E. Community/Health Care Provider Materials

Figure E.1.1
Model Letter to Community Health Care Providers and Physicians

Dear Colleague:

[Institution] was honored to be selected by the National Institutes of Health as one of the centers to be part of the Women's Health Initiative (WHI). The WHI has been designed to fill the void in information about health issues affecting women, particularly chronic diseases in mature women.

The WHI is a multi-center study, funded by the National Institutes of Health, that will involve research institutions throughout the United States. The WHI has two components -- a Clinical Trial and an Observational Study. Both involve following women ages 50-79 years for 9-12 years. Primary study outcomes are coronary heart disease, breast and colorectal cancer, and hip fractures. Secondary outcomes include other cardiovascular diseases, endometrial and ovarian cancer, other fractures, venous thromboembolic diseases and diabetes mellitus. Those women who are eligible and interested will be enrolled in the Clinical Trial; all others will be invited to enter the Observational Study. Clinical Trial participants will be in contact with the Clinical Center at least twice annually, while Observational participants will be followed mainly by mail and telephone contacts.

Nationwide, 63,000 women will participate in the Clinical Trial and a further 100,000 women will be recruited into the Observational Study. The [location] Clinical Center will enroll approximately 1,400 women in the Clinical Trial and 2,225 women in the Observational Study.

The philosophy of the WHI is that the sponsorship and collaboration of local medical professionals is essential to the success of the study. All interested women will be encouraged to discuss the question of participation with their gynecologist or their primary care physician. Participants will always be referred to their own physician if a potential medical or surgical problem is identified during a Clinical Center visit. In the event the woman experiences symptoms potentially related to a trial assignment, Clinical Center medical staff will work directly with her doctor to resolve the problem.

We believe that women will take pride in participating in this major effort to learn how to improve women's health. We would greatly appreciate your referral of women patients to the study. The [institution] would like to work with women and their physicians to make the WHI a rewarding experience.

Enclosed is a summary sheet regarding the study. If you have any questions, please feel free to call us at the numbers listed below.

Sincerely,

_____
Principal Investigator

Figure E.1.2
Model WHI Fact Sheet

The Women's Health Initiative (WHI), a multi-center study funded by the National Institutes of Health, will involve research institutions throughout the United States. The [Institution], under the direction of [Principal Investigator], has been chosen as one of the centers to be part of this study.

The WHI has two components -- a Clinical Trial and an Observational Study. Both will involve following women ages 50-79 years for 9-12 years. Participants will be encouraged to enroll in those arms of the Clinical Trial for which they meet eligibility requirements.

THE CLINICAL TRIAL: Will test the benefits and risks of hormone replacement therapy, dietary modification, and calcium plus vitamin D supplementation in relation to the overall health and quality of life of post-menopausal women.

- Participants in the hormone replacement arm of the Clinical Trial will be randomly selected to take estrogen 0.625 mg/day alone or estrogen 0.625 mg/day plus progestin 2.5 mg/day, or placebo. Women with a hysterectomy will not be randomized to the estrogen plus progestin arm. All women will have baseline and annual pelvic exams and pap smears; all non-hysterectomized women will receive an endometrial biopsy at baseline and a proportion will have the procedure repeated annually (women randomized to estrogen only and a sample of those taking estrogen plus progestin or placebo will have repeat aspirations).
- Participants in the dietary modification arm of the Clinical Trial will be randomized into two groups; high fiber/low fat diet, or their normal diet. Women being asked to modify their diets will learn how to accomplish this by attending group sessions led by registered dietitians.
- A year after enrollment in one or both of the trial arms described above, WHI women will be invited to enroll in the calcium/vitamin D arm of the trial. They will be randomized into two groups: calcium/vitamin D supplementation (1000 mg calcium with 400 IU vitamin D_3) or placebo.

THE OBSERVATIONAL STUDY:

- Will follow women who are unable or ineligible to participate in the Clinical Trial.
- After measurement of baseline characteristics, these women will be followed mainly by mail and phone contacts to ascertain clinical events.

All WHI participants will complete questionnaires, undergo limited screening measurements (e.g., height, weight, blood pressure), and provide blood specimens periodically. In addition, Clinical Trial participants will receive clinical breast examinations and electrocardiograms. They will also be asked to obtain regular mammograms.

As in previous studies, the collaboration and cooperation of the medical community in and around [City] is essential to the success of the Women's Health Initiative. All interested women will be encouraged to discuss their participation with their primary care provider.

With your support we anticipate that hundreds of women will want to be part of WHI and to "be part of the answer" to the many questions about appropriate care of post-menopausal women!

Figure E.1.3
Model National Press Release

In September 1993, the National Institutes of Health launched the most ambitious clinical study in history, the Women's Health Initiative (WHI). This $625,000 million, 15-year project will help decide how diet, hormone therapy and calcium and vitamin D might prevent heart disease, cancer and bone fractures in women. More than 160,000 post-menopausal women ages 50 - 79 years, from all socioeconomic and racial backgrounds, will be invited to participate in this landmark study.

