual flow can be calculated for every participant each month. The diaries are optical recognition forms, known as Teleforms, and will be scanned using a machine. There are specific instructions for the completion of the diaries, which are provided in Chapter 9.

8.4.2 Participant Registration Form

This form is to be completed by clinical center staff immediately following the baseline visit. This form will serve to register the participants in the study, and contains information about the participants' name, address and phone number, primary physician, age, race/ethnicity, stage of cancer, date of birth, date of baseline visit, and the participant's identification number and acrostic.

8.4.3 Chart Review Form

A medical chart review will be completed on all participants following the baseline clinic visit. The information to be obtained includes the: date of breast cancer diagnosis, stage and grade, size and number of positive lymph nodes, estrogen and progesterone receptors (positive and negative), current medications, comorbid conditions, and patients' height and weight. Specific instructions for the completion of this form are provided in Chapter 7.

CHAPTER 9

INSTRUCTIONS FOR MENSTRUAL DIARIES

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9.1.2	Filling in Letters, Numbers, and Check boxes	1
9.2	HANDLING THE MENSTRUAL DIARIES	1
9.3	INSTRUCTION SHEET FOR PARTICIPANTS	2

9.1 INSTRUCTIONS FOR COMPLETION

The menstrual diaries will be collected on an optical recognition form, known as a Teleform, and will be scanned by a machine. Therefore, to ensure that the machine will be able to read the participants' responses accurately, it is imperative that the form be completed according to the guidelines provided. The proper completion of this form is essential to the successful interpretation of the data.

9.1.1. Using the Right Pen

An important element in the scanner being able to read the diaries is the type of pen that is used to complete the form.

Pen Type: The teleform scanners have difficulty reading broken, discontinuous lines. A **felt tip pen with a fine point** is strongly recommended. Ball-point pens can provide good results as long as they produce solid, continuous lines. Avoid pencils and faulty ball-point pens.

Pen Color: **Black ink** should be used when filling out the diaries. Other colors, especially light blue, are not picked up well and will cause interpretation errors.

9.1.2 Filling in Letters, Numbers and Check boxes

Attached are examples of the correct ways in which to complete the teleform menstrual diaries. In general:

- Print letters and numbers neatly within the boxes without touching any sides.
- Print letters and numbers without broken lines.
- Make a distinct "X" within boxes.
- Use liquid "white out" to correct any mistakes.
- Best results are achieved when **upper-case letters** are used.
- Numbers do not have to be drawn *exactly* as shown.

9.2. HANDLING THE MENSTRUAL DIARIES

Careful handling of the teleform diaries is essential. If the forms are damaged and stained in any way, the scanner may not be able to read the responses written on the diaries. As a reminder, the

menstrual diaries are not to be:

- folded
- torn
- stapled
- stained (coffee, food)

Careful adherence to these guidelines will help ensure the timely and accurate data entry of this information.

9.3. INSTRUCTION SHEET FOR PARTICIPANTS

Attached is an information sheet to be distributed to the participants each time the menstrual diaries are provided to the participants. At baseline, it will be the responsibility of the clinical center staff to ensure that the participants are provided with these instructions. The clinical coordinating center staff will be responsible for enclosing these instructions when the menstrual diaries are mailed to the participants homes at 3 month intervals during the follow-up period.

Filling in Letters and Numbers

When hand printing upper case letters and numbers in constrained print field and image zones, use block letters such as:

A	B	C	D	E	F	G	H	I	J	K	L	M
N	O	P	Q	R	S	T	U	V	W	X	Y	Z

0	1	2	3	4	5	6	7	8	9

The following section provides correct and incorrect examples of how to fill in constrained print fields. (Although lower case characters are shown, the best recognition occurs when all upper-case letters are used.)

First Name

D	a	v	e						

Incorrect. Letter "D" touches line

First Name

D	a	v	e						

Incorrect. Letter lines are broken up.

How to Mark the Boxes

Although Teleform has been designed to accept boxes that have been marked with "✓" or "X", the best results are obtained when the boxes are darkened completely.

Preferred:



Acceptable:



Boxes should never be circled, because Teleform scanners will not look outside the boxes for any marked information.



You are to indicate your bleeding pattern for everyday of each month. This includes days that you had no bleeding, be sure to mark the box that indicates "no bleeding".

Draft

Patient I.D.:

 - -

Acrostic:

Each day, please check the appropriate box referring to information on any vaginal BLEEDING you may have. A BLEEDING day is defined as a day on which your blood loss requires the use of a tampon or pad. A SPOTTING day is a day on which your blood loss does not require use of a tampon or pad.

DECEMBER 1997

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
	1 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	2 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	3 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	4 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	5 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	6 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy
7 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	8 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	9 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	10 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	11 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	12 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	13 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy
4 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	15 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	16 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	17 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	18 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	19 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	20 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy
21 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	22 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	23 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	24 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	25 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	26 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	27 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy
28 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	29 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	30 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy	31 ☐ No Bleeding ☐ Spotting Bleeding: ☐ Light ☐ Medium ☐ Heavy			

IF AT ANY TIME YOU HAVE ANY UNUSUAL BLEEDING IN TERMS OF FREQUENCY, DURATION OR THE AMOUNT, PLEASE CALL YOUR PRIVATE PHYSICIAN!

CHAPTER 10
DOD FOLLOW-UP

10.1	OVERVIEW	1
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10.3	MEDICAL CHART REVIEWS	3
10.4	FOLLOW-UP ALERT VALUES SAFETY MONITORING.	3

10.1 OVERVIEW

All participant follow-up will be completed centrally by staff persons at the Clinical Coordinating Center. Routine follow-up for all participants will take place at six month intervals from the date the participant completed the baseline visit until the end of the data collection phase in April of 2001. All participants will be followed for at least 24 months, although some participants who are enrolled in the study early in the recruitment phase will be followed for a maximum of 36 months.

Participant follow-up will consist of a packet of questionnaires that will be sent to the participants' homes for them to complete and return to the Clinical Coordinating Center. Each follow-up contact will be scheduled to occur within a two-week window (plus or minus two weeks) around the target contact date. The target contact date is the corresponding anniversary, (for example, six or twelve months), of when the participant completed the baseline visit and data forms. For example, if a participant was enrolled on January 1, 1998, the target date for her six-month follow-up would be July 1, 1998. This women should complete the 6 month follow-up questionnaires within the two-week window extending from June 15, 1998 to July 15, 1998. Form completion outside of the window will be kept to a minimum because of the potential adverse impact on data analysis. A computerized tracking system has been developed to assist coordinating center staff in mailing out forms to the participants on schedule.

In the event the participant does not return the completed forms within two weeks of the date the forms were mailed, the Coordinating Center Project Manager or Assistant Project Manager will call the participant to check on the form status and/or perform the data collection activities in a telephone interview, if necessary.

The measures described below will be mailed to the participants during the follow-up period:

1. Demographic and Contact Information: Updates
2. Medical and Reproductive History: Updates will be completed on the patients' co-morbid status, menstrual cycling, contraceptive use, pregnancies and outcomes, and plans for future childbearing.
3. Arm and Hand Swelling Form
4. Personal Habits: Updates on patients' smoking and alcohol use status, height and weight, and exercise habits.
5. Health-Related Quality of Life Forms:
 - SF-12 Health Status Profile
 - Functional Assessment of Cancer Therapy-Breast (FACT-B)
 - Beck Depression Inventory
 - Sleep Disturbance Scale
 - Watts Sexual Functioning Questionnaire (Desire and Satisfaction Subscales)
 - Self-Concept Scale
 - Spirituality Subscale
6. Physical Symptoms Checklist
7. MOS Social Support Questionnaire

10.2. MENSTRUAL BLEEDING DIARIES

The monthly menstrual bleeding diaries will be completed each month from the patients' time of enrollment (i.e., completion of the baseline visit and forms) to the end of the study data collection period (i.e., April, 2001). Patients will be instructed to return the diaries to the Clinical Coordinating Center every three months. The Coordinating Center will, in turn, mail the participants the next consecutive, three months of diaries each quarter. Unusual bleeding patterns will be determined, and the principal investigators of the participating institutions will be notified, if necessary. (See section 10.4 below.)

10.3. MEDICAL CHART REVIEW

Medical chart reviews will be performed during the follow-up period on patients who have serious complications resulting from treatment, who undergo additional treatment(s) and/or have a cancer recurrence during the study period. Information to be obtained on these individuals includes the stage and grade of cancer, size and number of positive lymph nodes, estrogen and progesterone receptors, prescribed treatment, medications, and comorbidities.

10.4. FOLLOW-UP ALERT VALUES SAFETY MONITORING

During the course of the study certain safety monitoring procedures will be maintained to detect unusual bleeding patterns and higher than average rates of depressive symptomatology. The operational definitions of these two alert values are described below:

a) Unusual Bleeding Patterns. Participants' bleeding patterns will be recorded on the monthly bleeding diaries. Alert values for bleeding and spotting have been defined as follows:

1. Any episode of bleeding lasting longer than eight days. (A bleeding episode is defined as two or more consecutive days of bleeding or spotting bounded by at least two bleeding-free days.)
2. An interval between bleeding episodes of less than twenty-four days.
3. "On and off" bleeding within a 15 day period (e.g., 3 days bleeding, 2 days no bleeding, 4 days of bleeding).

A notice has also been placed on the bottom of the bleeding diary form asking the women to call their physician if they experience any unusual bleeding in terms of frequency, duration, or amount.

B) Depressive Symptomatology. The Beck Depression Inventory will be used, in part, as a screen for clinical depression. A cutoff score of 16 or greater is indicative of individuals who are

experiencing higher than average depressive symptomatology, which could indicate the presence of clinical depression.

Item 9, (Question 101 on the Baseline Quality of Life Form), response choices #3 on the Beck Depression Inventory also concerns whether the person is considering suicide. Persons who mark either response #3 ("I would kill myself if I had the chance.") will be referred for immediate consultation.

C) Process of Referral for Alert Values. At the follow-up assessments, the Principal Investigators of the clinical centers will be contacted should any of their participants have an unusual bleeding pattern (as described above), a Beck Depression Inventory score of 16 or greater and/or if the participant marked response "3" on question 9 of this form. The Principal Investigators will then be responsible for contacting the patients' designated physician for further follow-up.

CHAPTER 11
DATA MANAGEMENT

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11.3.1 Hardware and Software Components	3
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11.1

DATA IDENTIFIERS

Certain items will appear on every form and will serve as unique identifiers for the participants. These items are the Participant Identification Number, the Participant Acrostic Code, and the Visit Name Code.

11.1.1 Participant Identification Number

The Participant identification number is composed of 6 digits, and includes codes for the following: the clinical center code, the specific hospital or clinic code of the participating clinical center, and the participant identification code. The participant identification number will be denoted as given below:

_____ - _____
center clinic participant code

- Clinical Center Code: Each Clinical Center has been assigned a code number by the Coordinating Center. This number, the first digit of the participant's ID number, should be clearly entered in the space provided on all forms. Codes for each Clinical Center are listed below:

<u>Clinical Center</u>	Code
Memorial Sloan-Kettering Cancer Center	1
MD Anderson Cancer Center of the University of Texas in Houston	2
Wake Forest University School of Medicine	3

- Clinic Code: Patients may be recruited from several clinics and/or affiliated hospitals at each clinical center. In order to identify from which clinic a woman was recruited, the individual clinics within a clinical center will be assigned a code, which will be the second number of the participants' identification number. This code will be assigned by the clinical coordinating center, as needed.
- Participant Identification Code: The last four digits of the participants' identification number will be the participant identification code. As patients are screened/enrolled in the study, they should be assigned consecutive numbers, ranging from 0001 to as many as are needed to meet recruitment goals.

An example of a participant identification number for a participant at the Wake Forest University School of Medicine would be:

31-0007

This identification number then becomes the assigned number and should be written on the top of all pages of participants' baseline forms.

11.1.2 Participant Acrostic

This 6-letter alphabetic code will serve as a double-check of each participant's ID number. It will consist of the first three letters of the participant's last name, the first two letters of her first name, and her middle initial. For example, the acrostic for Myrtle Pauline Gooch would be GOOMYP. If a participant's last name is less than three letters, then a hyphen (-) will be used to fill in each blank space. Likewise, if the woman does not have a middle name, a hyphen (-) will appear in the last space. Even if a participant changes her name during the course of the trial, her acrostic will remain the same.

If an error is made in assigning the acrostic at the beginning of the trial and discovered later, it should not be corrected.

The acrostic code must be written on every page of each study form.

11.1.3 Visit Name

The type of visit should be marked on every page of the form as follows: BV = baseline, 6 months, 12 months, 18 months, 24 months, 30 months, or 36 months.

Clinical center staff will only be administering the baseline data forms, and therefore, only the box labeled "BV" or "baseline" should be marked by clinical center staff.

Follow-up data collection will be completed by the clinical coordinating center. Coordinating center staff must remember to mark the appropriate box designating the specific follow-up assessment.

11.2 DATA TRACKING AND INVENTORY

In addition to the main study data, an inventory will be maintained at the Coordinating Center containing participant contact information, follow-up status information, and form completion date information. This inventory will form the core of the data and participant tracking system. Most study management reports, including recruitment reports, missed visit reports, and missing form

reports will be generated from this inventory. Lists of participants due for mailings will also be generated from the tracking system.

11.3 MAINTAINING COMPUTER DATA FILES

11.3.1 Hardware and Software Components

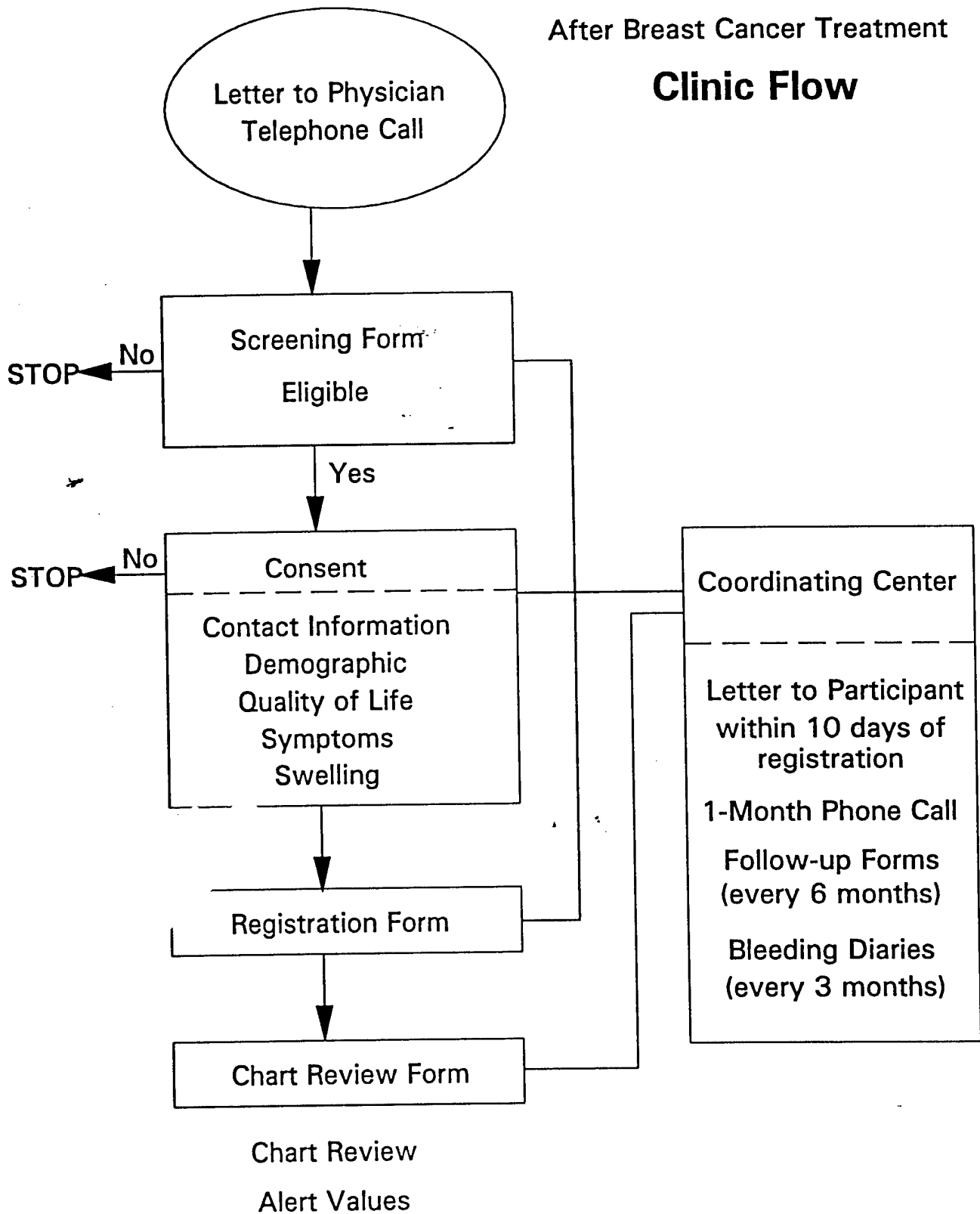
The data management system will be implemented on a Sun SparcServer 1000E at the Department of Public Health Sciences at the Wake Forest University School of Medicine. The data entry application for the questionnaires will be developed using the Foxpro relational database management system. Quality assurance checks and routine study reports will also be done in Foxpro and SAS. Bleeding diary information will be recorded on forms designed to be read through optical scanning using the Teleform software. Statistical analyses will be done using SAS and Splus.

11.3.2 System Backups

All data will reside on the SparcServer's disk drives. Full system backups to tape are made each week night. Backups to tape of the Teleform data will be done at the end of each day of scanning. In general, in the event of a hard disk failure no more than a day's worth of work will need to be repeated.