"Today we are entering a new age in women's health research. In terms of medical research, women have been ignored far too long," says Dr. Bernadine Healy, former director of the National Institutes of Health. For years, research has systematically excluded women from Clinical Trials even though certain diseases disproportionately affect women. This initiative will attempt to redress the vast inequities that exist in research and provide practical information to women and their physicians about hormone replacement therapy, dietary patterns and supplements, and exercise.

Through the Women's Health Initiative, the NIH has placed women's health issues at the top of the nation's research agenda. The information derived from these studies will provide scientifically valid information about disease prevention for women, their families and their communities. The results of the WHI will have a direct impact on women's health behaviors for generations to come.

For more information, contact Media Relations, NIH 301-402-3168.

Figure E.1.4
Model Letter to HRT Participant Health Care Provider

Dear Physician and Health Care Provider,

Your patient has expressed an interest in the Hormone Replacement Trial portion of the Women's Health Initiative (WHI). It is important that she do this under the guidance and full knowledge of her usual health care provider. This letter will explain what the WHI entails, eligibility guidelines, and what would be involved for you and your patient.

It is the policy of the WHI that clinics work closely with the women's own primary care providers and gynecologists in following these participants. The WHI will not provide primary health care to participants.

The Women's Health Initiative is a large clinical trial and observational study funded by the National Institutes of Health. Over 160,000 postmenopausal women across the United States who are between the ages of 50 and 79 are expected to participate in the WHI. It will study the effect of hormone replacement therapy, dietary modification of fat intake, and calcium and vitamin D supplementation on a woman's risk for heart disease, cancer and osteoporosis. In addition, the observational study will document clinical and public health issues for women.

The Hormone Replacement Trial (HRT) is designed to address the effect of estrogen replacement therapy on cardiovascular disease - the leading cause of death for women. It consists of three arms - some participants will take pills that contain estrogen only, others will take a combination estrogen/progestin pill (only women with a uterus) and still others will take a placebo. In order to be randomized to one of these arms, the woman must be postmenopausal, have no contraindications to taking hormone medications (not on anticoagulants, Tamoxifen, or steroid preparations and no history of hormone-related cancers such as breast and endometrial), and not currently on any hormone replacement therapy.

If a woman currently on hormones is interested in participating in the HRT, it is necessary for her to "wash-out" of her medications for three months prior to entering. This would mean that she would taper down and then be off **all** hormones for these three months. Some women might experience some perimenopausal-type symptoms that you could treat symptomatically. Others might have severe persistent symptoms of hormone withdrawal. Severe symptoms would make a woman ineligible for the HRT Study because she would not be able to tolerate being randomized to placebo. Women not eligible for the HRT Study could still participate in the Diet Modification Intervention or Observational Study arms of the WHI.

Once your patient has been enrolled in the HRT component of WHI, it is important that any estrogen or progestin treatment she receives is according to WHI protocol. She should generally not receive any estrogen or progestin other than those she has been randomized to receive in the trial, since these will interfere with the evaluation of the trial results, and could also result in the woman receiving an excessive overall dose of hormone. This "rule" applies to all forms of estrogen, including the patch and vaginal creams. However, there may occasions when symptoms such as vaginal bleeding or estrogen deficiency symptoms necessitate short courses of non-trial hormone medications. We would like to work with you to resolve such symptoms in a manner consistent with the WHI protocol.

Yearly follow-up exams will include mammograms, clinical breast exams, and pelvic exams (the latter only in women with a uterus). In addition, all women with a uterus will be asked to have a pap smear at least every three years while in the study. A selected subsample of participants will undergo additional screening every three years, including blood screening, ECG, cognitive and functional status, and endometrial aspiration. If an aspiration is unattainable, a

transvaginal uterine ultrasound will be ordered. Safety monitoring will be according to recommendations suggested by the 1993 American College of Obstetricians and Gynecologists Technical Bulletin on HRT, and the College of Physicians guidelines for HRT. The costs of these exams and tests will be covered by the woman's insurance or the WHI. All results of these studies will be forwarded to your office upon receiving your patient's signed permission. If any problem is found during these exams or if your patient should develop any problems not related to HRT, she will be referred back to your office for care. The participant may elect that you perform her annual pelvic exam and/or tri-annual Pap smear.

The participation of your patient will have a great impact upon the future of health care for all women. Your support and collaboration are critical to the success of the WHI and our ability to answer important questions on women's' health. If you should have any questions regarding the Women's Health Initiative, please call us at _____.

Sincerely,

_____ _____

Clinical Center Principal Investigator Clinical Center Co-Investigator

E.1.5
Model Letter Sent with Chart Labels to Health Care Providers

[Clinic Name and Address] [WHI Logo]

Dear Physician and Health Care Provider,

Your patient _____ has been enrolled in the Women's Health Initiative (WHI), a multi-center study funded by the National Institutes of Health. The WHI has two components -- a Clinical Trial and an Observational Study. Both involve following women ages 50-79 years for 9-12 years. Primary study outcomes are coronary heart disease, breast and colorectal cancer, and hip fractures. Secondary outcomes include other cardiovascular diseases, endometrial and ovarian cancer, other fractures, venous thromboembolic diseases and diabetes mellitus.