Menstrual Cycle Maintenance
And Quality Of Life
After Breast Cancer Treatment

Clinic Flow



Menstrual Cycle Maintenance
And Quality of Life
After Breast Cancer Treatment

Clinic Flow

Recruitment: Jan 1, 1998 - April 30, 1999 (16 months)

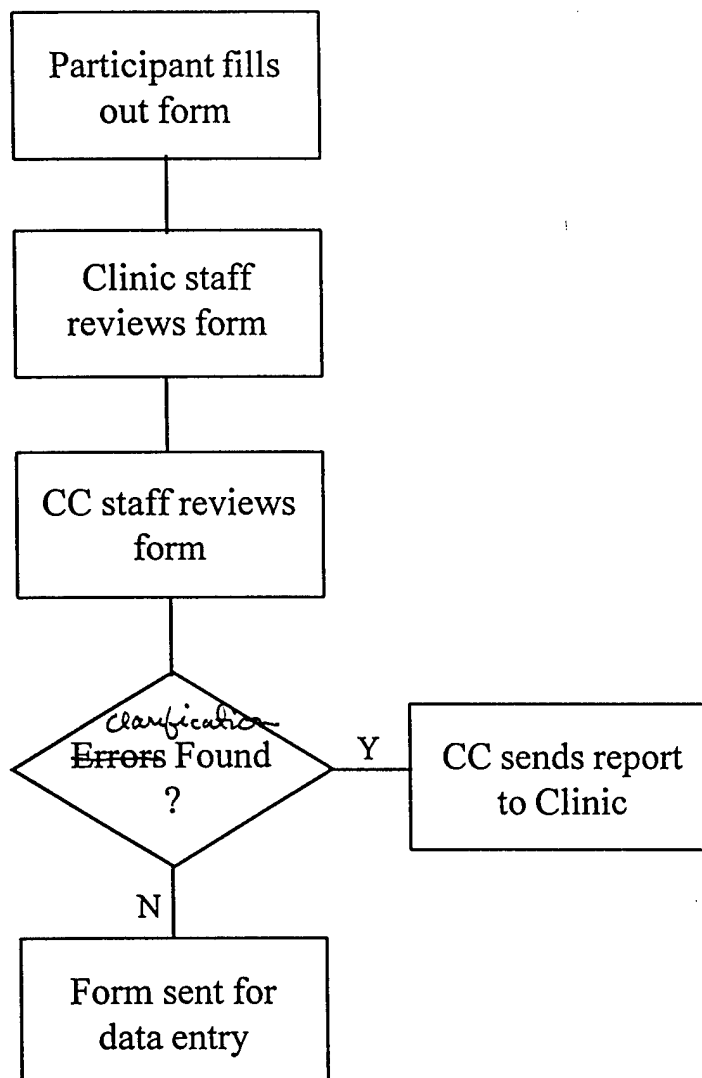
Follow-up: Jan 1, 1998 - April 30, 2001 (40 months)

		<u>Mos. 1-6</u>	<u>Mos.7-16</u>
Sloan-Kettering	360 (45%)	9/week	4/week
MD Anderson	252 (32%)	6/week	3/week
Wake Forest Univ.	188 (23%)	4/week	2/week
All	800	19/week 76/month 456/6 mos.	9/week 36/month 360/10 mos.

Assuming 80% of the participants will complete the study,

240 will have 36 months of follow-up, and
640 will have 24 months of follow-up

Form Path



Data Editing

IDs and Acrostics

- Double check for accuracy.
- Clear and easily readable.

Missing Information

- Questions answered.
- Skip patterns followed.

Range Checks

- Dates and other continuous variables, such as age, are within proper range.
- Multiple choice answers are within correct range.

Quality Control

Data Completeness

- All questions answered where appropriate.
- All forms completed and sent to CC.

Timeliness

- • Fax screening form to CC the same day.
- Mail baseline participant forms to CC on the 15th and 30th of each month.
- Follow through on CC requests as promptly as possible, including data editing forms and questions.

Reliability & Quality

- Be aware of the skip patterns on the forms.
- Look for possible inconsistencies when reviewing the forms.
- “An ounce of prevention is worth more than a pound of cure.”

CHAPTER 12

QUALITY CONTROL

12.1	CLINICAL CENTER ACTIVITIES	1
12.2	DATA QUALITY	1
12.3	COORDINATING CENTER ACTIVITIES	2
12.4	STUDY-WIDE REPORTS	2

12.1 CLINICAL CENTER ACTIVITIES

Specific quality control activities to be carried out by Clinical Center staff include:

- Recording of patient identifiers on the top of each questionnaire prior to their completion at the baseline clinic visit.
- Review of completed baseline questionnaires and forms for incomplete or inconsistent responses prior to shipment to the clinical coordinating center.
- Reporting of quality control concerns to the clinical coordinating center for prompt resolution.

The clinical center coordinator should regularly review this manual of procedures to be sure that activities are being carried out properly and with consideration for the participant. Corrective action should be taken immediately if problems are observed.

The clinical center coordinators are encouraged to communicate with the clinical coordinating center about quality control or other concerns.

12.2 DATA QUALITY

Each individual participating in the study will be assigned a participant identification number and a participant acrostic, (as described in Chapter 11). Individual forms are further identified by a code indicating the time at which the forms were completed, (for example, baseline, 18 months, etc.). The data entry system ensures that the participant identification number and participant acrostic are unique by permitting only one ID number and acrostic to be entered for each questionnaire/form at each data collection point.

Clinical center staff are asked to review all of the participants' questionnaires at baseline, prior to ending the baseline clinic visit. Forms must be completed correctly, and every question should be answered. Written responses to any items on the questionnaires/forms should be legible.

Review of the completed forms will be done again at the coordinating center by the Project Manager or Assistant Project Manager. The Project Manager will verify that the forms are legible, and that they have been filled out correctly and completely. Any problems identified will be resolved before the data entry step. If necessary, the clinic or participant will be contacted to provide missing information or to correct invalid responses on the forms.

The data entry screens will be designed to mirror the paper data collection forms to allow smooth flow from item to item and thereby minimize errors with data entry. Verification of participant identifiers and visit numbers will be incorporated into the data entry system, in addition to gross range checking of fields. Initially, a random 10% sample of study forms will be selected for duplicate data entry. Reports of data entry errors rates will be provided to the Principal

Investigator of the coordinating center. The target error rates will be $\leq 0.2\%$ per field. Error rates in excess of this level will support the need for additional training for data entry staff, double keying of all study data, or double entry of key study variables.

The clinical coordinating center will regularly perform internal comparisons of the entered data to detect missing records or suspicious or invalid data. These comparisons will include logical consistency checks of data within and across forms/questionnaires. Error reports will be generated and sent to the Principal Investigator and Project Manager of the coordinating center for resolution and for re-entry of corrected data.

10.3 COORDINATING CENTER ACTIVITIES

Quality assurance will be a major activity of the clinical coordinating center throughout the study. Activities will include:

- Training/retraining of clinical center staff in data collection procedures.
- Rechecking all completed questionnaires/forms sent by the clinical centers prior to data entry.
- Entering identifying patient and visit information on follow-up forms prior to mailing them to the participants.
- Data control (filing, manual editing, special coding efforts)
- Monitoring of data entry activities and error rates
- Documentation of data base changes.

Quality control and monitoring reports will also be generated by the clinical coordinating center. These reports will include:

- Recruitment yields at each Clinical Center
- Missed follow-up assessments, refusals, losses to follow-up
- Timeliness of data transmission
- Data error levels
- Deviations from protocol

The Coordinating Center personnel will be responsible for reviewing these reports in a timely basis and initiating actions needed to remedy any problems. If necessary, this may require performing site visits at the clinical centers, with follow-up evaluations of actions taken.

10.4 STUDY-WIDE REPORTS

During the recruitment period, monthly reports of recruitment activities by each clinical center will be provided to the principal investigators of the clinical centers.

During all phases, monitoring reports and analyses will be generated for each clinical center and for the whole study. These will be reported to all investigators and staff.

Quality control data will be summarized by the clinical coordinating center for annual reporting.

LIST OF REVISIONS MADE TO THE DOD QUESTIONNAIRES

12-15-97

All Questionnaires

The header information on all questionnaires has been revised to reflect the correct number of boxes needed for the participant ID number and acrostic.

In general, we tried to accommodate all requests for question changes and additions. Some questions were not changed, however, because they are standard items and/or part of established questionnaires where question changes are prohibited.

Chart Review

The chart review form has been revised to only include the initial pathology regarding diagnosis and definitive surgery. Information regarding the specific treatment(s) the patients received will be reserved for the 1 year chart review form that the group decided to create at the training session.

Contact Information Form

Minor editing.

Demographic Form

This form was revised to include questions on the number of persons currently living in the household (question 8), and the participant's religious preference (question 9).

Eligibility Form

The eligibility form was revised according to the discussion at the training session. All of the inclusion criteria are listed on the form, and instructions have been made more clear for the clinic staff persons.

Medical and Reproductive History

Question #20 in Part III of this form has been added. This questionnaire asks women to report the number of hot flushes they have experienced in the past week.

Part IV has been added to this form to collect information on the participants' use of prescription and non-prescription medications, in addition to the breast cancer treatment therapies.

Personal Habits

Questions 9, 10, and 13 have been added to include changes in weight patterns since the participant's cancer diagnosis.

Question 14 about walking outside the home: A one month time frame has now been added to these questions.

Questions about mild, moderate, and severe exercise could not be changed, because they are standard items. We did, however, add the words "mild," "moderate," and "severe" to the statement introducing the questions, so that the participants would know that they would be asked about all levels of activity.

Quality of Life

The quality of life form has been reformatted to make it somewhat easier to read.

The sleep questions now appear after the sexuality items, (in front of the spirituality items.)

Registration

The participant acrostic has now been added to the registration form.

Social Support

Minor editing.

Swelling

The Swelling Form has been revised per Jeanne's and Electra's comments. The form is now shorter and more "stream lined."

Symptoms

Minor editing.

MENSTRUAL CYCLE MAINTENANCE AND QUALITY OF LIFE BASELINE SURVEY



Clinical Centers

**M.D. Anderson
Cancer Center
Houston, Texas**

**Memorial Sloan-Kettering
Cancer Center
New York, New York**

**Presbyterian Hospital
Of Dallas
Dallas, Texas**

**Wake Forest University
Baptist Medical Center
Winston-Salem, NC**

Appendix J
Revised October 1998 Annual Report
DAMD 17-96-1-6292
J. Petrek

**Funded by
The U.S. Army Medical Research and Material Command:
Breast Cancer Research Program A**

Patient I.D. _____

Patient Acrostic: _____

DEMOGRAPHIC FORM

YOUR BACKGROUND

The following questions are about your background. This information will help us describe, in general terms, the women who are participating in the study. Please mark the appropriate box for each question.

1. What is your marital status?

- ☐ Never married
- ☐ Presently married
- ☐ Living in a marriage-like relationship
- ☐ Divorced or separated
- ☐ Widowed

2. What category below best describes your racial/ethnic background? If you are of mixed racial/ethnic background, choose the category with which you most closely identify yourself.

- ☐ **White (Not Hispanic)** (Persons having origins (ancestry) in any of the original people of Europe, North Africa, or the Middle East.)
- ☐ **Black or African American (Not Hispanic)** (Persons having origins (ancestry) in any of the Black racial groups of Africa.)
- ☐ **Hispanic** (Persons of Mexican, Puerto Rican, Cuban, Central or South American or other Spanish culture or origin (ancestry), regardless of race.)
- ☐ **Asian or Pacific Islander** (Persons from or having ancestors from the Far East, Southeast Asia, the Indian subcontinent, or the Pacific Islands. This area includes, for example, China, India, Japan, the Philippine Islands, Korea, Samoa, etc.)
- ☐ **American Indian or Alaskan Native** (Persons from or having ancestors from any of the original peoples of North America and who maintain cultural identification through tribal affiliation or community recognition.)

3. What is your date of birth?

		-			-				

Month Day Year

4. Which category below best describes the highest level of formal education you have completed?
(Choose the one best answer).

- ☐ No formal education
- ☐ Grade school (1st through 8th grade)
- ☐ Some high school (9th through 11th grade)
- ☐ High school diploma or G.E.D.
- ☐ Business or vocational training school after high school graduation
- ☐ Some college (but a college degree was not obtained)
- ☐ Associate Degree (A.D. or A.A.)
- ☐ College graduate or Baccalaureate Degree (B.A. or B.S.)
- ☐ Some college or professional school after college graduation
- ☐ Master's Degree
- ☐ Doctoral Degree (Ph.D., M.D., J.D., D.D.S., etc.)

5. What was your total family income (before taxes) from all sources last year? (Check one box below.
This information is important for describing the women in the study as a group and is kept strictly confidential).

- ☐ Less than \$10,000
- ☐ \$10,000 to \$19,999
- ☐ \$20,000 to \$34,999
- ☐ \$35,000 to \$49,999
- ☐ \$50,000 to \$74,999
- ☐ \$75,000 to \$100,000
- ☐ More than \$100,000

Patient I.D. _____

Patient Acrostic: _____

6. What is your current employment status? (*Check the box that best describes you.*)

- ☐ Unemployed/Looking for work → (Go to question 8)
- ☐ Retired → (Go to question 8)
- ☐ Full-time Homemaker → (Go to question 8)
- ☐ Employed - full-time → (Go to question 7)
- ☐ Employed - part-time → (Go to question 7)
- ☐ Disabled, unable to work → (Go to question 8)
- ☐ Student → (Go to question 8)
- ☐ Other (Please list: _____) → (Go to question 8)

7. If you are employed, which category best describes your occupation? (*If you are not employed currently, go to Question 8*).

- ☐ **Professional, Technical & Related Occupations** (such as teachers/professors, nurses, lawyers, physicians & engineers)
- ☐ **Managers, Administrators, or Proprietors** (such as sales managers, real estate agents, or postmasters)
- ☐ **Clerical & Related Occupations** (such as secretaries, clerks or mail carriers)
- ☐ **Sales Occupations** (such as in salespersons, demonstrators, agents and brokers)
- ☐ **Service Occupations** (such as police, cooks, or hairdressers)
- ☐ **Skilled Crafts, Service Repair Persons, & Related Occupations** (such as carpenters, appliance repair, or telephone line workers)
- ☐ **Equipment or Vehicle Operators & Related Occupations** (such as drivers, railroad brakemen or sewer workers)
- ☐ **Laborers** (such as helpers, longshoremen, or warehouse workers)
- ☐ **Farmers** (owners, managers, operators or tenants)
- ☐ **Members of the military**
- ☐ **Other** (please describe): _____

8. Including yourself, what is the total number of persons who are living in your household currently?

Persons

9. What is your religious preference?

☐

Catholic

☐

Jewish

☐

Protestant: (Indicate which denomination below:

Baptist, Church of Christ, Episcopalian, Methodist, Moravian,
Mormon, Presbyterian, Unitarian, etc., OR Inter-Denominational
OR Non-Denominational)

☐

Muslim

☐

Hindu

☐

Greek Orthodox

☐

Russian Orthodox

☐

Buddhist

☐

Other: (Please specify: _____)

☐

None

10. Today's date is:

Month

Day

Year

Patient I.D. _____ - _____

Patient Acrostic: _____

MEDICAL AND REPRODUCTIVE HISTORY QUESTIONNAIRE

PART 1. MEDICAL HISTORY

1. Has a doctor told you that you have any of the following conditions? (Please mark **all** that apply.)

☐ Diabetes requiring pills	☐ Underactive thyroid gland
☐ Diabetes requiring insulin shots	☐ Stomach or duodenal ulcer
☐ Diabetes treated with diet alone	☐ Diverticulitis
☐ Glaucoma	☐ Ulcerative colitis or Crohn's disease
☐ Arthritis	☐ Systemic erythematosus ("lupus" or SLE)
☐ Hypertension or high blood pressure requiring pills	☐ Pancreatitis (inflamed pancreas)
☐ High cholesterol requiring pills	☐ Gallbladder disease or gallstones
☐ Asthma	☐ Operation to remove gallbladder
☐ Emphysema or chronic bronchitis	☐ Migraine headaches
☐ Kidney or bladder stones (renal or urinary calculi)	☐ Amyotrophic Lateral Sclerosis (ALS, motor neuron disease, or Lou Gehrig's disease)
☐ High blood calcium	☐ Multiple sclerosis
☐ Kidney or renal failure requiring kidney dialysis or a kidney transplant	☐ None of the above
☐ Overactive thyroid gland	

2. Has a doctor ever told you that you have heart problems, problems with your blood circulation, or blood clots?

☐ No ----> (Go to question 3)

☐ Yes ----> (Answer question 2a. below)

2a. Please mark all the conditions or procedures below that a doctor said you had:

- ☐ Angina (chest pains from a heart problem)
- ☐ Heart attack (coronary, myocardial infarction, or MI)
- ☐ Heart failure or congestive heart failure
- ☐ Heart bypass operation or coronary bypass surgery for blocked or clogged arteries in your heart
- ☐ Angioplasty of the coronary arteries (opening the arteries of the heart with a balloon or other device sometimes called a PTCA)
- ☐ Carotid endarterectomy or carotid angioplasty (operation for blocked or narrowed arteries to the legs)
- ☐ Claudication or peripheral artery disease (poor blood flow to the legs or blocked or narrowed arteries to the legs)
- ☐ Deep vein thrombosis or DVT (a blood clot in the legs, does not include varicose veins)
- ☐ Pulmonary embolism (a blood clot in the lungs)
- ☐ Other problem with the heart or blood circulation

(Specify): _____

Patient I.D. _____
 Patient Acrostic: _____

PART II. FAMILY HISTORY

Please answer the following questions about the **history of breast cancer** among your female relatives. If you **do not** have a full-blooded relative in one of the categories listed below, please check **Does Not Apply**. (MARK ONLY ONE BOX PER LINE.)

3. Did this relative have breast cancer?	Does Not Apply	No	Yes			Don't know if she had breast cancer	
			How old was she when her <u>first</u> breast cancer occurred?				
			Less than 45	45 or older	Don't know age		
a. Mother	☐	☐	☐	☐	☐	☐	
b. Sister 1	☐	☐	☐	☐	☐	☐	
c. Sister 2	☐	☐	☐	☐	☐	☐	
d. Sister 3	☐	☐	☐	☐	☐	☐	
e. Sister 4	☐	☐	☐	☐	☐	☐	
f. Daughter 1	☐	☐	☐	☐	☐	☐	
g. Daughter 2	☐	☐	☐	☐	☐	☐	
h. Daughter 3	☐	☐	☐	☐	☐	☐	
i. Daughter 4	☐	☐	☐	☐	☐	☐	
j. Maternal grandmother (your mother's mother)	☐	☐	☐	☐	☐	☐	
k. Paternal grandmother (your father's mother)	☐	☐	☐	☐	☐	☐	

Please answer the following questions about the **history of ovarian cancer** among your female relatives. If you do not have a full-blooded relative in one of the categories listed below, please check **Does Not Apply**. (MARK ONLY ONE BOX PER LINE.)

4. Did this relative have ovarian cancer?	Does Not Apply	No	Yes			Don't know if she had ovarian cancer	
			How old was she when her <u>first</u> ovarian cancer occurred?				
			Less than 45	45 or older	Don't know age		
a. Mother	☐	☐	☐	☐	☐	☐	
b. Sister 1	☐	☐	☐	☐	☐	☐	
c. Sister 2	☐	☐	☐	☐	☐	☐	
d. Sister 3	☐	☐	☐	☐	☐	☐	
e. Sister 4	☐	☐	☐	☐	☐	☐	
f. Daughter 1	☐	☐	☐	☐	☐	☐	
g. Daughter 2	☐	☐	☐	☐	☐	☐	
h. Daughter 3	☐	☐	☐	☐	☐	☐	
i. Daughter 4	☐	☐	☐	☐	☐	☐	
j. Maternal grandmother (your mother's mother)	☐	☐	☐	☐	☐	☐	
k. Paternal grandmother (your father's mother)	☐	☐	☐	☐	☐	☐	

Patient I.D. _____ - _____
Patient Acrostic: _____

PART III. REPRODUCTIVE HISTORY

The following questions ask about your menstrual cycles and reproductive history. We are very interested in this information so that we can understand more about women's health during their childbearing years. Some of the questions ask you to give dates or ages when certain things happened. If you are not sure about the exact date or age, please give your best estimate.

1. At what age did you have your first menstrual period?

years old

2. What was the date of the first day of your last menstrual period (your best guess)?

 - -

Month Day Year

3. What was the date of the first day of your last menstrual cycle prior to your diagnosis of breast cancer?

 - -

Month Day Year

4. Prior to your breast cancer diagnosis, had you ever been told by a health professional that you might not be able to have a baby?

☐

No

☐

Yes (If yes, what was the reason?) _____

☐

Do not know

5. Have you ever tried for 12 consecutive months to become pregnant and not been able to conceive?

☐

No

☐

Yes ---> (If yes, how old were you at the time? years)

6. Have you ever been pregnant (including full-term pregnancies, miscarriages, and abortions)?

☐ No ---> (If no, go to Question 12)

☐ Yes

7. How many times have you ever been pregnant?

Pregnancies

8. How many full-term pregnancies (lasting at least six months) have you had? (If you have never had a full-term pregnancy, please write a "0" in the box.)

Full-term pregnancies

9. Please list the date of birth of all your children:

Sons:

Date of Birth: - -
Month Day Year

Date of Birth: - -
Month Day Year

Date of Birth: - -
Month Day Year

Date of Birth: - -
Month Day Year

Daughters:

Date of Birth: - -
Month Day Year

Date of Birth: - -
Month Day Year

Date of Birth: - -
Month Day Year

Date of Birth: - -
Month Day Year

Patient I.D. _____

Patient Acrostic: _____

10. How old were you at your first full-term pregnancy?

Years old

11. Did you have complications with any of your full-term pregnancies?

☐ No

☐ Yes (If yes, describe below)

12. Which method of birth control are you and your partner using currently? (Mark all that apply.)

☐ No method

☐ Condoms (rubbers)

☐ Birth control pills

☐ Foams/jellies/suppositories

☐ Sponge

☐ Withdrawal (pulling out)

☐ Diaphragm

☐ Safe periods (rhythm or counting days)

☐ Norplant

☐ Cervical cap

☐ Tubal ligation (tubes tied)

☐ Vasectomy

☐ Other (Please describe: _____)

☐ Don't know

13. Which method of birth control were you using just before your diagnosis of breast cancer? (Mark all that apply.)

☐ No method

☐ Condoms (rubbers)

☐ Birth control pills

☐ Foams/jellies/suppositories

☐ Sponge

☐ Withdrawal (pulling out)

☐ Diaphragm

☐ Safe periods (rhythm or counting days)

☐ Norplant

☐ Cervical cap

☐ Tubal ligation (tubes tied)

☐ Vasectomy

☐ Other (Please describe: _____)

☐ Don't know

14. Have you had a tubal ligation? (Tubes tied to prevent future pregnancies.)

☐

No

☐

Yes ---> If yes, when?

Month

Year

15. During the past month, how many times have you had sexual intercourse without using contraception?

Times

16. Are you planning to try to get pregnant in the future?

☐

No ---> (Go to Question 17)

☐

Yes ---> (Go to question 16a)

☐

Not sure ---> (Go to question 17)

16a. If you want to get pregnant, when do you think you might try to get pregnant?

☐

In the next 6 months

☐

In the next year

☐

In the next two years or more

17. In the eight months prior to your diagnosis of breast cancer, did you want to have a child or more children in the future?

☐

No

☐

Yes

☐

Undecided

18. Has the diagnosis of breast cancer influenced your decision to have children?

☐

No

☐

Yes

Patient I.D. _____
Patient Acrostic: _____

19. Have you had any type of surgery involving your reproductive organs or pelvic region of the body?
(For example, the removal of an ovary or uterine fibroids.)

☐ No
☐ Yes ----> (If yes, please describe below:)

Type of Surgery:

Date: - -
Month Day Year

Date: - -
Month Day Year

Date: - -
Month Day Year

20. In the past month, have you had any hot flashes or night sweats (hot flashes that occur during sleep)?

☐ No
☐ Yes ----> (If yes, how many have you had in the **past week**?)

hot flashes/night sweats

PART IV. CURRENT MEDICATIONS

This section of the questionnaire asks you to list all of the prescription and non-prescription medications and supplements you take on a regular basis.

1. Please list below all of the **prescription medications** you are taking currently, **other than those you are taking as part of your breast cancer treatment.**

Drug Name	Dosage	How many <u>months</u> have you been taking this medication?
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

2. Please list below all of the **non-prescription medications or supplements** you are taking currently.

Drug Name	Dosage	How many <u>months</u> have you been taking this medication?
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

Patient I.D.: _____

Patient Acrostic: _____

Visit Type: ☐ Baseline ☐ 6 month ☐ 12 month ☐ 18 month ☐ 24 month ☐ 30 month ☐ 36 month

SYMPTOMS QUESTIONNAIRE

Below are statements about symptoms some people may experience. For each statement, check the appropriate box for the response that best describes how bothersome the symptom was for you **during the past month**. If you did not have the problem, check the box under the column titled "symptom did not occur". Please do not skip any questions. **Mark only one box on each line.**

If you experienced the symptom, use the following key to indicate how bothersome it was:

Mild = symptom did not interfere with usual activities.
Moderate = symptom interfered somewhat with usual activities.
Severe = symptom was so bothersome that usual activities could not be performed.

Symptom	Symptom did not occur	Symptom Occurred and Was:		
		Mild	Moderate	Severe
1. Fatigue or low energy level				
2. Mouth ulcers				
3. Restless sleep				
4. Sleeping too much				
5. Nervousness or shakiness inside				
6. Mood changes				
7. Feeling depressed				
8. Lightheadedness when standing up				
9. Faintness or dizziness at rest				
10. Headaches				
11. Swelling of ankles or feet				
12. Diarrhea				

Symptom	Symptom did not occur	Symptom Occurred and Was:		
		Mild	Moderate	Severe
13. Constipation				
14. Abdominal pain/cramps				
15. Vaginal dryness				
16. Muscle pain/ache/or cramp				
17. Weight gain				
18. Weight loss				
19. General aches and pains				
20. Hot flashes				
21. Joint pains				
22. Night sweats				
23. Aches in back of neck and skull				
24. Forgetfulness				
25. Difficulty concentrating				
26. Increased appetite				
27. Short temper				
28. Decreased efficiency				
29. Loss of interest in work/activities				
30. Lowered work performance				
31. Blind spots, fuzzy vision				
32. Breast sensitivity/tenderness				
33. Avoidance of social affairs				
34. Cold sweats				
35. Decreased appetite				
36. Feelings of suffocation				
37. Difficulty healing				
38. Bloating				

Patient I.D. _____

Patient Acrostic: _____

SWELLING FORM

The following questions concern swelling in your arm and/or hand. Please mark the appropriate box(es) for each question.

1. Since your treatment for breast cancer, has any swelling occurred in your arm or hand on the same side that you had your lumpectomy or mastectomy?

☐

No → (Go to question 10)

☐

Yes → (Continue to question 2)

☐

Don't know → (Go to question 10)

2. How soon after you had surgery and/or began treatment did this swelling occur?

☐

Less than 1 week

☐

1 week to 4 weeks

☐

1 month to 3 months

☐

4 months to 6 months

3. Where does the swelling occur? (Check all that apply)

☐

Hand

☐

Upper Arm

☐

Lower Arm

4. Would you consider the swelling to be mostly?

☐

Mild

☐

Moderate

☐

Severe

5. Does the swelling interfere with any of the following?

Yes No

☐☐

Clothing that you wear

☐☐

Your ability to do routine activities, such as household chores or grooming.

☐☐

Exercise

☐☐

Your appearance

☐

Other, please describe: _____

6. Do you believe the start of your swelling was related to any of the following?

Yes

No

Don't
Know

☐☐☐

Radiation treatment

☐☐☐

Breast reconstruction

☐☐☐

Infection or injury to arm / hand

☐☐☐

Weather changes

☐☐☐

General use of your arm

☐☐☐

Exercise

☐☐☐

Airplane travel

☐

Other: Please describe: _____

Patient I.D. _____

Patient Acrostic: _____

7. Did (or does) swelling seem to get worse with any of the following?

Yes	No	Don't Know	
☐	☐	☐	Hot weather
☐	☐	☐	General use of your arm
☐	☐	☐	Exercise
☐	☐	☐	Sauna / Jacuzzi / Hot bath
☐	☐	☐	Airplane travel
☐	☐	☐	Specific foods
☐	☐	☐	Mental / emotional stress

Other: Please describe: _____

8. Did you seek treatment for this swelling?

☐

No → If no, why not?

☐

Yes → If yes, what type of treatment did you receive? (**Check all that apply**)

☐

Compression therapy by machine

☐

Glove / Sleeve Compression / Garment

☐

Physical therapy

☐

Manual lymphatic drainage

☐

Bandaging technique

☐

Other, please describe: _____

9. Do you have swelling now?

☐ No → (Go to question 10)

☐ Yes → (Continue to 9a)

9a. If yes, how long have you had swelling?

☐ Less than 1 week

☐ 2 - 4 weeks

☐ 1 - 3 months

☐ 4 - 6 months

10. Since your treatment for breast cancer, do you remember any particular breaks in your skin, slight skin injuries, or infected hang nails in your arm or hand on the same side that you had your lumpectomy or mastectomy, which improved by themselves and for which antibiotics were not given?

☐ No

☐ Yes

☐ Don't know

11. Since your treatment for breast cancer, have you had any infection in the arm or hand on the same side that you had your lumpectomy or mastectomy for which you:

11a. received antibiotics by mouth?

☐ No

☐ Yes

☐ Don't know

11b. received antibiotics by injection?

☐ No

☐ Yes

☐ Don't know

Patient I.D.: _ _ - _ _ _ _ _
Patient Acrostic: _ _ _ _ _
Visit Type: ☐ Baseline ☐ 6 month ☐ 12 month ☐ 18 month ☐ 24 month ☐ 30 month ☐ 36 month

QUALITY OF LIFE FORM

1. In general, would you say your health is: **(Check one)**

Excellent	Very good	Good	Fair	Poor
☐	☐	☐	☐	☐

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? **(Check one)**

2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.

Limited a lot	Limited a little	Not limited at all
☐	☐	☐

3. Climbing several flights of stairs.

Limited a lot	Limited a little	Not limited at all
☐	☐	☐

During the **past four weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**? **(Check one)**

	Yes	No
4. Accomplished less than you would like.	☐	☐
5. Had difficulty performing the work or other activities, for example, it took extra effort.	☐	☐

During the **past four weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of emotional problems** (such as feeling depressed or anxious)? **(Check one)**

	Yes	No
6. Accomplished less than you would like.	☐	☐

- Yes No
7. Didn't do work or other activities as carefully as usual. ☐ ☐
8. During the past four weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? **(Check one)**
- Not at all Slightly Moderately Quite a bit Extremely
- ☐ ☐ ☐ ☐ ☐
9. During the past four weeks, how much did pain interfere with your normal activities (including both work outside the home, housework and family activities)? **(Check one)**
- Not at all Slightly Moderately Quite a bit Extremely
- ☐ ☐ ☐ ☐ ☐

These questions are about how you feel and how things have been with you **during the past four weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the **past four weeks**:

10. Have you felt calm and peaceful? **(Check one)**
- All of the time Most of the time A good bit of the time Some of the time A little of the time None of the time
- ☐ ☐ ☐ ☐ ☐ ☐
11. Did you have a lot of energy? **(Check one)**
- All of the time Most of the time A good bit of the time Some of the time A little of the time None of the time
- ☐ ☐ ☐ ☐ ☐ ☐
12. Have you felt downhearted and blue? **(Check one)**
- All of the time Most of the time A good bit of the time Some of the time A little of the time None of the time
- ☐ ☐ ☐ ☐ ☐ ☐

Patient I.D. _____

Patient Acrostic: _____

Below is a list of statements that other people with your illness have said are important. Please circle the number that best describes how true each statement has been for you during the past 7 days.

Physical Well-Being	Not At All	A Little Bit	Some-what	Quite a bit	Very Much
13. I had a lack of energy.	1	2	3	4	5
14. I had nausea.	1	2	3	4	5
15. I had trouble meeting the needs of my family.	1	2	3	4	5
16. I had pain.	1	2	3	4	5
17. I was bothered by side effects of treatment.	1	2	3	4	5
18. In general, I felt sick.	1	2	3	4	5
19. I was forced to spend time in bed.	1	2	3	4	5

20. How much does your Physical Well-Being affect your quality of life? (Circle one number.)

Not At All 0 1 2 3 4 5 6 7 8 9 10 Very Much So

Social/Family Well-Being	Not At All	A Little Bit	Some-what	Quite a bit	Very Much
21. I felt distant from my friends.	1	2	3	4	5
22. I got emotional support from my family.	1	2	3	4	5
23. I got support from my friends and neighbors.	1	2	3	4	5
24. My family had accepted my illness.	1	2	3	4	5
25. Family communication about my illness was poor.	1	2	3	4	5

If you have a spouse/partner, or are sexually active, please answer questions 26-27. Otherwise, go to question 28.

26. I felt close to my partner (or main support).	1	2	3	4	5
27. I was satisfied with my sex life.	1	2	3	4	5

28. How much does your Social/Family Well-Being affect your quality of life? (Circle one number.)

Not At All 0 1 2 3 4 5 6 7 8 9 10 Very Much So

Relationship With Doctor	Not At All	A Little Bit	Some-what	Quite a bit	Very Much							
29. I had confidence in my doctor(s).	1	2	3	4	5							
30. My doctor was available to answer my questions.	1	2	3	4	5							
31. How much does your <u>Relationship with your Doctor</u> affect your quality of life? (Circle one number.)												
Not At All	0	1	2	3	4	5	6	7	8	9	10	Very Much So

										Not At All	A Little Bit	Some-what	Quite a bit	Very Much
Emotional Well-Being														
32. I felt sad.										1	2	3	4	5
33. I was proud of how I'm coping with my illness.										1	2	3	4	5
34. I was losing hope in the fight against my illness.										1	2	3	4	5
35. I felt nervous.										1	2	3	4	5
36. I worried about dying.										1	2	3	4	5
37. How much does your <u>Emotional Well-Being</u> affect your quality of life? (Circle one number.)														
Not At All	0	1	2	3	4	5	6	7	8	9	10	Very Much So		

Functional Well-Being	Not At All	A Little Bit	Some-what	Quite a bit	Very Much							
38. I was able to work (include work in home).	1	2	3	4	5							
39. My work (include work in home) was fulfilling.	1	2	3	4	5							
40. I was able to enjoy life “in the moment.”	1	2	3	4	5							
41. I had accepted my illness.	1	2	3	4	5							
42. I was sleeping well.	1	2	3	4	5							
43. I enjoyed my usual leisure pursuits.	1	2	3	4	5							
44. I was content with the quality of my life right now.	1	2	3	4	5							
45. How much does your <u>Functional Well-Being</u> affect your quality of life? (Circle one number.)												
Not At All	0	1	2	3	4	5	6	7	8	9	10	Very Much So

Patient I.D. _____
 Patient Acrostic: _____

Additional Concerns	Not At All	A Little Bit	Some-what	Quite a bit	Very Much
46. I was short of breath.	1	2	3	4	5
47. I was self-conscious about the way I dressed.	1	2	3	4	5
48. My arms were swollen or tender.	1	2	3	4	5
49. I felt sexually attractive.	1	2	3	4	5
50. I was bothered by hair loss.	1	2	3	4	5
51. I worried about the risk of cancer in other family members.	1	2	3	4	5
52. I worried about the effect of stress on my illness.	1	2	3	4	5
53. I was bothered by a change in weight.	1	2	3	4	5
54. I was able to feel like a woman.	1	2	3	4	5

55. How much do these Additional Concerns affect your quality of life? (Circle one number.)

Not At All 0 1 2 3 4 5 6 7 8 9 10 Very Much So

PART II. YOUR APPEARANCE

This section asks you about your general perceptions regarding your body. Right now, how satisfied are you with these parts of your body? Please check the appropriate box for the response that best describes your satisfaction with each body part.