Nationwide, 63,000 women will participate in the Clinical Trial and an additional 100,000 women will be recruited into the Observational Study. There are three components to the Clinical Trial: hormone replacement, dietary modification, and calcium and vitamin D supplementation. Women are enrolled in these components based on their interest and eligibility following a series of screening visits.

Your patient has been enrolled in the (HRT, DM, CaD, OS) Study. Enclosed is a label briefly summarizing the study component(s) your patient is enrolled in that you can place with your patient's medical records. The purpose of the label is to remind you of your patient's participation in the study during her health care visits and to serve as a request that you notify us if there is any change in her health status. Contact information has been included on the label(s).

[For women enrolled in HRT:]

The Hormone Replacement Trial is designed to address the effect of hormone replacement therapy on cardiovascular disease - the leading cause of death for women - and on osteoporotic fractures. It consists of two studies: women with uteri will be randomly assigned to take either progesterone and estrogen or a placebo; women without uteri will be randomly assigned to take either estrogen or a placebo. To be randomized, the woman must be postmenopausal, have no contraindications to taking hormone medications (not on anticoagulants, Tamoxifen, or steroid preparations, and no history of hormone-related cancers such as breast and endometrium), and not currently on any hormone replacement therapy. The WHI investigators have developed a rigorous protocol that maintains the scientific integrity of the study while assuring participant safety. The clinical center clinicians hope to assure your patient receives appropriate monitoring and follow-up by developing a collaborative relationship with you, her health care provider.

Now that your patient has been enrolled in the HRT, it is important that any estrogen or progestin treatment she receives is according to WHI protocol. She should generally not receive any estrogen or progestin other than those she has been randomized to receive in the trial, since these will interfere with the evaluation of the trial results, and could also result in her receiving an excessive overall dose of hormone. These guidelines apply to all forms of estrogen, including the patch and vaginal creams. However, there may be occasions when symptoms such as vaginal bleeding or estrogen deficiency symptoms necessitate short courses of non-trial hormone medications. We would like to work with you to resolve such symptoms in a manner consistent with the WHI protocol.

The WHI will follow your patient for approximately 9-12 years. To assure her safety and appropriate data collection, she will be questioned at least every 6 months about any symptoms or problems she is having. She will also have yearly examinations, including resting pulse and blood pressure, height, weight, waist and hip measurements, ECG, clinical breast exam, mammogram, and pelvic exam (in women with uteri only). Every three years, women with a uterus will have a Pap smear and a small subsample will have endometrial aspirations. The costs of these exams and tests will be covered by your patient's insurance or the WHI. All results of these studies will be forwarded to your office upon receiving your patient's signed permission. If any problems are found during these exams or if your patient should develop any problems not related to HRT, she will be referred back to your office for care. It may be possible for you to perform or arrange some of these yearly exams.

[For women enrolled in DM:]

The Dietary Modification Study is designed to study the effect of a diet low in fat and high in fruits, vegetables, and grains on cancer and cardiovascular disease. Women in this study are randomized into two groups: dietary change (intervention) or usual diet (control). Women in the dietary change group will attend group sessions led by registered dietitians.

The WHI will follow your patient for approximately 9-12 years. To assure her safety and appropriate data collection, she will have yearly examinations, including resting pulse and blood pressure, height, weight, waist and hip measurements, ECG, and clinical breast exam, and every other year she will have a mammogram. The costs of these exams and tests will be covered by your patient's insurance or the WHI. All results of these studies will be forwarded to your office upon receiving your patient's signed permission. If any problem is found during these exams or if your patient should develop any problems not related to her participation in the study, she will be referred back to your office for care. It may be possible for you to perform or arrange some of these exams, such as the mammogram.

[For women enrolled in CaD (sent in a separate letter at time of CaD enrollment):]

Your patient has been enrolled in the Calcium and Vitamin D Study, designed to study the effect of calcium and vitamin D supplementation on the development of osteoporosis (measured by incidence of hip fractures). Women in this study are randomly assigned to one of two groups: one that takes calcium and vitamin D pills and one that takes placebos. Your patient should not take supplemental vitamin D in a dosage equal to or greater than 600 IU, since this dosage combined with the study pill could be potentially toxic.

[For women enrolled in OS:]

The Observational Study is designed to study the impact of various lifestyle and risk factors on the development of cancer, cardiovascular disease, fractures, and other major illnesses. This will be achieved by relating information obtained on baseline characteristics to subsequent illness events and mortality. The WHI will follow your patient for approximately 9-12 years by means of annual self-administered mailed questionnaires. These questionnaires will update information on hospitalization(s) and the occurrence of other outcomes of interest during the previous year and record changes in a few key exposure variables. Three years following her enrollment, she will be seen at the clinical center for physical measurements, such as blood pressure and weight, and to provide a blood sample.

[All Participants:]

The participation of your patient will have a great impact upon the future of health care for all women. Your support and collaboration are critical to the success of the WHI and our ability to answer important questions on women's health. If you should have any questions regarding the Women's Health Initiative or your patient's participation, please call us at _____. Thank you.