	Very dissatisfied	Somewhat dissatisfied	Neutral	Somewhat satisfied	Very satisfied
56. Hair					
57. Breasts					
58. Arms					
59. Face					
60. Waist					
61. Hips					
62. Thighs					
63. Overall body					

How much do you agree or disagree with the following statement? (Check the appropriate box.)

64. The appearance of my breast area is important to me.

Strongly
Disagree

☐

Disagree

☐

Neither Agree
or Disagree

☐

Agree

☐

Strongly
Agree

☐

65. I view myself as a:

☐

Very overweight person

☐

Moderately overweight person

☐

Normal weight person

☐

Moderately thin person

☐

Very thin person

PART III. SEXUALITY

These next questions are about the way health problems may interfere with your sex life. These questions are personal, but your answers are important in understanding how health problems may affect women's sexuality.

66. Have you been sexually active with a partner during the last 6 months?

☐

No ----> (If no, skip to Question 79).

☐

Yes ----> (If yes, continue to Question 67).

67. How many times have you had sexual intercourse in the past month?

☐

0 times

☐

1 - 4 times

☐

5 - 10 times

☐

11 or more

Patient I.D. _____

Patient Acrostic: _____

For the following questions, please check the box for the response that best describes your sexual feelings and experiences **DURING THE PAST MONTH.**

	Never	Almost Never	Sometimes	Almost Always	Always
68. How often were you aware of wetness in your vagina as you became sexually excited?					
69. How often did it take a long time for your vagina to become wet or slippery as you became sexually excited?					
70. During sexual relations, how frequently did you notice dryness of your vagina?					
71. How often did you feel pain or discomfort during vaginal penetration?					
72. How often did you feel satisfied after sexual activity?					
73. How often were you satisfied with the frequency of sexual activity?					
74. How frequently did you feel tense or nervous after a sexual experience?					

For the following questions, please check the box for the response that best describes your sexual feelings and experiences **DURING THE PAST MONTH.**

	Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
75. I avoid having my breast area fondled or kissed.					
76. My partner avoids fondling or kissing my breast area.					
77. I notice I don't hug or kiss my partner much.					
78. I notice my partner doesn't hug and kiss me much.					

PART IV. SLEEP HABITS

The next group of questions ask about your sleep habits. Please check the appropriate box for the one response that best describes how often you experienced these situations in **THE PAST 4 WEEKS**.

79. Did you have trouble falling asleep?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

80. Did you wake up several times a night?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

81. Did you wake up earlier than you planned to?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

82. Did you have trouble getting back to sleep after you woke up too early?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

Patient I.D. _____

Patient Acrostic: _____

83. Overall, how was your typical night's sleep during the past 4 weeks?

- ☐ Very sound or restful
☐ Sound or restful
☐ Average quality
☐ Restless
☐ Very restless

84. About how many hours of sleep did you get on a typical night during the past 4 weeks?

- ☐ 5 or less hours
☐ 6 hours
☐ 7 hours
☐ 8 hours
☐ 9 hours
☐ 10 or more hours

PART V. SPIRITUAL BELIEFS

The following questions are about spiritual beliefs. Please check the appropriate box indicating how true the statement has been for you during **THE PAST WEEK**.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
85. I felt peaceful.					
86. I had a reason for living.					
87. I felt a sense of purpose in my life.					
88. I was able to reach down deep into myself for comfort.					
89. I felt a sense of harmony within myself.					
90. I found comfort in my faith.					
91. I found strength in my faith.					

- 5 -4 -3 -2 -1 0 +1 +2 +3 +4 +5
- Worse Same as before Better

The following questions consist of groups of statements. After reading each group of statements carefully, check the box next to the one statement in each group which **best** describes the way you have been feeling **the past week, including today**. If several statements within a group seem to apply equally, check each one. **Be sure to read all the statements in each group before making your choice.**

- Quality of Life 5/98*

Patient I.D. _____

Patient Acrostic: _____

97. ☐ I don't feel particularly guilty.
☐ I feel guilty a good part of the time.
☐ I feel quite guilty most of the time.
☐ I feel guilty all of the time.
98. ☐ I don't feel I am being punished.
☐ I feel I may be punished.
☐ I expect to be punished.
☐ I feel I am being punished.
99. ☐ I don't feel disappointed in myself.
☐ I am disappointed in myself.
☐ I am disgusted with myself.
☐ I hate myself.
100. ☐ I don't feel I am any worse than anybody else.
☐ I am critical of myself for my weaknesses or mistakes.
☐ I blame myself all the time for my faults.
☐ I blame myself for everything bad that happens.
101. ☐ I don't have any thoughts of killing myself.
☐ I have thoughts of killing myself, but I would not carry them out.
☐ I would like to kill myself.
☐ I would kill myself if I had the chance.
102. ☐ I don't cry anymore than usual.
☐ I cry more now than I used to.
☐ I cry all the time now.
☐ I used to be able to cry, but now I can't cry even though I want to.

103. ☐ I am no more irritated now than I ever am.
☐ I get annoyed or irritated more easily than I used to.
☐ I feel irritated all the time now.
☐ I don't get irritated at all by the things that used to irritate me.
104. ☐ I have not lost interest in other people.
☐ I am less interested in other people than I used to be.
☐ I have lost most of my interest in other people.
☐ I have lost all of my interest in other people.
105. ☐ I make decisions about as well as I ever could.
☐ I put off making decisions more than I used to.
☐ I have greater difficulty in making decisions than before.
☐ I can't make decisions at all anymore.
106. ☐ I don't feel I look any worse than I used to.
☐ I am worried that I am looking old or unattractive.
☐ I feel that there are permanent changes in my appearance that make me look unattractive.
☐ I believe that I look ugly.
107. ☐ I can work about as well as before.
☐ It takes an extra effort to get started at doing something.
☐ I have to push myself very hard to do anything.
☐ I can't do any work at all.
108. ☐ I can sleep as well as usual.
☐ I don't sleep as well as I used to.
☐ I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
☐ I wake up several hours earlier than I used to and cannot get back to sleep.

Patient I.D. _____

Patient Acrostic: _____

109. ☐ I don't get more tired than usual.
☐ I get tired more easily than I used to.
☐ I get tired from doing almost anything.
☐ I am too tired to do anything.
110. ☐ My appetite is no worse than usual.
☐ My appetite is not as good as it used to be.
☐ My appetite is much worse now.
☐ I have no appetite at all anymore.
111. ☐ I haven't lost much weight, if any, lately.
☐ I have lost more than five (5) pounds.
☐ I have lost more than ten (10) pounds.
☐ I have lost more than fifteen (15) pounds.
112. ☐ I am no more worried about my health than usual.
☐ I am worried about physical problems such as aches and pains; or upset stomach; or constipation.
☐ I am very worried about physical problems and it's hard to think of much else.
☐ I am so worried about my physical problems that I cannot think about anything else.
113. ☐ I have not noticed any recent change in my interest in sex.
☐ I am less interested in sex than I used to be.
☐ I am much less interested in sex now.
☐ I have lost interest in sex completely.

Patient I.D.: _____ - _____

Patient Acrostic: _____

Visit Type: ☐ Baseline ☐ 6 month ☐ 12 month ☐ 18 month ☐ 24 month ☐ 30 month ☐ 36 month

SOCIAL SUPPORT FORM

The following are questions about the support that is available to you.

1. At the present time, about how many close friends and close relatives do you have (people you feel at ease with and can talk to about what is on your mind)? **(Please write the number in the boxes below.)**

Number of close friends and close relatives

People sometimes look to others for companionship, assistance, or other types of support. Currently, how often is each of the following kinds of support available to you if you need it? (Check one box for each statement.)

	None of the time	A little of the time	Some of the time	Most of the time	All of the time
2. Someone to help you if you were confined to bed.					
3. Someone you can count on to listen to you when you need to talk.					
4. Someone to give you good advice about a crisis.					
5. Someone to take you to the doctor if you needed it.					
6. Someone who shows you love and affection.					
7. Someone to have a good time with.					
8. Someone to give you information to help you understand a situation.					
9. Someone to confide in or talk to about yourself or your problems.					

	None of the time	A little of the time	Some of the time	Most of the time	All of the time
10. Someone who hugs you.					
11. Someone to get together with for relaxation.					
12. Someone to prepare your meals if you were unable to do it yourself.					
13. Someone whose advice you really want.					
14. Someone to do things with to help you get your mind off things.					
15. Someone to help with daily chores if you were sick.					
16. Someone to share your most private worries and fears with.					
17. Someone to turn to for suggestions about how to deal with a personal problem.					
18. Someone to do something enjoyable with.					
19. Someone who understands your problems.					
20. Someone to love you and make you feel wanted.					

Patient I.D. _____

Patient Acrostic: _____

For the following questions, please check the box that is the most true for you at the present time.
(Check only one box for each statement.)

Of the people who are important to you, how many:

	None	One	Some	Most	All
21. Don't understand you.					
22. Get on your nerves.					
23. Ask too much of you.					
24. Argue with you.					
25. Don't include you.					
26. Show that they don't like you.					
27. Boss you.					
28. Try to get you to do things you don't want to do.					

Patient I.D. _____ - _____

Patient Acrostic: _____

PERSONAL HABITS FORM

These questions are about habits that may affect your health (smoking, alcohol use, weight, and exercise). Please answer each question as accurately as possible. There are no right or wrong answers.

1. Have you ever smoked more than 100 cigarettes in your life?

☐

No ---> (Go to Question 6)

☐

Yes, I am a former smoker. ---> (Go to Question 2)

☐

Yes, I am a current smoker. ---> (Go to Question 3)

2. As a former smoker, how many years did you smoke?

A. _____ Years

B. How many cigarettes did you smoke per day? (1 pack = 20 cigarettes)

☐

I smoked occasionally

☐

0 - 5 cigarettes a day

☐

6 - 20 cigarettes a day

☐

21 - 30 cigarettes a day

☐

31 - 40 cigarettes a day

☐

more than 40 cigarettes a day

(Go to question 4.)

3. As a current smoker, how many years have you been smoking?

A. _____ Years B. How many cigarettes do you smoke per day? (1 pack = 20 cigarettes)

- ☐ I smoke occasionally.
- ☐ 0 - 5 cigarettes a day
- ☐ 6 - 20 cigarettes a day
- ☐ 21 - 30 cigarettes a day
- ☐ 31 - 40 cigarettes a day
- ☐ more than 40 cigarettes a day

4. Were you smoking cigarettes at the time of your diagnosis of breast cancer?

- ☐ No ---> (Go to Question 6)
- ☐ Yes ---> (Go to Question 5)

5. How many cigarettes were you smoking per day at the time of your diagnosis? (1 pack = 20 cigarettes)

- ☐ I smoked occasionally.
- ☐ 0 - 5 cigarettes a day
- ☐ 6 - 20 cigarettes a day
- ☐ 21 - 30 cigarettes a day
- ☐ 31 - 40 cigarettes a day
- ☐ more than 40 cigarettes a day

6. Have you ever drank alcoholic beverages?

- ☐ No ---> (Go to Question 8)
- ☐ Yes ---> (Go to Question 6a)

6a. If yes, about how many alcoholic beverages (beer, wine, or mixed drinks) do you currently drink in an average month?

Beverages per month

Patient I.D. _____

Patient Acrostic: _____

7. Were you drinking alcoholic beverages prior to your diagnosis of breast cancer?

☐

No ---> (Go to question 8)

☐

Yes ---> (Go to question 7a)

7a. If yes, on average how many beverages per month were you drinking prior to your diagnosis?

beverages per month

8. A woman's weight changes during her adult life. Mark the one answer that best describes you during your adult life prior to your diagnosis with breast cancer. Please don't include times when you were pregnant or sick. **(Mark only one.)**

☐

Weight has stayed about the same (within 10 pounds) ---> (Go to question 9)

☐

Steady gain in weight ---> (Go to Question 9)

☐

Lost weight as an adult and kept it off ---> (Go to Question 9)

☐

Weight has gone up and down again by more than 10 pounds ---> (Go to Question 8a)

8a. About how many times has your weight gone up and down by more than 10 pounds? Please don't include times when you were pregnant or sick.

times

9. Have you gained any weight since you were diagnosed with breast cancer?

☐

No ----> (Go to question 10)

☐

Yes ----> (Go to question 9a)

9a. If yes, how many pounds have you gained?

pounds

10. Have you lost any weight since you were diagnosed with breast cancer?

☐ No ----> (Go to question 11)

☐ Yes ----> (Go to question 10a)

10a. If yes, how many pounds have you lost?

pounds

11. What is your height?

(feet) (inches) .

12. What is your current weight?

pounds

13. What was your usual weight prior to your diagnosis with breast cancer?

pounds

13a. How long had you been at this weight?

years --- months

The following questions are about your usual physical activity and exercise. This includes walking and sports.

14. Think about the walking you do outside the home. In the past month, how often did you walk outside the home for more than 10 minutes without stopping? (Mark only one.)

- ☐ Rarely or never ----> (Go to Question 15)
- ☐ 1-3 times each month ----> (Go to Question 14a)
- ☐ 1 time each week ----> (Go to Question 14a)
- ☐ 2-3 times each week ----> (Go to Question 14a)
- ☐ 4-6 times each week ----> (Go to Question 14a)
- ☐ 7 or more times each week ----> (Go to Question 14a)

Patient I.D. _____

Patient Acrostic: _____

- 14a. When you walked outside the home for more than 10 minutes without stopping, how many minutes did you usually walk?

- ☐ Less than 20 minutes
☐ 20-39 minutes
☐ 40-59 minutes
☐ 1 hour or more

- 14b. What was your usual speed?

- ☐ Casual strolling or walking (less than 2 miles an hour)
☐ Average or normal (2-3 miles an hour)
☐ Fairly fast (3-4 miles an hour)
☐ Very fast (more than 4 miles an hour)
☐ Don't know

Following are three categories of exercise, (strenuous, moderate, and mild). Not including walking outside the home, how often each week (7 days) do you usually do the following strenuous, moderate, and mild types of exercise?

15. **STRENUOUS OR VERY HARD EXERCISE.** (You work up a sweat and your heart beats fast.)
For example, aerobics, aerobic dancing, jogging, tennis, swimming laps.

☐	None	--->	(Go to Question 16)
☐	1 day per week	--->	(Go to Question 15a)
☐	2 days per week	--->	(Go to Question 15a)
☐	3 days per week	--->	(Go to Question 15a)
☐	4 days per week	--->	(Go to Question 15a)
☐	5 or more days per week	--->	(Go to question 15a)

15a. How long do you usually exercise like this at one time?

- ☐ Less than 20 minutes
- ☐ 20-39 minutes
- ☐ 40-59 minutes
- ☐ 1 hour or more

16. **MODERATE EXERCISE** (Not exhausting). For example, biking outdoors, using an exercise machine (like a stationary bike or treadmill), calisthenics, easy swimming, popular or folk dancing.

- ☐ None ---> (Go to Question 17)
- ☐ 1 day per week ---> (Go to Question 16a)
- ☐ 2 days per week ---> (Go to Question 16a)
- ☐ 3 days per week ---> (Go to Question 16a)
- ☐ 4 days per week ---> (Go to Question 16a)
- ☐ 5 or more days per week ---> (Go to Question 16a)

16a. How long do you usually exercise like this at one time?

- ☐ Less than 20 minutes
- ☐ 20-39 minutes
- ☐ 40-59 minutes
- ☐ 1 hour or more

Patient I.D. _____ - _____

Patient Acrostic: _____

17. **MILD EXERCISE.** For example, slow dancing, bowling, golf.

☐	None	--->	(Go to Question 18)
☐	1 day per week	--->	(Go to Question 17a)
☐	2 days per week	--->	(Go to Question 17a)
☐	3 days per week	--->	(Go to Question 17a)
☐	4 days per week	--->	(Go to Question 17a)
☐	5 or more days per week	--->	(Go to Question 17a)

17a. How long do you usually exercise like this at one time?

☐	Less than 20 minutes
☐	20-39 minutes
☐	40-59 minutes
☐	1 hour or more

Patient I.D. _____ - _____

Patient Acrostic: _____

CONTACT INFORMATION FORM

We would like some information about you and two relatives or friends so that we can keep in touch with you during the study. This information is very important, so please answer these questions completely. Please print the information in the space provided or mark the appropriate box.

1. Your full legal name: _____
First MI Last

2. Name you prefer to use: (if different) _____

3. What is your maiden name? _____
Last

4. What is your date of birth: / /
Month Day Year

5. Social Security Number: _____ - _____ - _____

6. Your Mailing Address:

7. Telephone Numbers: Home: Area Code (____) _____ - _____

Work: Area Code (____) _____ - _____

Other: Area Code (____) _____ - _____

8. When is the best time to contact you?

Where is the best place to contact you?

_____ time(s)
Day of week

- ☐ At home
☐ At work
☐ Other

_____ time(s)
Day of week

- ☐ At home
☐ At work
☐ Other

9. What is your husband's (partner's) legal name? (This information will help us keep in contact with you during the study. Please leave this blank if you are not currently married or with a long-term partner.)