Sincerely,

_____ _____

Clinical Center Principal Investigator

Clinical Center Co-Investigator [or Consulting Gynecologist]

Figure E.1.6
Model Primary Care Provider Letter for HERS Information

Dear Healthcare Provider

The results of the Heart and Estrogen/progestin Replacement Study (HERS) were recently publicized. The Women's Health Initiative (WHI) scientists would like to share our review of and response to HERS because of the involvement of your patient, _____, in the Hormone Replacement Therapy Trial (HRT) portion of the WHI.

HERS participants had a documented history of coronary heart disease (CHD) and were randomized to either conjugated estrogen 0.625 mg and medroxyprogesterone acetate 2.5 mg OR placebo to investigate the effects of these drugs on CHD.[1,2] (No hysterectomized women were eligible for HERS.) Overall, there was no significant difference in reducing heart attacks between the two groups after an average of 4.1 years. The active hormone group showed a time trend with more CHD events in year 1 and fewer events in years 4 and 5. As expected, more women in the hormone group reported venous thromboembolic events (VTE) and gallbladder disease.

After re-examination of the WHI HRT protocol in light of these neutral findings, WHI scientists have determined that all participants could continue in the HRT trial regardless of previously reported heart disease status. The WHI Data and Safety Monitoring Board, a group of independent scientists who monitor the WHI, confirmed this decision.

We will provide each HRT participant with a newsletter updating her on HERS and its results. Each participant was also informed about the increased risk of VTE and gallbladder disease during the initial consenting process. The HERS group published its preliminary findings about an increased incidence of VTE in 1997, [3] and those WHI HRT participants who had a history of VTE were also given more information on symptoms of VTE, ways to decrease risk, and individual counseling. All HRT participants were encouraged to discuss these issues with you, their care provider.

The neutral HERS findings serve to re-enforce our conviction that a long-term study like the Women's Health Initiative is important and necessary. We appreciate your cooperation and your support of study efforts. We hope to continue this type of communication with you in the future. If you should have any questions regarding the HERS results, the HRT, or any other aspect of WHI, please do not hesitate to contact me.

Sincerely,

Principal Investigator

[1] Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. *JAMA*. 1998;280:605-613.

[2] Petitti DB. Hormone replacement therapy and heart disease prevention: Experimentation trumps observation. *JAMA* [editorial]. 1998;280:650-652.

[3] Grady D, Hulley SB, Furberg C. Venous thromboembolic events associated with hormone replacement therapy. *JAMA* [letter]. 1997;278:477.

Figure E.1.7
Model Primary Care Provider Letter on Unblinding

Dear (*Health Care Provider*),

We wanted to remind you about **(*participant's name*)** and her participation in the Hormone Replacement Therapy (HRT) trial of the Women's Health Initiative (WHI). The HRT trial will provide critical guidance about HRT indications such as prevention of cardiovascular disease and rates of bone fractures. Because it is a double blind study, with participants randomized to either active hormones or placebo, neither investigators nor participants know their assignment group.

During the WHI HRT trial (like other clinical trials), any decision to reveal a participant's study assignment is considered very carefully. We avoid giving the participant information that might reveal what type of pill she is on. The data collected and the ability of the study to find significant results can be biased when a participant's assignment to active or placebo is known. The WHI protocol contains very specific safety measures to protect your patient during her participation in the HRT trial, even while maintaining the double blind. For example, her health history is reviewed every six months to ensure she has not developed any contraindications to HRT.

If you can treat your patient for specific health concerns without unblinding (or if knowing the assignment would not affect your general plan of care), we would appreciate your cooperation in supporting the blind.

Also, when the participant is informed of "estrogenic effects" on lab results such as mammograms or pap smears, she is effectively unblinded. If at all possible, we ask that you not inform the study clinic or your patient of such comments. If your patient asks you about vaginal bleeding that may be occurring, be assured that the clinic will evaluate and coordinate with you any necessary follow-up. Please feel welcome to call the clinic and discuss any concerns you might have.

We appreciate your efforts and know that you will value the findings from this large, long-term clinical trial of HRT. Thank you for your support.

Please contact the WHI Clinical Center with any concerns you may have. We can be reached at:

(CC contact and phone number)

E.2 Participant Recruitment Materials

Figure E.2.1
Model Initial Contact Letter

Today's Date

Dear Friend,

You are invited to consider joining the Women's Health Initiative (WHI), an important and exciting new study sponsored by the National Institutes of Health. You may already know about the study from newspaper, radio and TV accounts. The Women's Health Initiative has generated a great deal of interest and enthusiasm among women across the country. This is the largest study ever to provide answers to important questions about women's health.

The [Institution] has been a leader in research on women's health for several decades and is well known for its research in _____ and other diseases. We are honored to have been selected as one of the centers nationwide to carry out the Women's Health Initiative.

The WHI will study how to prevent heart disease, cancer and bone fractures, some of the main causes of poor health and death in women. The study will examine the possible effect of low-fat diet in preventing breast and colon cancer, the possible value of hormone replacement therapy on major health events and the effect of calcium and vitamin D supplements on preventing bone loss.

You are one of a select group of women in the [Location] area who have a chance to join in this landmark study. If you are between the ages of 50 and 79, in good health, have gone through menopause (the change of life), and if you expect to be in the [Location] area for the next three years, you may be eligible to join.