_____ MI _____
First Last

10. Please provide the names of two relatives or friends, not living in your household, who are likely to know how to contact you if we are unable to reach you.

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

Patient I.D. _____
Patient Acrostic: _____

11. Please provide the name of the physician you go to for most of your general health care needs. (For example, your family physician or a gynecologist).

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

12. Please provide the name of your oncologist.

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

13. Please provide the name of your breast surgeon, (if applicable).

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

14. Please provide the name of your radiologist, (if applicable).

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

Appendix K
Revised October 1998 Annual Report
DAMD 17-96-1-6292
J. Petrek

MENSTRUAL CYCLE MAINTENANCE AND QUALITY OF LIFE

6-Month Follow-up Survey



Clinical Coordinating Center

**Wake Forest University School of Medicine
Department of Public Health Sciences
Winston-Salem, North Carolina 27157-1063
(336) 716-2116**



**Funded by
The U.S. Army Medical Research and Material Command:
Breast Cancer Research Program A**

Patient I.D. _____

Patient Acrostic: _____

PART I

**MEDICAL and REPRODUCTIVE HISTORY
FOLLOW-UP QUESTIONNAIRE**

The following questions ask about health professionals you may have seen in the past 6 months. This information will help us describe in general terms the kinds of services being used.

1. In the past six months, which of the following doctors or other health professionals have you seen?
(Please Check all that apply)

☐ None	☐ Family Therapist
☐ Acupuncturist	☐ Nutritionist
☐ Allergist	☐ Obstetrician
☐ Cardiologist	☐ Medical Oncologist/Chemotherapist
☐ Chiropractor	☐ Orthopedic Surgeon
☐ Dentist	☐ Homeopathic/Herbalist/Naturopathic
☐ Dermatologist	☐ Pain Control Professional
☐ Ear/Nose/Throat Doctor	☐ Alternative Therapist (Homeopath, herbalist, naturopathologist, etc.)
☐ Eye Doctor	☐ Physical Therapist
☐ Marital Counselor	☐ Plastic Surgeon
☐ Gastroenterologist	☐ Psychiatrist
☐ General Practitioner	☐ Clinical Psychologist
☐ Gynecologist	☐ Radiologist
☐ Infertility Specialist	☐ Rheumatologist
☐ Internist	☐ Social Worker
☐ Massage Therapist	☐ Organized Support Group
☐ Neurologist	☐ Surgeon
☐ Sexual Therapist	☐ Urologist
	☐ Other: _____

2. In the past 6 months, have you been seen at an emergency room?

☐ No

☐ Yes → For what reason: _____

3. In the past 6 months, have you been hospitalized or had surgery? Please mark one box for each line item (a) and (b).

	No	Yes	If yes, for what reason?
(a) Hospitalized?			
(b) Had surgery?			

4. Has anything else changed regarding either your mental or physical health status? Please mark one box for each line item (a) and (b).

	No	Yes	What has changed?
(a) Mental Health?			
(b) Physical Health?			

Patient I.D. _____ - _____

Patient Acrostic: _____

5. Have you had any biopsies in the past 6 months?

☐ No

☐ Yes → If yes, what was biopsied? _____

Why was this biopsied? _____

6. In the past 6 months, have you had a re-occurrence of breast cancer?

☐ No

☐ Yes → If yes, how was this diagnosis made. (For example, biopsy, lab tests)?

7. Have you been diagnosed with any other cancer in the past 6 months?

☐ No

☐ Yes → If yes, what type? _____

How was this diagnosis made? (For example, biopsy, lab tests)?

8. Today's date is:

 /

 /

Month Day Year

Patient I.D. _____

Patient Acrostic: _____

PART II

REPRODUCTIVE HISTORY

The following questions ask about your menstrual cycles and reproductive history. We are very interested in this information so that we can understand more about women's health during their childbearing years. Some of the questions ask you to give dates or the number of times when certain things happened. If you are not sure about the exact date or number of times, please give your best estimate.

1. What was the date of the first day of your last menstrual period (your best guess)?

		-			-				
Month			Day			Year			

2. In the past 6 months, have you been sexually active with a male partner:

☐ No → Go to question 6

☐ Yes → Go to question 3

3. Which method of birth control are you and your partner using currently? (**Check all that apply.**)

- ☐ No method
- ☐ Condoms (rubbers)
- ☐ Birth control pills
- ☐ Foams/jellies/suppositories
- ☐ Sponge
- ☐ Withdrawal (pulling out)
- ☐ Diaphragm

- ☐ Safe periods (rhythm or counting days)
- ☐ Norplant
- ☐ Cervical cap
- ☐ Tubal ligation (tubes tied)
- ☐ Vasectomy
- ☐ Other (Please describe: _____)
- ☐ Don't know

4. In the past month, how many times have you had sexual intercourse without using contraception?

Times

5. In the past 6 months, have you become pregnant?

☐ No

☐ Yes → If yes, are you pregnant now?

☐ No

☐ Yes

6. In the past month, have you had any hot flashes or night sweats (hot flashes that occur during sleep)?

☐ No

☐ Yes ----> If yes, how many have you had in the **past week**?

hot flashes/night sweats

Patient I.D. _____
Patient Acrostic: _____

PART III

CURRENT MEDICATIONS

1. Please list below all of the **prescription medications** you are taking currently. (Write "none" if you are not taking any prescription medications at this time.)

Drug Name	Dosage
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

2. Please list below all of the **non-prescription medications or supplements** you are taking currently. (Write "none" if are not taking any non-prescription medications or supplements at this time.)

Drug Name	Dosage
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

Patient I.D. _____

Patient Acrostic: _____

SWELLING FORM

The following questions concern swelling in your arm and/or hand. Please mark the appropriate box(es) for each question.

1. In the past 6 months, has any swelling occurred in your arm or hand on the same side that you had your lumpectomy or mastectomy?

☐

No → (Go to question 8)

☐

Yes → (Continue to question 2)

☐

Don't know → (Go to question 8)

2. Do you believe the start of your swelling was related to any of the following?

Yes

☐

No

☐

Don't
Know

☐

Radiation treatment

☐☐☐

Breast reconstruction

☐☐☐

Infection or injury to arm / hand

☐☐☐

Weather changes

☐☐☐

General use of your arm

☐☐☐

Exercise

☐☐☐

Airplane travel

☐

Other: Please describe: _____

2a. How soon after you had surgery and/or began treatment did this swelling occur?

- ☐ Less than 1 week
- ☐ 1 week to 4 weeks
- ☐ 1 month to 3 months
- ☐ 4 months to 6 months
- ☐ 7 months to 9 months
- ☐ 10 months to 12 months
- ☐ 13 months to 15 months

2b. Where does (did) the swelling occur? **(Check all that apply)**

- ☐ Hand
- ☐ Upper Arm
- ☐ Lower Arm

2c. Do (did) you consider the swelling to be mostly?

- ☐ Mild
- ☐ Moderate
- ☐ Severe

3. Does (did) the swelling interfere with any of the following?

Yes	No	
☐	☐	Clothing that you wear
☐	☐	Your ability to do routine activities, such as household chores or grooming.
☐	☐	Exercise
☐	☐	Your appearance
☐		Other, please describe: _____

Patient I.D. _____

Patient Acrostic: _____

4. Does (did) swelling seem to get worse with any of the following?

Yes	No	Don't Know	
☐	☐	☐	Hot weather
☐	☐	☐	General use of your arm
☐	☐	☐	Exercise
☐	☐	☐	Sauna / Jacuzzi / Hot bath
☐	☐	☐	Airplane travel
☐	☐	☐	Specific foods
☐	☐	☐	Mental / emotional stress
☐			Other: Please describe: _____

5. Prior to your breast cancer diagnosis, did you notice swelling in your hand and/or arm with any of the following? **(Check all that apply)**

Yes	No	Don't Know	
☐	☐	☐	Exercise
☐	☐	☐	Household Chores
☐	☐	☐	Heat/Humidity
☐	☐	☐	Eating salty foods
☐	☐	☐	Drinking alcoholic beverages
☐			Other: Please describe: _____

6. Did you seek treatment for this swelling in the past 6 months?

☐

No → If no, why not?

☐

Yes → If yes, what type of treatment did you receive? **(Check all that apply)**

☐

Compression therapy by machine

☐

Glove / Sleeve Compression / Garment

☐

Physical therapy

☐

Manual lymphatic drainage

☐

Bandaging technique

☐

Other, please describe: _____

7. Do you have swelling now?

☐

No → (Go to question 8)

☐

Yes → (Continue to question 7a)

7a. If yes, how long have you had swelling?

☐

Less than 1 week

☐

2 - 4 weeks

☐

1 - 3 months

☐

4 - 6 months

☐

7 - 9 months

☐

10 - 12 months

Patient I.D. _____

Patient Acrostic: _____

8. In the past 6 months, do you remember any breaks in your skin, infected hang nails, or slight skin injuries in your arm or hand on the same side that you had your lumpectomy or mastectomy?

- ☐ No → (Go to question 9)
- ☐ Yes → (Continue to question 8a)
- ☐ Don't Know → (Continue to question 9)

8a. If yes, did you receive antibiotics?

- ☐ Yes
- ☐ No
- ☐ Don't know

9. In the past 6 months, did you have any infection in the arm or hand on the same side that you had your lumpectomy or mastectomy?

- ☐ No → (Go to question 10)
- ☐ Yes → (Continue to question 9a)
- ☐ Don't Know → (Continue to question 10)

If yes, did you:

9a. receive antibiotics by mouth?

- ☐ No
- ☐ Yes
- ☐ Don't know

If yes, did you:

9b. receive antibiotics by injection?

☐

No

☐

Yes

☐

Don't know

10. Do you have pain in the affected arm and/or hand? (**Check one box for each site**)

	Yes	No
hand		
arm		
hand and arm		

Patient I.D. : _____ - _____

Patient Acrostic: _____

SYMPTOMS QUESTIONNAIRE

Below are statements about symptoms some people may experience. For each statement, check the appropriate box for the response that best describes how bothersome the symptom was for you **during the past month**. If you did not have the problem, check the box under the column titled "symptom did not occur". Please do not skip any questions. **Mark only one box on each line.**

If you experienced the symptom, use the following key to indicate how bothersome it was:

Mild = symptom did not interfere with usual activities.
Moderate = symptom interfered somewhat with usual activities.
Severe = symptom was so bothersome that usual activities could not be performed.

Symptom	Symptom did not occur	Symptom Occurred and Was:		
		Mild	Moderate	Severe
1. Fatigue or low energy level				
2. Mouth ulcers				
3. Restless sleep				
4. Sleeping too much				
5. Nervousness or shakiness inside				
6. Mood changes				
7. Feeling depressed				
8. Lightheadedness when standing up				
9. Faintness or dizziness at rest				
10. Headaches				
11. Swelling of ankles or feet				
12. Diarrhea				

Symptom	Symptom did not occur	Symptom Occurred and Was:		
		Mild	Moderate	Severe
13. Constipation				
14. Abdominal pain/cramps				
15. Vaginal dryness				
16. Muscle pain/ache/or cramp				
17. Weight gain				
18. Weight loss				
19. General aches and pains				
20. Hot flashes				
21. Joint pains				
22. Night sweats				
23. Aches in back of neck and skull				
24. Forgetfulness				
25. Difficulty concentrating				
26. Increased appetite				
27. Short temper				
28. Decreased efficiency				
29. Loss of interest in work/activities				
30. Lowered work performance				
31. Blind spots, fuzzy vision				
32. Breast sensitivity/tenderness				
33. Avoidance of social affairs				
34. Cold sweats				
35. Decreased appetite				
36. Feelings of suffocation				
37. Difficulty healing				
38. Bloating				

Patient I.D. _____

Patient Acrostic: _____

QUALITY OF LIFE FORM

1. In general, would you say your health is: **(Check one)**

Excellent

☐

Very good

☐

Good

☐

Fair

☐

Poor

☐

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.

Limited a lot

☐

Limited a little

☐

Not limited at all

☐

3. Climbing several flights of stairs.

Limited a lot

☐

Limited a little

☐

Not limited at all

☐

During the past four weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	Yes	No
4. Accomplished less than you would like.	☐	☐
5. Had difficulty performing the work or other activities, for example, it took extra effort.	☐	☐

During the past four weeks, have you had any of the following problems with your work or other regular daily activities as a result of emotional problems (such as feeling depressed or anxious)?

	Yes	No
6. Accomplished less than you would like.	☐	☐
7. Didn't do work or other activities as carefully as usual.	☐	☐

8. During the past four weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? **(Check one)**

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

9. During the past four weeks, how much did pain interfere with your normal activities (including both work outside the home, housework and family activities)? **(Check one)**

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

These questions are about how you feel and how things have been with you during the past four weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past four weeks:

10. Have you felt calm and peaceful? **(Check one)**

All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐	☐

11. Did you have a lot of energy? **(Check one)**

All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐	☐

12. Have you felt downhearted and blue? **(Check one)**

All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐	☐

Patient Acrostic: _____

Physical Well-Being	Not At All	A Little Bit	Some-what	Quite a bit	Very Much
13. I had a lack of energy.	1	2	3	4	5
14. I had nausea.	1	2	3	4	5
15. I had trouble meeting the needs of my family.	1	2	3	4	5
16. I had pain.	1	2	3	4	5
17. I was bothered by side effects of treatment.	1	2	3	4	5
18. In general, I felt sick.	1	2	3	4	5
19. I was forced to spend time in bed.	1	2	3	4	5

0	1	2	3	4	5	6	7	8	9	10
										Very Much So

Social/Family Well-Being	Not At All	A Little Bit	Some-what	Quite a bit	Very Much
21. I felt distant from my friends	1	2	3	4	5
22. I got emotional support from my family.	1	2	3	4	5
23. I got support from my friends and neighbors.	1	2	3	4	5
24. My family had accepted my illness.	1	2	3	4	5
25. Family communication about my illness was poor.	1	2	3	4	5

26. I felt close to my partner (or main support).	1	2	3	4	5
27. I was satisfied with my sex life.	1	2	3	4	5

0	1	2	3	4	5	6	7	8	9	10
										Very Much So

Relationship With Doctor	Not At All	A Little Bit	Some-What	Quite a bit	Very Much
29. I had confidence in my doctor(s).	1	2	3	4	5
30. My doctor was available to answer my questions.	1	2	3	4	5
31. How much does your <u>Relationship with your Doctor</u> affect your quality of life? (Circle one number.)					
0	1	2	3	4	5
6	7	8	9	10	
Not at all					Very Much So

Emotional Well-Being	Not at All	A Little Bit	Some-what	Quite a bit	Very Much
32. I felt sad.	1	2	3	4	5
33. I was proud of how I'm coping with my illness.	1	2	3	4	5
34. I was losing hope in the fight against my illness.	1	2	3	4	5
35. I felt nervous.	1	2	3	4	5
36. I worried about dying.	1	2	3	4	5
37. How much does your <u>Emotional Well-Being</u> affect your quality of life? (Circle one number.)					
0	1	2	3	4	5
6	7	8	9	10	
Not at all					Very Much So

Functional Well-Being	Not at All	A Little Bit	Some-what	Quite a bit	Very Much
38. I was able to work (include work in home).	1	2	3	4	5
39. My work (include work in home) was fulfilling.	1	2	3	4	5
40. I was able to enjoy life "in the moment."	1	2	3	4	5
41. I had accepted my illness.	1	2	3	4	5
42. I was sleeping well.	1	2	3	4	5
43. I enjoyed my usual leisure pursuits.	1	2	3	4	5
44. I was content with the quality of my life right now.	1	2	3	4	5
45. How much does your <u>Functional Well-Being</u> affect your quality of life? (Circle one number.)					
0	1	2	3	4	5
6	7	8	9	10	
Not at all					Very Much So

Patient I.D. _____

Patient Acrostic: _____

Additional Concerns

	Not At All	A Little Bit	Some- what	Quite a bit	Very Much
46. I was short of breath.	1	2	3	4	5
47. I was self-conscious about the way I dressed.	1	2	3	4	5
48. My arms were swollen or tender.	1	2	3	4	5
49. I felt sexually attractive.	1	2	3	4	5
50. I was bothered by hair loss.	1	2	3	4	5
51. I worried about the risk of cancer in other family members.	1	2	3	4	5
52. I worried about the effect of stress on my illness.	1	2	3	4	5
53. I was bothered by a change in weight.	1	2	3	4	5
54. I was able to feel like a woman.	1	2	3	4	5

55. How much do these Additional Concerns affect your quality of life? (Circle one number.)

0 1 2 3 4 5 6 7 8 9 10
Not at all Very Much So

YOUR APPEARANCE

This section asks you about your general perceptions regarding your body. Right now, how satisfied are you with these parts of your body? Please check the appropriate box for the response that best describes your satisfaction with each body part.

	Very dissatisfied	Somewhat dissatisfied	Neutral	Somewhat satisfied	Very satisfied
56. Hair					
57. Breasts					
58. Arms					
59. Face					
60. Waist					
61. Hips					
62. Thighs					
63. Overall body					

How much do you agree or disagree with the following statement? (Check the appropriate box.)

64. The appearance of my breast area is important to me.

**Strongly
Disagree**

☐

Disagree

☐

**Neither Agree
or Disagree**

☐

Agree

☐

**Strongly
Agree**

☐

65. I view myself as a:

☐

Very overweight person

☐

Moderately overweight person

☐

Normal weight person

☐

Moderately thin person

☐

Very thin person

PART III. SEXUALITY

These next questions are about the way health problems may interfere with your sex life. These questions are personal, but your answers are important in understanding how health problems may affect women's sexuality.

66. Have you been sexually active with a partner during the last 6 months?

☐

No ----> (If no, skip to Question 79).

☐

Yes ----> (If yes, continue to Question 67).