The enclosed brochure describes what you will be asked to do if you join the Women's Health Initiative and how you can benefit yourself and others by participating. We urge you to read the enclosed brochure which explains the study in more detail. For more information, complete the return postage pre-paid postcard or call [Phone Number]. You are under no obligation to join the study. All information will be kept confidential.

We hope that you will consider joining 160,000 women from communities across the country in this pioneer effort. Your participation may improve your health and the health of women for generations to come. We hope that you will choose to "be part of the answer."

Sincerely,

Figure E.2.2
Model Interest Survey

Please complete this form and return it in the enclosed return envelope to the Women's Health Initiative Clinical Center.

1 **No**, I am not interested because *(please specify and return this survey; you do not need to fill out the form below)*:

1 **Yes**, I am interested *(please complete the form below)*

1. Name: _____
2. Address: _____
3. Home Phone: (__ __ __) __ __ __ - __ __ __ __
4. Work Phone: (__ __ __) __ __ __ - __ __ __ __
5. When and where are the best times to contact you by phone?

Day(s) of week:_____ _____ Morning 1 at home

_____ Afternoon or

_____ Evening 1 at work

6. Date of Birth: _____
7. Age: _____
8. Female: 1 Yes 1 No
9. If you would like additional Interest Surveys for other friends and family members, please let us know how many you would like, and we will send them to you.

I would like _____ additional Interest Surveys.

Thank You For Your Interest!

Please use the enclosed envelope to return this survey.

Figure E.2.3
Model Prescreen

Please return this questionnaire in the enclosed prepaid envelope whether or not you are interested in participating in the study.

1. Name (Please print): _____ _____ _____
   First M.I. Last

2. What is your date of birth? Month_____/Day_____/Year_____

3. What is your age now? _____years

4. Home Phone: ( ) ____ - _____ Work Phone: ( ) ____ - _____

		Yes	No	Don't Know
5.	Do you think you will be living in this area for the next 3 years?	____	____	
6.	Have you gone through menopause (the change of life?)	____	____	
7.	Do you currently take female hormones like estrogen (Premarin) or Progestin (Provera)?:	____	____	
8.	Did a doctor ever say that you had any cancer within the past ten years?	____	____	____
	If yes, please specify: _____			
9.	Are 10 or more of your meals each week prepared away from home?	____	____	
10.	Will you be able to get to our clinic?	____	____	

Figure E.2.4
Model How to Fill Out Form 2 - Eligibility Screen

How to fill out Form 2 - Eligibility Screen

- Please use the #2 pencil provided to fill out the form. Be sure to completely fill in the ovals on the form. We use a machine to read the marks. Please do not fold this questionnaire or it cannot be read by the machine.
- Feel free to make any comments or add any additional information on the back of this questionnaire.
- Page 1 is for office use only. You can start on Page 2.
- If you have any questions, please ask the WHI staff. If you are filling out the form at home, call us and we will be happy to help you.
- If there is an arrow by your answer, follow it to the next question. Sometimes the arrow will skip some questions and other times you will go to a box with more questions. The arrows help you decide which questions to answer.
- For number answers like "54," fill in the "50" oval and the "4" oval. Do not fill in the "5" and "4."
- On question 16 about how you heard about the study, give only **one answer**: the source that made you decide to contact us.
- If you are filling out this form at home, please return it in the envelope provided. We will pay for postage. Include the cardboard that came with the form so that it will not bend.

NOTES:

- If you are **interested in the hormone replacement part of the study** and you are taking female hormones now, you will need to stop taking hormones for three months before your first screening visit.
- If you are **interested in the dietary part of the study**, you will need to come to frequent meetings for one year.

Figure E.2.5
Model CaD Recruitment Letter

Dear (*WHI Participant*),

We are at a critical turning point in the Calcium and Vitamin D Study (CaD) of the Women's Health Initiative. Our objective in sending you this letter is to ask you to seriously consider joining the study.

The scientific goals of the Calcium/Vitamin D Study are to examine the effect of CaD supplements on hip fractures, colorectal cancer and breast cancer. These are major health concerns of women: 1 in 6 women will fracture their hip in her lifetime. Breast cancer is the second leading cause of death in women, colorectal cancer, the third. Although many women are taking calcium supplements to prevent osteoporosis, there are still a number of unanswered questions. Critical to the success of the WHI CaD Study is the enrollment of a sufficient number of women, 40, 000 women across the 40 WHI centers. This means the *(Clinic Name)* must enroll approximately *(number)* women. Thus far, we have enrolled about *(number)* women, so we need about *(number)* additional women to enroll from our Center.

No additional visits or time beyond what you currently spend in the other parts of the WHI Study will be required once you join CaD. If you join the CaD Study, you may continue to take any calcium supplements you are taking in addition to the study pills. We have two types of study pills for you to choose from, one is a swallowable pill and the other is a chewable one. You may choose which suits you best.

If you want more information, please let us know by completing the enclosed postcard. You can also directly contact either your practitioner by calling *(phone number)* or your nutritionist by calling *(phone number)* with your questions.

By joining CaD, you will be among a pioneering group of women seeking and finding answers to these important health concerns in postmenopausal women.

Sincerely,

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E.3 Participant Contact Materials

Figure E.3.1
Model SV1 Reminder Letter

WOMEN'S HEALTH INITIATIVE
[CC NAME AND ADDRESS]

February 16, 2012

[Participant's Name and Address]

Dear [Participant Name]

Thank you for your interest in taking part in the Women's Health Initiative. This study is looking at how to improve the health of women 50 to 79 years of age.

Your visit to the [CC Name] is scheduled for _____, _____ at _____.

This visit is to tell you more about the study, answer any questions, and see if you would be able to join the study. It will take about 3 to 4 hours of your time.

Please complete the enclosed forms. Use a #2 pencil (enclosed) to complete the mark-sense forms (like the Food Frequency Questionnaire). Be sure to completely fill in the ovals on the mark-sense forms because they are read by a machine that picks up the marks in the ovals. After your complete the forms, keep them in the mailing envelope so the forms are not folded.

If you decide to take part in this study, a fasting blood sample will be taken during your clinic visit. It is important that you take no aspirin or anti-inflammatory drugs (prescribed or over-the-counter) for 48 hours before the clinic visit and have nothing but water to eat or drink during the 12 hours before the clinic visit. If you usually take medications in the morning, you may take them with water at the usual time.

The address of the [CC Name] is: _____
_____
_____

A map to the Clinical Center is included with this letter. *[Include parking and child and adult care information, if available, and any other CC-specific information that may be of assistance to the participant.*]

Things To Remember for Your WHI Visit:

1. Complete and keep all of the enclosed forms in the mailing envelope. Bring them with you to the Clinical Center.
2. Use the enclosed medication bag to carry all of your prescription and over-the-counter medications that you are taking currently. We would like them to be in their original bottles. Be sure to bring any hormone medications, vitamins, minerals, laxatives, and fiber medications (like Metamucil) that you are currently taking.
3. To have a blood sample taken, you must refrain from vigorous exercise, fast for 12 hours before your WHI visit (no food or drink, except water), and take no aspirin or nonsteroidal anti-inflammatory medications (like ibuprofen) for 48 hours before your visit. You should not smoke one hour before your blood draw. You may take your regular prescription medicines, but hold any medicine for diabetes until after your blood draw or as your physician advises.
4. Wear light, loose, comfortable two-piece clothing, if possible.

If you have any questions or need to contact us for any reason, please call _____ at ( ) _____.

_____

Signature

Enclosures

Figure E.3.2
Model Appointment Card

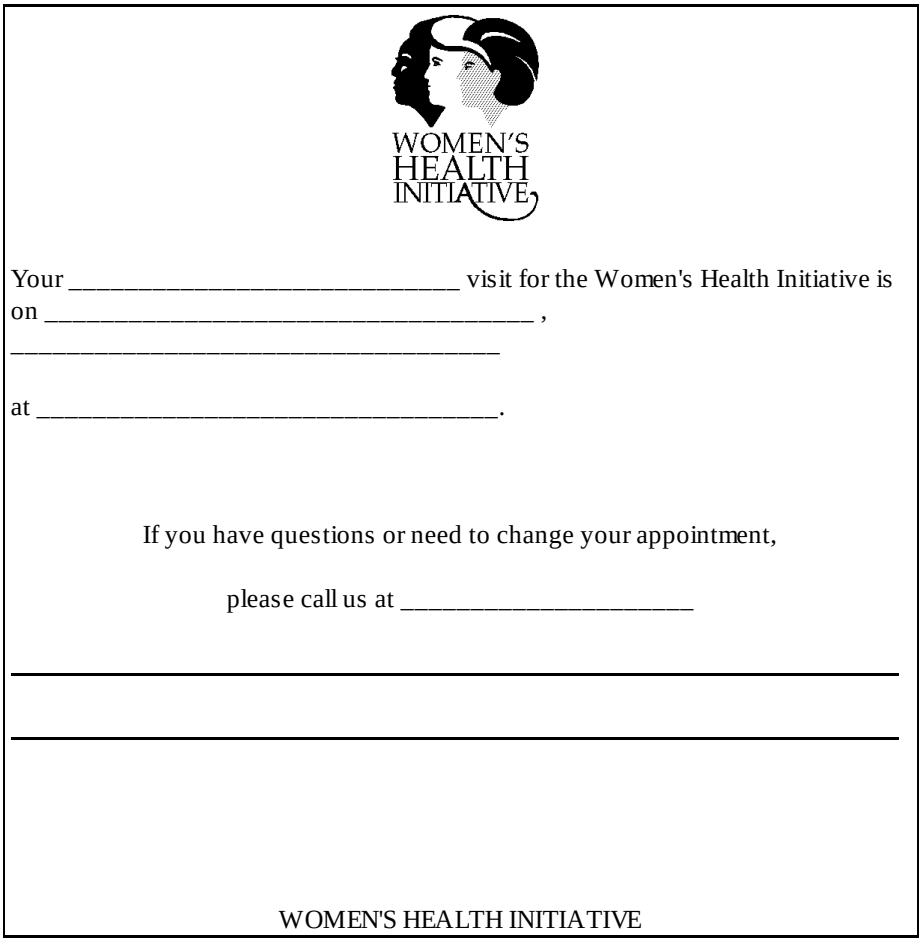

Figure E.3.3
Model Ineligible Letter

[To Follow.]