67. How many times have you had sexual intercourse in the past month?

☐

0 times

☐

1 - 4 times

☐

5 - 10 times

☐

11 or more

Patient I.D. _____

Patient Acrostic: _____

For the following questions, please check the box for the response that best describes your sexual feelings and experiences **DURING THE PAST MONTH.**

	Never	Almost Never	Sometimes	Almost Always	Always
68. How often were you aware of wetness in your vagina as you became sexually excited?					
69. How often did it take a long time for your vagina to become wet or slippery as you became sexually excited?					
70. During sexual relations, how frequently did you notice dryness of your vagina?					
71. How often did you feel pain or discomfort during vaginal penetration?					
72. How often did you feel satisfied after sexual activity?					
73. How often were you satisfied with the frequency of sexual activity?					
74. How frequently did you feel tense or nervous after a sexual experience?					

For the following questions, please check the box for the response that best describes your sexual feelings and experiences **DURING THE PAST MONTH.**

	Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
75. I avoided having my breast area fondled or kissed.					
76. My partner avoided fondling or kissing my breast area.					
77. I notice I didn't hug or kiss my partner much.					
78. I notice my partner didn't hug and kiss me much.					

PART IV. SLEEP HABITS

The next group of questions ask about your sleep habits. Please check the appropriate box for the one response that best describes how often you experienced these situations in **THE PAST 4 WEEKS**.

79. Did you have trouble falling asleep?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

80. Did you wake up several times a night?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

81. Did you wake up earlier than you planned to?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

82. Did you have trouble getting back to sleep after you woke up too early?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

Patient I.D. _____

Patient Acrostic: _____

83. Overall, how was your typical night's sleep during the past 4 weeks?

- ☐ Very sound or restful
- ☐ Sound or restful
- ☐ Average quality
- ☐ Restless
- ☐ Very restless

84. About how many hours of sleep did you get on a typical night during the past 4 weeks?

- ☐ 5 or less hours
- ☐ 6 hours
- ☐ 7 hours
- ☐ 8 hours
- ☐ 9 hours
- ☐ 10 or more hours

PART V. SPIRITUAL BELIEFS

The following questions are about spiritual beliefs. Please check the appropriate box indicating how true the statement has been for you during **THE PAST WEEK**.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
85. I felt peaceful.					
86. I had a reason for living.					
87. I felt a sense of purpose in my life.					
88. I was able to reach down deep into myself for comfort.					
89. I felt a sense of harmony within myself.					
90. I found comfort in my faith.					
91. I found strength in my faith.					

92. Where would you place yourself on the following scale, if "0" means that your life is just the way it was before your breast cancer, "+5" means that everything is totally different but better, and "-5" means that everything is totally different but worse. **(Please circle ONE number).**

-5	-4	-3	-2	-1	0	+1	+2	+3	+4	+5
Worse					Same as before					Better

PART VI. EMOTIONAL FEELINGS

The following questions consist of groups of statements. After reading each group of statements carefully, check the box next to the one statement in each group which **best** describes the way you have been feeling **the past week, including today**. If several statements within a group seem to apply equally, check each one. **Be sure to read all the statements in each group before making your choice.**

93. ☐ I do not feel sad.
☐ I feel sad.
☐ I am sad all the time and I can't snap out of it.
☐ I am so sad or unhappy that I can't stand it.
94. ☐ I am not particularly discouraged about the future.
☐ I feel discouraged about the future.
☐ I feel I have nothing to look forward to.
☐ I feel that the future is hopeless and that things cannot improve.
95. ☐ I do not feel like a failure.
☐ I feel I have failed more than the average person.
☐ As I look back on my life, all I can see is a lot of failures.
☐ I feel I am a complete failure as a person.
96. ☐ I get as much satisfaction out of things as I used to.
☐ I don't enjoy things the way I used to.
☐ I don't get real satisfaction out of anything anymore.
☐ I am dissatisfied or bored with everything.

Patient I.D. _____ - _____

Patient Acrostic: _____

97. ☐ I don't feel particularly guilty.
☐ I feel guilty a good part of the time.
☐ I feel quite guilty most of the time.
☐ I feel guilty all of the time.
98. ☐ I don't feel I am being punished.
☐ I feel I may be punished.
☐ I expect to be punished.
☐ I feel I am being punished.
99. ☐ I don't feel disappointed in myself.
☐ I am disappointed in myself.
☐ I am disgusted with myself.
☐ I hate myself.
100. ☐ I don't feel I am any worse than anybody else.
☐ I am critical of myself for my weaknesses or mistakes.
☐ I blame myself all the time for my faults.
☐ I blame myself for everything bad that happens.
101. ☐ I don't have any thoughts of killing myself.
☐ I have thoughts of killing myself, but I would not carry them out.
☐ I would like to kill myself.
☐ I would kill myself if I had the chance.
102. ☐ I don't cry anymore than usual.
☐ I cry more now than I used to.
☐ I cry all the time now.
☐ I used to be able to cry, but now I can't cry even though I want to.

103. ☐ I am no more irritated now than I ever am.
☐ I get annoyed or irritated more easily than I used to.
☐ I feel irritated all the time now.
☐ I don't get irritated at all by the things that used to irritate me.
104. ☐ I have not lost interest in other people.
☐ I am less interested in other people than I used to be.
☐ I have lost most of my interest in other people.
☐ I have lost all of my interest in other people.
105. ☐ I make decisions about as well as I ever could.
☐ I put off making decisions more than I used to.
☐ I have greater difficulty in making decisions than before.
☐ I can't make decisions at all anymore.
106. ☐ I don't feel I look any worse than I used to.
☐ I am worried that I am looking old or unattractive.
☐ I feel that there are permanent changes in my appearance that make me look unattractive.
☐ I believe that I look ugly.
107. ☐ I can work about as well as before.
☐ It takes an extra effort to get started at doing something.
☐ I have to push myself very hard to do anything.
☐ I can't do any work at all.
108. ☐ I can sleep as well as usual.
☐ I don't sleep as well as I used to.
☐ I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
☐ I wake up several hours earlier than I used to and cannot get back to sleep.

Patient I.D. _____

Patient Acrostic: _____

109. ☐ I don't get more tired than usual.
☐ I get tired more easily than I used to.
☐ I get tired from doing almost anything.
☐ I am too tired to do anything.
110. ☐ My appetite is no worse than usual.
☐ My appetite is not as good as it used to be.
☐ My appetite is much worse now.
☐ I have no appetite at all anymore.
111. ☐ I haven't lost much weight, if any, lately.
☐ I have lost more than five (5) pounds.
☐ I have lost more than ten (10) pounds.
☐ I have lost more than fifteen (15) pounds.
112. ☐ I am no more worried about my health than usual.
☐ I am worried about physical problems such as aches and pains; or upset stomach; or constipation.
☐ I am very worried about physical problems and it's hard to think of much else.
☐ I am so worried about my physical problems that I cannot think about anything else.
113. ☐ I have not noticed any recent change in my interest in sex.
☐ I am less interested in sex than I used to be.
☐ I am much less interested in sex now.
☐ I have lost interest in sex completely.

Patient I.D. _____

Patient Acrostic: _____

SOCIAL SUPPORT FORM

The following are questions about the support that is available to you.

1. At the present time, about how many close friends and close relatives do you have (people you feel at ease with and can talk to about what is on your mind)? **(Please write the number in the boxes below.)**

Number of close friends and close relatives

People sometimes look to others for companionship, assistance, or other types of support. Currently, how often is each of the following kinds of support available to you if you need it? (Check one box for each statement.)

	None of the time	A little of the time	Some of the time	Most of the time	All of the time
2. Someone to help you if you were confined to bed.					
3. Someone you can count on to listen to you when you need to talk.					
4. Someone to give you good advice about a crisis.					
5. Someone to take you to the doctor if you needed it.					
6. Someone who shows you love and affection.					
7. Someone to have a good time with.					
8. Someone to give you information to help you understand a situation.					
9. Someone to confide in or talk to about yourself or your problems.					

	None of the time	A little of the time	Some of the time	Most of the time	All of the time
10. Someone who hugs you.					
11. Someone to get together with for relaxation.					
12. Someone to prepare your meals if you were unable to do it yourself.					
13. Someone whose advice you really want.					
14. Someone to do things with to help you get your mind off things.					
15. Someone to help with daily chores if you were sick.					
16. Someone to share your most private worries and fears with.					
17. Someone to turn to for suggestions about how to deal with a personal problem.					
18. Someone to do something enjoyable with.					
19. Someone who understands your problems.					
20. Someone to love you and make you feel wanted.					

Patient I.D. _____
 Patient Acrostic: _____

For the following questions, please check the box that is the most true for you at the present time.
 (Check only one box for each statement.)

Of the people who are important to you, how many:

	None	One	Some	Most	All
21. Don't understand you.					
22. Get on your nerves.					
23. Ask too much of you.					
24. Argue with you.					
25. Don't include you.					
26. Show that they don't like you.					
27. Boss you.					
28. Try to get you to do things you don't want to do.					

Patient I.D. _____

Patient Acrostic: _____

PERSONAL HABITS FORM

These questions are about habits that may affect your health (smoking, alcohol use, weight, and exercise). Please answer each question as accurately as possible.

1. Do you smoke currently?

☐

No

☐

Yes

If yes, how many cigarettes do you smoke per day? (1 pack = 20 cigarettes)

☐

I smoke occasionally.

☐

0 - 5 cigarettes a day

☐

6 - 20 cigarettes a day

☐

21 - 30 cigarettes a day

☐

31 - 40 cigarettes a day

☐

more than 40 cigarettes a day

2. Do you currently drink alcoholic beverages?

☐

No

☐

Yes

If yes, about how many alcoholic beverages (beer, wine, or mixed drinks) do you currently drink in an average month?

Beverages per month

3. What is your current weight?

pounds

The following questions are about your usual physical activity and exercise. This includes walking and sports.

4. Think about the walking you do outside the home. In the past month, how often did you walk outside the home for more than 10 minutes without stopping? (Mark only one.)

☐	Rarely or never	--->	(Go to Question 5)
☐	1-3 times each month	--->	(Go to Question 4a)
☐	1 time each week	--->	(Go to Question 4a)
☐	2-3 times each week	--->	(Go to Question 4a)
☐	4-6 times each week	--->	(Go to Question 4a)
☐	7 or more times each week	--->	(Go to Question 4a)

4a. When you walked outside the home for more than 10 minutes without stopping, how many minutes did you usually walk?

☐	Less than 20 minutes
☐	20-39 minutes
☐	40-59 minutes
☐	1 hour or more

4b. What was your usual speed?

☐	Casual strolling or walking (less than 2 miles an hour)
☐	Average or normal (2-3 miles an hour)
☐	Fairly fast (3-4 miles an hour)
☐	Very fast (more than 4 miles an hour)
☐	Don't Know

Patient I.D. _____

Patient Acrostic: _____

Following are three categories of exercise, (strenuous, moderate, and mild). Not including walking outside the home, how often each week (7 days) do you usually do the following strenuous, moderate, and mild types of exercise?

5. **STRENUOUS OR VERY HARD EXERCISE.** (You work up a sweat and your heart beats fast.)
For example, aerobics, aerobic dancing, jogging, tennis, swimming laps.

☐	None	--->	(Go to Question 6)
☐	1 day per week	--->	(Go to Question 5a)
☐	2 days per week	--->	(Go to Question 5a)
☐	3 days per week	--->	(Go to Question 5a)
☐	4 days per week	--->	(Go to Question 5a)
☐	5 or more days per week	--->	(Go to question 5a)

5a. How long do you usually exercise like this at one time?

☐	Less than 20 minutes
☐	20-39 minutes
☐	40-59 minutes
☐	1 hour or more

6. **MODERATE EXERCISE** (Not exhausting). For example, biking outdoors, using an exercise machine (like a stationary bike or treadmill), calisthenics, easy swimming, popular or folk dancing.

☐	None	--->	(Go to Question 7)
☐	1 day per week	--->	(Go to Question 6a)
☐	2 days per week	--->	(Go to Question 6a)
☐	3 days per week	--->	(Go to Question 6a)
☐	4 days per week	--->	(Go to Question 6a)
☐	5 or more days per week	--->	(Go to Question 6a)

6a. How long do you usually exercise like this at one time?

- ☐ Less than 20 minutes
- ☐ 20-39 minutes
- ☐ 40-59 minutes
- ☐ 1 hour or more

7. **MILD EXERCISE.** For example, slow dancing, bowling, golf.

- ☐ None
- ☐ 1 day per week ----> (Go to Question 7a)
- ☐ 2 days per week ----> (Go to Question 7a)
- ☐ 3 days per week ----> (Go to Question 7a)
- ☐ 4 days per week ----> (Go to Question 7a)
- ☐ 5 or more days per week ----> (Go to Question 7a)

7a. How long do you usually exercise like this at one time?

- ☐ Less than 20 minutes
- ☐ 20-39 minutes
- ☐ 40-59 minutes
- ☐ 1 hour or more

Patient I.D. _____ - _____

Patient Acrostic: _____

CONTACT INFORMATION FORM

We would like you to update your contact information so that we can keep in touch with you during the study. This information is very important, so please answer these questions completely. Please print the information in the space provided or mark the appropriate box.

1. **Has your address changed since our last mailing to you?**

☐ No ☐ Yes → **If yes, please provide current mailing address**

Your Current Mailing Address?

2. Telephone Numbers: Home: Area Code (____) _____ - _____

Work: Area Code (____) _____ - _____

Other: Area Code (____) _____ - _____

3. When is the best time to contact you?

Day of week time(s)

Day of week time(s)

Where is the best place to contact you?

☐ At home
☐ At work
☐ Other

☐ At home
☐ At work
☐ Other

4. In case we might ever need to contact you by telephone, may we leave a message for you on your answering machine, (if you have one), if we are unable to reach you directly?

☐ No
☐ Yes

5. What is your husband's or partner's legal name? (This information will help us keep in contact with you during the study. Please leave this blank if you are not currently married or with a long-term partner.)

First MI Last

6. Please provide the names of two relatives or friends, not living in your household, who are likely to know how to contact you if we are unable to reach you.

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

Relationship to you: _____

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

Relationship to you: _____

Appendix L
Revised October 1998 Annual Report
DAMD 17-96-1-6292
J. Petrek

MENSTRUAL CYCLE MAINTENANCE AND QUALITY OF LIFE

One-Year Follow-up Survey



Clinical Coordinating Center

**Wake Forest University School of Medicine
Department of Public Health Sciences
Winston-Salem, North Carolina 27157-1063
(336) 716-2116**



**Funded by
The U.S. Army Medical Research and Materiel Command:
Breast Cancer Research Program A**

Patient I.D. _____

Patient Acrostic: _____

DEMOGRAPHIC FOLLOW-UP FORM

YOUR BACKGROUND

The following questions are about your background. We would like to see if you have had any changes in your personal situation in the past year. Please mark the appropriate box for each question.

1. What is your marital status?

- ☐ Never married
- ☐ Presently married
- ☐ Living in a marriage-like relationship
- ☐ Divorced
- ☐ Separated
- ☐ Widowed

2. Which category below best describes the highest level of formal education you have completed?
(Choose the one best answer).

- ☐ No formal education
- ☐ Grade school (1st through 8th grade)
- ☐ Some high school (9th through 11th grade)
- ☐ High school diploma or G.E.D.
- ☐ Business or vocational training school after high school graduation
- ☐ Some college (but a college degree was not obtained)
- ☐ Associate Degree (A.D. or A.A.)
- ☐ College graduate or Baccalaureate Degree (B.A. or B.S.)
- ☐ Some college or professional school after college graduation
- ☐ Master's Degree
- ☐ Doctoral Degree (Ph.D., M.D., J.D., D.D.S., etc.)

3. What was your total family income (before taxes) from all sources last year? (Check one box below. This information is important for describing the women in the study as a group and is kept strictly confidential).

- ☐ Less than \$10,000
- ☐ \$10,000 to \$19,999
- ☐ \$20,000 to \$34,999
- ☐ \$35,000 to \$49,999
- ☐ \$50,000 to \$74,999
- ☐ \$75,000 to \$100,000
- ☐ More than \$100,000

4. What type of health insurance do you have? (If you have more than one type of insurance, please mark the box for your primary source of insurance.)

- ☐ HMO
- ☐ Group Health Insurance
- ☐ V.A./Military Sponsored
- ☐ Individual Health Insurance (includes CHAMPUS)
- ☐ Medicaid
- ☐ Disability Insurance
- ☐ None
- ☐ Other (Please list: _____)

5. What is your current employment status? (Check the box that best describes you.)

- ☐ Unemployed/Looking for work → (Go to question 8)
- ☐ Retired → (Go to question 8)
- ☐ Full-time Homemaker → (Go to question 8)
- ☐ Employed - full-time → (Go to question 6)
- ☐ Employed - part-time → (Go to question 6)
- ☐ Disabled, unable to work → (Go to question 8)
- ☐ Student → (Go to question 8)
- ☐ Other (Please list: _____) → (Go to question 8)

Patient I.D. _____

Patient Acrostic: _____

6. If you are employed, which category best describes your occupation?

- ☐ Professional, Technical & Related Occupations (such as teachers/professors, nurses, lawyers, physicians & engineers)
- ☐ Managers, Administrators, or Proprietors (such as sales managers, real estate agents, or postmasters)
- ☐ Clerical & Related Occupations (such as secretaries, clerks or mail carriers)
- ☐ Sales Occupations (such as salespersons, demonstrators, agents and brokers)
- ☐ Service Occupations (such as police, cooks, or hairdressers)
- ☐ Skilled Crafts, Service Repair Persons, & Related Occupations (such as carpenters, appliance repair, or telephone line workers)
- ☐ Equipment or Vehicle Operators & Related Occupations (such as drivers, railroad brakemen or sewer workers)
- ☐ Laborers (such as helpers, longshoremen, or warehouse workers)
- ☐ Farmers (owners, managers, operators or tenants)
- ☐ Members of the military
- ☐ Other (please describe): _____

7. This following is a list of employment issues that a person might have. For each statement, indicate whether this has happened to you since your diagnosis. If it did occur, indicate whether you believe this situation was related to your diagnosis. (Circle the answers that are most true for you on each line.)