Figure E.3.4
Model Follow-Up Appointment Reminder Letter

Date

Dear _____:

This is a reminder that you have an appointment for a six-month/annual visit at your Women's Health Initiative Clinical Center on [Date and Time].

The following checked items are important for you to remember:

- ☐ Return all completed forms.
- ☐ Bring all medications to your visit—both prescribed (those that a doctor has given you) and those you have purchased over-the-counter—and any vitamins or minerals, laxatives and fiber medications (like Metamucil) you may take that you have used within the two weeks before your visit. Included with this letter is a bag for carrying your medications.
- ☐ Do not eat or drink anything but water for 12 hours before your appointment, as you are scheduled for a fasting blood test. If you are on insulin or oral diabetic medicines, do not take them the morning of your appointment, but bring them to the Clinical Center.
- ☐ Do not take any aspirin or non-aspirin substitutes for 48 hours before the visit. Also do not do any vigorous exercise for 12 hours before the visit.
- ☐ Please wear loose clothing that can be easily moved to take measures.
- ☐ Please bring your HRT Calendar. (HRT only)
- ☐ Please call us to schedule a mammogram so that it will be done before your appointment.
- ☐ You are scheduled to have a pelvic exam with a Pap smear. (Select HRT participants only)
- ☐ You are scheduled to have a sampling of the lining of your uterus (biopsy). (Select HRT participants only)

We look forward to seeing you again! If you need to change your appointment time or have any questions, please call us as soon as possible at [Phone Number].

Thank you for your participation in the Women's Health Initiative.

_____
[CC staff name]

Figure E.3.5
Model No-Contact Mailing Postcard

WHI

1. Have you had any major health problems since we last saw you?

   ☐ No

   ☐ Yes Please describe: _____

   _____

2. Is this address label correct?

   ☐ Yes

   ☐ No

   Change to: _____

   _____

3. Are you interested in rejoining the WHI study? ☐ No ☐ Yes

4. I have some questions. ☐ No ☐ Yes

   Please call me at: _____

   Best times to call: _____

Figure E.3.6.
Model Cover Letter to Include in *Form 49 - E+P Survey* Mailing

Dear Participant,

Thanks to your time and effort, women and health care providers worldwide learned in July 2002 some important new information about how estrogen plus progestin affects the risk of disease in postmenopausal women. As the news began to settle, important scientific questions arose:

What happens when women stop hormones?

- Do they feel better, worse, or the same?
- Do they have symptoms of menopause?
- Is there an effect on sexual function?
- How do women take care of themselves after they stop?

No large study has addressed these kinds of questions. In addition to the ongoing medical information you are providing about the effects of stopping hormones on disease, WHI has a golden opportunity to learn answers to these other important questions about women's health and well-being.

The enclosed survey is being sent to participants, like you, who are in the Women's Health Initiative Estrogen plus Progestin study and were asked to stop taking study pills in July 2002. As we have said several times, you are still a WHI VIP (Very Important Participant) and can provide much valuable information about hormones and women's health.

Whether you were taking active or placebo study pills, the information you provide is critical for helping us learn, scientifically, about the experiences of women after they stop hormones.

Some of the questions ask about personal topics, but they are important. For example, a sexual relationship is important to many women, yet little is known about the combined effects of aging, stopping hormones, and partner issues on a woman's sexual life. For some women sex is not an important part of their life, and that is okay too. The questions in this survey deal with these personal topics in a matter-of-fact fashion. As always, the answers are confidential. If you are uncomfortable answering a question, you may choose not to answer it.

Please remember that there are no right or wrong answers – just data to help us understand hormones and postmenopausal women's health. We can learn a great deal from this survey to help women and their health care providers in the future. Thank you for your support and contributions toward continued success in WHI!

Warmest regards,

PI

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E.4 Clinical Center Contact Materials

Figure E.4.1
Model SV0 Checklist

Date/time Begun:	____ ____:____ ____ (hr/min)
	____ - ____ - ____ (M/D/Y)
Date/time Completed:	____ ____:____ ____ (hr/min)
	____ - ____ - ____ (M/D/Y)
Final Review:	____ ____:____ ____ (hr/min)
	____ - ____ - ____ (M/D/Y)

- Affix label here-

Clinical Center/ID: __ __ __ __ - ___ ___ ___ - __

First Name _____M.I._____

Last Name _____

Initial each activity when completed or write "NA" if not applicable.