Since your diagnosis have you:	Occurred			If yes, was it	
	since diagnosis?			related to your	
	No	Yes	-->	No	Yes
a. believed you could not change jobs for fear of losing your health insurance?	No	Yes	-->	No	Yes
b. lost your health insurance due to sick leave?	No	Yes	-->	No	Yes
c. been fired or laid off?	No	Yes	-->	No	Yes
d. been demoted?	No	Yes	-->	No	Yes
e. been denied a promotion?	No	Yes	-->	No	Yes
f. been denied a wage increase?	No	Yes	-->	No	Yes
g. had your work responsibilities limited unnecessarily?	No	Yes	-->	No	Yes
h. been promoted?	No	Yes	-->	No	Yes

8. This following is a list of insurance issues that a person might have. For each statement, indicate whether this has happened to you since your diagnosis. If it did occur, indicate whether you believe this situation was related to your diagnosis. (Circle the answers that are most true for you on each line.)

Since your diagnosis have:

- a. you been denied health insurance?
- b. you been denied life insurance?
- d. your health insurance rates increased?
- d. your life insurance rates increased?
- e. you had a health benefit payment denied?
- f. you had trouble changing from group health to individual health insurance?

Occurred since diagnosis?			<u>If yes</u> , was it related to your diagnosis?	
No	Yes	-->	No	Yes
No	Yes	-->	No	Yes
No	Yes	-->	No	Yes
No	Yes	-->	No	Yes
No	Yes	-->	No	Yes
No	Yes	-->	No	Yes
No	Yes	-->	No	Yes

9. Please give the date you completed this form:

		/			/				
Month			Day			Year			

Patient I.D.: _____

Patient Acrostic: _____

PART 1

MEDICAL & REPRODUCTIVE HISTORY FOLLOW-UP QUESTIONNAIRE

The following questions ask about health professionals you may have seen in the past 6 months. This information will help us describe in general terms the kinds of services being used.

1. In the past six months, which of the following doctors or other health professionals have you seen?
(Please Check all that apply)

☐ None	☐ Family Therapist
☐ Acupuncturist	☐ Nutritionist
☐ Allergist	☐ Obstetrician
☐ Cardiologist	☐ Medical Oncologist/Chemotherapist
☐ Chiropractor	☐ Orthopedic Surgeon
☐ Dentist	☐ Homeopathic/Herbalist/Naturopathic
☐ Dermatologist	☐ Pain Control Professional
☐ Ear/Nose/Throat Doctor	☐ Alternative Therapist (Homeopath, herbalist, naturopathologist, etc.)
☐ Eye Doctor	☐ Physical Therapist
☐ Marital Counselor	☐ Plastic Surgeon
☐ Gastroenterologist	☐ Psychiatrist
☐ General Practitioner	☐ Clinical Psychologist
☐ Gynecologist	☐ Radiologist
☐ Infertility Specialist	☐ Rheumatologist
☐ Internist	☐ Social Worker
☐ Massage Therapist	☐ Organized Support Group
☐ Neurologist	☐ Surgeon
☐ Sexual Therapist	☐ Urologist
	☐ Other: _____

2. In the past 6 months, have you been seen at an emergency room?

☐ No

☐ Yes → For what reason: _____

3. In the past 6 months, have you been hospitalized or had surgery? Please mark one box for each line item (a) and (b).

	No	Yes	If yes, for what reason?
(a) Hospitalized?			
(b) Had surgery?			

4. Has anything else changed regarding either your mental or physical health status? Please mark one box for each line item (a) and (b).

	No	Yes	What has changed?
(a) Mental Health?			
(b) Physical Health?			

Patient I.D.: _ _ - _ _ _ _

Patient Acrostic: _ _ _ _ _

5. Have you had any biopsies in the past 6 months?

☐ No

☐ Yes → If yes, what was biopsied? _____

Why was this biopsied? _____

6. In the past 6 months, have you had a re-occurrence of breast cancer?

☐ No

☐ Yes → If yes, how was this diagnosis made. (For example, biopsy, lab tests)?

7. Have you been diagnosed with any other cancer in the past 6 months?

☐ No

☐ Yes → If yes, what type? _____

How was this diagnosis made? (For example, biopsy, lab tests)?

Patient I.D. _____

Patient Acrostic: _____

PART II

REPRODUCTIVE HISTORY

The following questions ask about your menstrual cycles and reproductive history. We are very interested in this information so that we can understand more about women's health during their childbearing years. Some of the questions ask you to give dates or the number of times when certain things happened. If you are not sure about the exact date or number of times, please give your best estimate.

1. What was the date of the first day of your last menstrual period (your best guess)?

		-			-				

Month Day Year

2. In the past 6 months, have you been sexually active with a male partner:

☐ No → Go to question 6

☐ Yes → Go to question 3

3. Which method of birth control are you and your partner using currently? (Check all that apply.)

- ☐ No method
- ☐ Condoms (rubbers)
- ☐ Birth control pills
- ☐ Foams/jellies/suppositories
- ☐ Sponge
- ☐ Withdrawal (pulling out)
- ☐ Diaphragm

- ☐ Safe periods (rhythm or counting days)
- ☐ Norplant
- ☐ Cervical cap
- ☐ Tubal ligation (tubes tied)
- ☐ Vasectomy
- ☐ Other (Please describe: _____)
- ☐ Don't know

4. In the past month, how many times have you had sexual intercourse without using contraception?

 Times

5. In the past 6 months, have you become pregnant?

☐

No

☐

Yes → If yes, are you pregnant now?

☐

No

☐

Yes

6. In the past month, have you had any hot flashes or night sweats (hot flashes that occur during sleep)?

☐

No

☐

Yes ----> If yes, how many have you had in the **past week**?

hot flashes/night sweats

FAMILY HISTORY UPDATE

Please update the following grid about the **history of breast cancer** among your female relatives. If you do not have a full-blooded relative in one of the categories listed below, please leave that line blank. (MARK ONLY ONE BOX PER LINE.)

1. Did this relative have breast cancer?

	No	Yes			Don't know if she had breast cancer	
		How old was she when her first breast cancer occurred?				
		Less than 45	45 or older	Don't know age		
a. Mother	☐	☐	☐	☐	☐	
b. Sister 1	☐	☐	☐	☐	☐	
c. Sister 2	☐	☐	☐	☐	☐	
d. Sister 3	☐	☐	☐	☐	☐	
e. Sister 4	☐	☐	☐	☐	☐	
f. Daughter 1	☐	☐	☐	☐	☐	
g. Daughter 2	☐	☐	☐	☐	☐	
h. Daughter 3	☐	☐	☐	☐	☐	
i. Daughter 4	☐	☐	☐	☐	☐	
j. Maternal grandmother (your mother's mother)	☐	☐	☐	☐	☐	
k. Paternal grandmother (your father's mother)	☐	☐	☐	☐	☐	

Please update the following grid about the history of ovarian cancer among your female relatives. If you do not have a full-blooded relative in one of the categories listed below, please leave that line blank.
(MARK ONLY ONE BOX PER LINE.)

2. Did this relative have ovarian cancer?

	No	Yes			Don't know if she had ovarian cancer	
		How old was she when her first ovarian cancer occurred?				
		Less than 45	45 or older	Don't know age		
a. Mother	☐	☐	☐	☐	☐	
b. Sister 1	☐	☐	☐	☐	☐	
c. Sister 2	☐	☐	☐	☐	☐	
d. Sister 3	☐	☐	☐	☐	☐	
e. Sister 4	☐	☐	☐	☐	☐	
f. Daughter 1	☐	☐	☐	☐	☐	
g. Daughter 2	☐	☐	☐	☐	☐	
h. Daughter 3	☐	☐	☐	☐	☐	
i. Daughter 4	☐	☐	☐	☐	☐	
j. Maternal grandmother (your mother's mother)	☐	☐	☐	☐	☐	
k. Paternal grandmother (your father's mother)	☐	☐	☐	☐	☐	

Patient I.D. _____

Patient Acrostic: _____

CURRENT MEDICATIONS

1. Please list below all of the **prescription medications** you are taking currently. (Write "none" if you are not taking any prescription medications at this time.)

Drug Name

Dosage

2. Please list below all of the **non-prescription medications or supplements** you are taking currently. (Write "none" if are not taking any non-prescription medications or supplements at this time.)

Drug Name

Dosage

Patient I.D. _____

Patient Acrostic: _____

TREATMENT EXPECTATIONS

1. We are interested in your expectations regarding the treatments you received over the past year. For each of the treatments listed below, how did your expectations before treatment compare with the actual treatment you received? Better than expected, the same as you expected, or worse than you expected? (Mark one box for each line.)

	Not Applicable. (Did not have this treatment.)	Worse Than Expected	Same As Expected	Better Than Expected
Lumpectomy				
Mastectomy				
Reconstructive Surgery				
Radiation				
Chemotherapy				
Tamoxifen				
Bone Marrow Transplant				

Patient I.D. _____

Patient Acrostic: _____

SWELLING FORM

The following questions concern swelling in your arm and/or hand. Please mark the appropriate box(es) for each question.

1. In the past 6 months, has any swelling occurred in your arm or hand on the same side that you had your lumpectomy or mastectomy?

☐

No → (Go to question 8)

☐

Yes → (Continue to question 2)

☐

Don't know → (Go to question 8)

2. Do you believe the start of your swelling was related to any of the following?

Yes

☐

No

☐

Don't

Know

☐

Radiation treatment

☐☐☐

Breast reconstruction

☐☐☐

Infection or injury to arm / hand

☐☐☐

Weather changes

☐☐☐

General use of your arm

☐☐☐

Exercise

☐☐☐

Airplane travel

☐

Other: Please describe: _____

2a. How soon after you had surgery and/or began treatment did this swelling occur?

- ☐ Less than 1 week
- ☐ 1 week to 4 weeks
- ☐ 1 month to 3 months
- ☐ 4 months to 6 months
- ☐ 7 months to 9 months
- ☐ 10 months to 12 months
- ☐ 13 months to 15 months

2b. Where does (did) the swelling occur? (Check all that apply)

- ☐ Hand
- ☐ Upper Arm
- ☐ Lower Arm

2c. Do (did) you consider the swelling to be mostly?

- ☐ Mild
- ☐ Moderate
- ☐ Severe

3. Does (did) the swelling interfere with any of the following?

Yes	No	
☐	☐	Clothing that you wear
☐	☐	Your ability to do routine activities, such as household chores or grooming.
☐	☐	Exercise
☐	☐	Your appearance
☐		Other, please describe: _____

Patient I.D. _____

Patient Acrostic: _____

4. Does (did) swelling seem to get worse with any of the following?

Yes No Don't
Know

☐☐☐

Hot weather

☐☐☐

General use of your arm

☐☐☐

Exercise

☐☐☐

Sauna / Jacuzzi / Hot bath

☐☐☐

Airplane travel

☐☐☐

Specific foods

☐☐☐

Mental / emotional stress

☐

Other: Please describe: _____

5. Prior to your breast cancer diagnosis, did you notice swelling in your hand and/or arm with any of the following? (Check all that apply)

Yes No Don't
Know

☐☐☐

Exercise

☐☐☐

Household Chores

☐☐☐

Heat/Humidity

☐☐☐

Eating salty foods

☐☐☐

Drinking alcoholic beverages

☐

Other: Please describe: _____

6. Did you seek treatment for this swelling in the past 6 months?

☐ No → If no, why not?

☐ Yes → If yes, what type of treatment did you receive? (Check all that apply)

- ☐ Compression therapy by machine
- ☐ Glove / Sleeve Compression / Garment
- ☐ Physical therapy
- ☐ Manual lymphatic drainage
- ☐ Bandaging technique
- ☐ Other, please describe: _____

7. Do you have swelling now?

☐ No → (Go to question 8)

☐ Yes → (Continue to question 7a)

7a. If yes, how long have you had swelling?

- ☐ Less than 1 week
- ☐ 2 - 4 weeks
- ☐ 1 - 3 months
- ☐ 4 - 6 months
- ☐ 7 - 9 months
- ☐ 10 - 12 months

Patient I.D. _____

Patient Acrostic: _____

8. In the past 6 months, do you remember any breaks in your skin, infected hang nails, or slight skin injuries in your arm or hand on the same side that you had your lumpectomy or mastectomy?

- ☐ No → (Go to question 9)
- ☐ Yes → (Continue to question 8a)
- ☐ Don't Know → (Continue to question 9)

8a. If yes, did you receive antibiotics?

- ☐ Yes
- ☐ No
- ☐ Don't know

9. In the past 6 months, did you have any infection in the arm or hand on the same side that you had your lumpectomy or mastectomy?

- ☐ No → (Go to question 10)
- ☐ Yes → (Continue to question 9a)
- ☐ Don't Know → (Continue to question 10)

9a. If yes, did you receive antibiotics by mouth?

- ☐ No
- ☐ Yes
- ☐ Don't know

If yes, did you:

9b. receive antibiotics by injection?

☐

No

☐

Yes

☐

Don't know

10. Do you have pain in the affected arm and/or hand? (Check one box for each site)

	Yes	No
hand		
arm		
hand and arm		

Patient I.D. : _____ - _____

Patient Acrostic: _____

SYMPTOMS QUESTIONNAIRE

Below are statements about symptoms some people may experience. For each statement, check the appropriate box for the response that best describes how bothersome the symptom was for you **during the past month**. If you did not have the problem, check the box under the column titled "symptom did not occur". Please do not skip any questions. **Mark only one box on each line.**

If you experienced the symptom, use the following key to indicate how bothersome it was:

Mild = symptom did not interfere with usual activities.
 Moderate = symptom interfered somewhat with usual activities.
 Severe = symptom was so bothersome that usual activities could not be performed.

Symptom	Symptom did not occur	Symptom Occurred and Was:		
		Mild	Moderate	Severe
1. Fatigue or low energy level				
2. Mouth ulcers				
3. Restless sleep				
4. Sleeping too much				
5. Nervousness or shakiness inside				
6. Mood changes				
7. Feeling depressed				
8. Lightheadedness when standing up				
9. Faintness or dizziness at rest				
10. Headaches				
11. Swelling of ankles or feet				
12. Diarrhea				

Symptom	Symptom did not occur	Symptom Occurred and Was:		
		Mild	Moderate	Severe
13. Constipation				
14. Abdominal pain/cramps				
15. Vaginal dryness				
16. Muscle pain/ache/or cramp				
17. Weight gain				
18. Weight loss				
19. General aches and pains				
20. Hot flashes				
21. Joint pains				
22. Night sweats				
23. Aches in back of neck and skull				
24. Forgetfulness				
25. Difficulty concentrating				
26. Increased appetite				
27. Short temper				
28. Decreased efficiency				
29. Loss of interest in work/activities				
30. Lowered work performance				
31. Blind spots, fuzzy vision				
32. Breast sensitivity/tenderness				
33. Avoidance of social affairs				
34. Cold sweats				
35. Decreased appetite				
36. Feelings of suffocation				
37. Difficulty healing				
38. Bloating				

Patient I.D. _____

Patient Acrostic: _____

QUALITY OF LIFE FORM

1. In general, would you say your health is: (Check one)

Excellent

☐

Very good

☐

Good

☐

Fair

☐

Poor

☐

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.

Limited a lot

☐

Limited a little

☐

Not limited at all

☐

3. Climbing several flights of stairs.

Limited a lot

☐

Limited a little

☐

Not limited at all

☐

During the past four weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

4. Accomplished less than you would like.

Yes

☐

No

☐

5. Had difficulty performing the work or other activities, for example, it took extra effort.

☐☐

During the past four weeks, have you had any of the following problems with your work or other regular daily activities as a result of emotional problems (such as feeling depressed or anxious)?

6. Accomplished less than you would like.

Yes

☐

No

☐

7. Didn't do work or other activities as carefully as usual.

☐☐

8. During the past four weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? (Check one)

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

9. During the past four weeks, how much did pain interfere with your normal activities (including both work outside the home, housework and family activities)? (Check one)

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

These questions are about how you feel and how things have been with you during the past four weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past four weeks:

10. Have you felt calm and peaceful? (Check one)

All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐	☐

11. Did you have a lot of energy? (Check one)

All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐	☐

12. Have you felt downhearted and blue? (Check one)

All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐	☐

Relationship With Doctor	Not At All	A Little Bit	Some-What	Quite a bit	Very Much
29. I had confidence in my doctor(s).	1	2	3	4	5
30. My doctor was available to answer my questions.	1	2	3	4	5
31. How much does your <u>Relationship with your Doctor</u> affect your quality of life? (Circle one number.)					
0	1	2	3	4	5
6	7	8	9	10	
Not at all					Very Much So

Emotional Well-Being	Not at All	A Little Bit	Some-what	Quite a bit	Very Much
32. I felt sad.	1	2	3	4	5
33. I was proud of how I'm coping with my illness.	1	2	3	4	5
34. I was losing hope in the fight against my illness.	1	2	3	4	5
35. I felt nervous.	1	2	3	4	5
36. I worried about dying.	1	2	3	4	5
37. How much does your <u>Emotional Well-Being</u> affect your quality of life? (Circle one number.)					
0	1	2	3	4	5
6	7	8	9	10	
Not at all					Very Much So

Functional Well-Being	Not at All	A Little Bit	Some-what	Quite a bit	Very Much
38. I was able to work (include work in home).	1	2	3	4	5
39. My work (include work in home) was fulfilling.	1	2	3	4	5
40. I was able to enjoy life "in the moment."	1	2	3	4	5
41. I had accepted my illness.	1	2	3	4	5
42. I was sleeping well.	1	2	3	4	5
43. I enjoyed my usual leisure pursuits.	1	2	3	4	5
44. I was content with the quality of my life right now.	1	2	3	4	5
45. How much does your <u>Functional Well-Being</u> affect your quality of life? (Circle one number.)					
0	1	2	3	4	5
6	7	8	9	10	
Not at all					Very Much So

Patient Acrostic: _____

Not At All	A Little Bit	Some- what	Quite a bit	Very Much

46. I was short of breath.	1	2	3	4	5
47. I was self-conscious about the way I dressed.	1	2	3	4	5
48. My arms were swollen or tender.	1	2	3	4	5
49. I felt sexually attractive.	1	2	3	4	5
50. I was bothered by hair loss.	1	2	3	4	5
51. I worried about the risk of cancer in other family members.	1	2	3	4	5
52. I worried about the effect of stress on my illness.	1	2	3	4	5
53. I was bothered by a change in weight.	1	2	3	4	5
54. I was able to feel like a woman.	1	2	3	4	5

0 1 2 3 4 5 6 7 8 9 10
Not at all Very Much So

This section asks you about your general perceptions regarding your body. Right now, how satisfied are you with these parts of your body? Please check the appropriate box for the response that best describes your satisfaction with each body part.

	Very dissatisfied	Somewhat dissatisfied	Neutral	Somewhat satisfied	Very satisfied
56. Hair					
57. Breasts					
58. Arms					
59. Face					
60. Waist					
61. Hips					
62. Thighs					
63. Overall body					

How much do you agree or disagree with the following statement? (Check the appropriate box.)

64. The appearance of my breast area is important to me.

Strongly
Disagree

☐

Disagree

☐

Neither Agree
or Disagree

☐

Agree

☐

Strongly
Agree

☐

65. I view myself as a:

☐

Very overweight person

☐

Moderately overweight person

☐

Normal weight person

☐

Moderately thin person

☐

Very thin person

PART III. SEXUALITY

These next questions are about the way health problems may interfere with your sex life. These questions are personal, but your answers are important in understanding how health problems may affect women's sexuality.

66. Have you been sexually active with a partner during the last 6 months?

☐

No ----> (If no, skip to Question 79).

☐

Yes ----> (If yes, continue to Question 67).

67. How many times have you had sexual intercourse in the past month?

☐

0 times

☐

1 - 4 times

☐

5 - 10 times

☐

11 or more

Patient I.D. _____

Patient Acrostic: _____

For the following questions, please check the box for the response that best describes your sexual feelings and experiences **DURING THE PAST MONTH.**

	Never	Almost Never	Sometimes	Almost Always	Always
68. How often were you aware of wetness in your vagina as you became sexually excited?					
69. How often did it take a long time for your vagina to become wet or slippery as you became sexually excited?					
70. During sexual relations, how frequently did you notice dryness of your vagina?					
71. How often did you feel pain or discomfort during vaginal penetration?					
72. How often did you feel satisfied after sexual activity?					
73. How often were you satisfied with the frequency of sexual activity?					
74. How frequently did you feel tense or nervous after a sexual experience?					

For the following questions, please check the box for the response that best describes your sexual feelings and experiences **DURING THE PAST MONTH.**

	Strongly disagree	Disagree	Neither agree or disagree	Agree	Strongly agree
75. I avoided having my breast area fondled or kissed.					
76. My partner avoided fondling or kissing my breast area.					
77. I notice I didn't hug or kiss my partner much.					
78. I notice my partner didn't hug and kiss me much.					

PART IV. SLEEP HABITS

The next group of questions ask about your sleep habits. Please check the appropriate box for the one response that best describes how often you experienced these situations in **THE PAST 4 WEEKS**.

79. Did you have trouble falling asleep?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

80. Did you wake up several times a night?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

81. Did you wake up earlier than you planned to?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

82. Did you have trouble getting back to sleep after you woke up too early?

- ☐ No, not in the past 4 weeks
- ☐ Yes, less than once a week
- ☐ Yes, 1 or 2 times a week
- ☐ Yes, 3 or 4 times a week
- ☐ Yes, 5 or more times a week

Patient I.D. _____

Patient Acrostic: _____

83. Overall, how was your typical night's sleep during the past 4 weeks?

- ☐ Very sound or restful
☐ Sound or restful
☐ Average quality
☐ Restless
☐ Very restless

84. About how many hours of sleep did you get on a typical night during the past 4 weeks?

- ☐ 5 or less hours
☐ 6 hours
☐ 7 hours
☐ 8 hours
☐ 9 hours
☐ 10 or more hours

PART V. SPIRITUAL BELIEFS

The following questions are about spiritual beliefs. Please check the appropriate box indicating how true the statement has been for you during **THE PAST WEEK**.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
85. I felt peaceful.					
86. I had a reason for living.					
87. I felt a sense of purpose in my life.					
88. I was able to reach down deep into myself for comfort.					
89. I felt a sense of harmony within myself.					
90. I found comfort in my faith.					
91. I found strength in my faith.					

92. Where would you place yourself on the following scale, if "0" means that your life is just the way it was before your breast cancer, "+5" means that everything is totally different but better, and "-5" means that everything is totally different but worse. *(Please circle ONE number).*

-5	-4	-3	-2	-1	0	+1	+2	+3	+4	+5
Worse					Same as before					Better

PART VI. EMOTIONAL FEELINGS

The following questions consist of groups of statements. After reading each group of statements carefully, check the box next to the one statement in each group which **best** describes the way you have been feeling the past week, including today. If several statements within a group seem to apply equally, check each one. Be sure to read all the statements in each group before making your choice.

93. ☐ I do not feel sad.
☐ I feel sad.
☐ I am sad all the time and I can't snap out of it.
☐ I am so sad or unhappy that I can't stand it.
94. ☐ I am not particularly discouraged about the future.
☐ I feel discouraged about the future.
☐ I feel I have nothing to look forward to.
☐ I feel that the future is hopeless and that things cannot improve.
95. ☐ I do not feel like a failure.
☐ I feel I have failed more than the average person.
☐ As I look back on my life, all I can see is a lot of failures.
☐ I feel I am a complete failure as a person.
96. ☐ I get as much satisfaction out of things as I used to.
☐ I don't enjoy things the way I used to.
☐ I don't get real satisfaction out of anything anymore.
☐ I am dissatisfied or bored with everything.

Patient I.D. _____

Patient Acrostic: _____

97. ☐ I don't feel particularly guilty.
☐ I feel guilty a good part of the time.
☐ I feel quite guilty most of the time.
☐ I feel guilty all of the time.
98. ☐ I don't feel I am being punished.
☐ I feel I may be punished.
☐ I expect to be punished.
☐ I feel I am being punished.
99. ☐ I don't feel disappointed in myself.
☐ I am disappointed in myself.
☐ I am disgusted with myself.
☐ I hate myself.
100. ☐ I don't feel I am any worse than anybody else.
☐ I am critical of myself for my weaknesses or mistakes.
☐ I blame myself all the time for my faults.
☐ I blame myself for everything bad that happens.
101. ☐ I don't have any thoughts of killing myself.
☐ I have thoughts of killing myself, but I would not carry them out.
☐ I would like to kill myself.
☐ I would kill myself if I had the chance.
102. ☐ I don't cry anymore than usual.
☐ I cry more now than I used to.
☐ I cry all the time now.
☐ I used to be able to cry, but now I can't cry even though I want to.

103. ☐ I am no more irritated now than I ever am.
☐ I get annoyed or irritated more easily than I used to.
☐ I feel irritated all the time now.
☐ I don't get irritated at all by the things that used to irritate me.
104. ☐ I have not lost interest in other people.
☐ I am less interested in other people than I used to be.
☐ I have lost most of my interest in other people.
☐ I have lost all of my interest in other people.
105. ☐ I make decisions about as well as I ever could.
☐ I put off making decisions more than I used to.
☐ I have greater difficulty in making decisions than before.
☐ I can't make decisions at all anymore.
106. ☐ I don't feel I look any worse than I used to.
☐ I am worried that I am looking old or unattractive.
☐ I feel that there are permanent changes in my appearance that make me look unattractive.
☐ I believe that I look ugly.
107. ☐ I can work about as well as before.
☐ It takes an extra effort to get started at doing something.
☐ I have to push myself very hard to do anything.
☐ I can't do any work at all.
108. ☐ I can sleep as well as usual.
☐ I don't sleep as well as I used to.
☐ I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
☐ I wake up several hours earlier than I used to and cannot get back to sleep.

Patient I.D. _____

Patient Acrostic: _____

109. ☐ I don't get more tired than usual.
☐ I get tired more easily than I used to.
☐ I get tired from doing almost anything.
☐ I am too tired to do anything.
110. ☐ My appetite is no worse than usual.
☐ My appetite is not as good as it used to be.
☐ My appetite is much worse now.
☐ I have no appetite at all anymore.
111. ☐ I haven't lost much weight, if any, lately.
☐ I have lost more than five (5) pounds.
☐ I have lost more than ten (10) pounds.
☐ I have lost more than fifteen (15) pounds.
112. ☐ I am no more worried about my health than usual.
☐ I am worried about physical problems such as aches and pains; or upset stomach; or constipation.
☐ I am very worried about physical problems and it's hard to think of much else.
☐ I am so worried about my physical problems that I cannot think about anything else.
113. ☐ I have not noticed any recent change in my interest in sex.
☐ I am less interested in sex than I used to be.
☐ I am much less interested in sex now.
☐ I have lost interest in sex completely.

Patient I.D. _____

Patient Acrostic: _____

SOCIAL SUPPORT FORM

The following are questions about the support that is available to you.

1. At the present time, about how many close friends and close relatives do you have (people you feel at ease with and can talk to about what is on your mind)? (Please write the number in the boxes below.)

Number of close friends and close relatives

People sometimes look to others for companionship, assistance, or other types of support. Currently, how often is each of the following kinds of support available to you if you need it? (Check one box for each statement.)

	None of the time	A little of the time	Some of the time	Most of the time	All of the time
2. Someone to help you if you were confined to bed.					
3. Someone you can count on to listen to you when you need to talk.					
4. Someone to give you good advice about a crisis.					
5. Someone to take you to the doctor if you needed it.					
6. Someone who shows you love and affection.					
7. Someone to have a good time with.					
8. Someone to give you information to help you understand a situation.					
9. Someone to confide in or talk to about yourself or your problems.					

	None of the time	A little of the time	Some of the time	Most of the time	All of the time
10. Someone who hugs you.					
11. Someone to get together with for relaxation.					
12. Someone to prepare your meals if you were unable to do it yourself.					
13. Someone whose advice you really want.					
14. Someone to do things with to help you get your mind off things.					
15. Someone to help with daily chores if you were sick.					
16. Someone to share your most private worries and fears with.					
17. Someone to turn to for suggestions about how to deal with a personal problem.					
18. Someone to do something enjoyable with.					
19. Someone who understands your problems.					
20. Someone to love you and make you feel wanted.					

Patient I.D. _____

Patient Acrostic: _____

For the following questions, please check the box that is the most true for you at the present time.
(Check only one box for each statement.)

Of the people who are important to you, how many:

	None	One	Some	Most	All
21. Don't understand you.					
22. Get on your nerves.					
23. Ask too much of you.					
24. Argue with you.					
25. Don't include you.					
26. Show that they don't like you.					
27. Boss you.					
28. Try to get you to do things you don't want to do.					

Patient I.D. _____

Patient Acrostic: _____

PERSONAL HABITS FORM

These questions are about habits that may affect your health (smoking, alcohol use, weight, and exercise). Please answer each question as accurately as possible.

1. Do you smoke currently?

☐

No

☐

Yes

If yes, how many cigarettes do you smoke per day? (1 pack = 20 cigarettes)

☐

I smoke occasionally.

☐

0 - 5 cigarettes a day

☐

6 - 20 cigarettes a day

☐

21 - 30 cigarettes a day

☐

31 - 40 cigarettes a day

☐

more than 40 cigarettes a day

2. Do you currently drink alcoholic beverages?

☐

No

☐

Yes

If yes, about how many alcoholic beverages (beer, wine, or mixed drinks) do you currently drink in an average month?

Beverages per month

3. What is your current weight?

pounds

The following questions are about your usual physical activity and exercise. This includes walking and sports.

4. Think about the walking you do outside the home. In the past month, how often did you walk outside the home for more than 10 minutes without stopping? (Mark only one.)

☐	Rarely or never	--->	(Go to Question 5)
☐	1-3 times each month	--->	(Go to Question 4a)
☐	1 time each week	--->	(Go to Question 4a)
☐	2-3 times each week	--->	(Go to Question 4a)
☐	4-6 times each week	--->	(Go to Question 4a)
☐	7 or more times each week	--->	(Go to Question 4a)

4a. When you walked outside the home for more than 10 minutes without stopping, how many minutes did you usually walk?

☐	Less than 20 minutes
☐	20-39 minutes
☐	40-59 minutes
☐	1 hour or more

4b. What was your usual speed?

☐	Casual strolling or walking (less than 2 miles an hour)
☐	Average or normal (2-3 miles an hour)
☐	Fairly fast (3-4 miles an hour)
☐	Very fast (more than 4 miles an hour)
☐	Don't Know

Patient I.D. _____

Patient Acrostic: _____

Following are three categories of exercise, (strenuous, moderate, and mild). Not including walking outside the home, how often each week (7 days) do you usually do the following strenuous, moderate, and mild types of exercise?

5. **STRENUOUS OR VERY HARD EXERCISE.** (You work up a sweat and your heart beats fast.)
For example, aerobics, aerobic dancing, jogging, tennis, swimming laps.

☐	None	--->	(Go to Question 6)
☐	1 day per week	--->	(Go to Question 5a)
☐	2 days per week	--->	(Go to Question 5a)
☐	3 days per week	--->	(Go to Question 5a)
☐	4 days per week	--->	(Go to Question 5a)
☐	5 or more days per week	--->	(Go to question 5a)

5a. How long do you usually exercise like this at one time?

☐	Less than 20 minutes
☐	20-39 minutes
☐	40-59 minutes
☐	1 hour or more

6. **MODERATE EXERCISE** (Not exhausting). For example, biking outdoors, using an exercise machine (like a stationary bike or treadmill), calisthenics, easy swimming, popular or folk dancing.

☐	None	--->	(Go to Question 7)
☐	1 day per week	--->	(Go to Question 6a)
☐	2 days per week	--->	(Go to Question 6a)
☐	3 days per week	--->	(Go to Question 6a)
☐	4 days per week	--->	(Go to Question 6a)
☐	5 or more days per week	--->	(Go to Question 6a)

6a. How long do you usually exercise like this at one time?

- ☐ Less than 20 minutes
- ☐ 20-39 minutes
- ☐ 40-59 minutes
- ☐ 1 hour or more

7. **MILD EXERCISE.** For example, slow dancing, bowling, golf.

- ☐ None
- ☐ 1 day per week ---> (Go to Question 7a)
- ☐ 2 days per week ---> (Go to Question 7a)
- ☐ 3 days per week ---> (Go to Question 7a)
- ☐ 4 days per week ---> (Go to Question 7a)
- ☐ 5 or more days per week ---> (Go to Question 7a)

7a. How long do you usually exercise like this at one time?

- ☐ Less than 20 minutes
- ☐ 20-39 minutes
- ☐ 40-59 minutes
- ☐ 1 hour or more

Patient Acrostic:

1. What major challenges have you faced since your diagnosis?

2. What positive experiences have you had? (For example, things you learned about yourself, how you interact with your family, etc.)

Patient I.D. _____

Patient Acrostic: _____

LIFE EVENTS

Below are things that sometimes happen to people. Please try to think back over the **past year** to remember if any of these things happened. (Mark only one box on each line.)

Over the past year:	NO	YES, and it upset me:		
		Not too much	Moderately (Medium)	Very Much
1. Did you have any major problems with money.				
2. Did you or a family member or close friend lose their jobs or retire?				
3. Did you have a major conflict with children?				
4. Did you have a divorce or break-up with a spouse or partner?				
5. Did a family member or close friend have a divorce or breakup?				
6. Did a close friend or family member die or have a serious illness (other than your spouse or partner.)				
7. Did you have any major accidents, disasters, muggings, unwanted sexual experiences, robberies, or similar events?				
8. Did your spouse or partner die or have a serious illness?				
9. Were you physically abused by a family member or close friend?				
10. Were you verbally abused by a family member or close friend?				
11. Did a pet die?				

Patient I.D. _____

Patient Acrostic: _____

CONTACT INFORMATION FORM

We would like you to update your contact information so that we can keep in touch with you during the study. This information is very important, so please answer these questions completely. Please print the information in the space provided or mark the appropriate box.

1. Has your address changed since our last mailing to you?

☐ No ☐ Yes → If yes, please provide current mailing address

Your Current Mailing Address?

2. Telephone Numbers: Home: Area Code (____) ____ - ____
Work: Area Code (____) ____ - ____
Other: Area Code (____) ____ - ____

3. When is the best time to contact you?

Day of week time(s)

Day of week time(s)

Where is the best place to contact you?

☐ At home
☐ At work
☐ Other

☐ At home
☐ At work
☐ Other

Patient I.D. _____

Patient Acrostic: _____

4. In case we might ever need to contact you by telephone, may we leave a message for you on your answering machine, (if you have one), if we are unable to reach you directly?

☐

No

☐

Yes

5. What is your husband's or partner's legal name? (This information will help us keep in contact with you during the study. Please leave this blank if you are not currently married or with a long-term partner.)

First

MI

Last

6. Please provide the names of two relatives or friends, not living in your household, who are likely to know how to contact you if we are unable to reach you.

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

Relationship to you: _____

Name: _____

Address: _____

Phone Number: Area Code (____) _____ - _____

Relationship to you: _____