SV0

___ Distribute *Initial Consent Form*

___ Distribute *Form 2 - Eligibility Screen* or administer *Form 3 - Eligibility Phone Screen* (with #2 pencil)

___ Distribute *Form 20 - Personal Information*

___ Distribute *Form 60 - Food Frequency Questionnaire (FFQ)* (with #2 pencil)

___ Provide overview of WHI

___ View Introduction to WHI video

HRT Interest (Currently Taking Hormones) Only:

- ___ Discuss HRT washout, answer questions
  - ___ HRT introductory letter sent to participant
  - ___ HRT introductory letter sent to Primary Care Provider

___ Review completed *Form 2/3 - Eligibility Screen*

___ Review completed *Form 60 - Food Frequency Questionnaire (FFQ)*

___ Review completed *Form 20 - Personal Information*

___ Scan completed *Form 2/3 - Eligibility Screen*

___ Scan completed *Form 60 - Food Frequency Questionnaire (FFQ)*

___ Run Eligibility Determination for DM and HRT

___ Schedule Screening Visit 1 (SV1) or schedule for OS contact if ineligible for or uninterested in CT

___ Inform participant about the need to fast for blood draws at SV1

Figure E.4.2
Model SV1 Checklist

Date Begun: ____ - ____ - ____ (M/D/Y) Date Completed: ____ - ____ - ____ (M/D/Y) Final Review: ____ - ____ - ____ (M/D/Y)	**- Affix label here-** Clinical Center/ID: __ __ __ __ - ___ ___ ___ - __ First Name _____M.I._____ Last Name _____

Initial each activity when completed or write "NA" if not applicable.

SV1

PRE-VISIT PREPARATION

___ Prepare participant file

___ Distribute or mail cover letter, medication bag, directions to CC

___ Assemble forms and barcode labels for the specific components of the study

___ Make a reminder phone call regarding SV1

INITIAL INFORMED CONSENT

___ View Introduction to WHI video (if not already viewed)

___ Provide a description of the study (the following are the minimal key points to be covered)

- ___ Participation is voluntary
- ___ Withdrawal from study can occur at any time
- ___ Study information is confidential
- ___ Overview of screening requirements
- ___ Description and risks of screening clinical procedures

___ Participant is given ample opportunity to ask questions

___ Review and discuss *Initial Consent Form*

___ Obtain signatures on *Initial Consent Form* and provide one copy to participant

___ Complete *Form 11 - Consent Status*

___ Complete *Form 4 - HRT Washout* (HRT, as appropriate)

BLOOD AND URINE COLLECTION

___ Collect urine sample - BD sites only (*Form 101 - Urine Collection and Processing*)

___ Draw participant's fasting blood (*Form 100 - Blood Collection and Processing*)

___ Give participant a light snack

___ Process blood sample

___ Process urine sample - BD sites only

FORMS COMPLETION AND REVIEW

___ Obtain *General Medical Release* form signature

___ Begin *Form 6 - Final Eligibility Assessment*

___ Administer *Form 43 - Hormone Use*

MEDICATION REVIEW

___ Complete WHILMA Database *Task 44 - Current Medications*

___ Complete WHILMA Database *Task 45 - Current Supplements*

PHYSICAL MEASUREMENTS

___ Complete *Form 80 - Physical Measurements*

- ___ Resting pulse
- ___ Blood pressure measurement
- ___ Height measurement
- ___ Weight measurement
- ___ Waist measurement
- ___ Hip measurement

___ Complete *Form 87 - Bone Density Scan* - BD sites only

CT INFORMED CONSENT

___ Provide detailed description of CTs:

- ___ HRT
- ___ DM

___ View videos:

- ___ HRT
- ___ DM

END OF VISIT

___ Discuss current experience and future plans with the participant

___ Distribute CT forms:

- ___ *Form 30 - Medical History Questionnaire*
- ___ *Form 31 - Reproductive History Questionnaire*

CT ONLY:

___ Schedule Screening Visit 2 (SV2)

___ Schedule Bone Density Scan (Bone Density sites only)

___ Ensure participant has a signed copy of *Initial Consent Form*

___ Provide participant with copies of appropriate CT consent forms to read, sign, and return at SV2:

- ___ HRT

___ DM

OS ONLY:

___ Provide detailed description of OS and obtain signed consent

___ Ensure that participant has a signed copy of OS Consent Form

___ Distribute additional baseline questionnaires for completion at the CC or at home:

- ___ *Form 30 - Medical History Questionnaire*
- ___ *Form 31 - Reproductive History Questionnaire*
- ___ *Form 32 - Family History Questionnaire*
- ___ *Form 34 - Personal Habits Questionnaire*
- ___ *Form 37 - Thoughts and Feelings*
- ___ *Form 42 - OS Questionnaire*

___ Provide WHI memento, Exercise Brochure, and health education materials

POST VISIT

___ Key-enter/scan forms

___ Determine eligibility for HRT & DM

Figure E.4.3
Model SV2 Checklist

Date Begun: ____ - ____ - ____ (M/D/Y) Date Completed: ____ - ____ - ____ (M/D/Y) Final Review: ____ - ____ - ____ (M/D/Y)	**- Affix label here-** Clinical Center/ID: __ __ __ __ - ___ ___ ___ - __ First Name _____M.I._____ Last Name _____

Initial each activity when completed or write "NA" if not applicable.

SV2

PRE-VISIT PREPARATION

___ Check each participant's eligibility determination to confirm the components for which she is still eligible

___ Review lab results

- ___ CBC
- ___ Triglycerides (HRT, if done)

___ Assemble forms and barcode labels for the specific components of the study

___ Provide *HRT Endometrial Aspiration* sheet (HRT)

___ Send information to participant regarding fasting blood draws (if not completed at SV1)

___ Make reminder phone call regarding SV2

INFORMED CONSENT

___ Review and discuss appropriate informed consent form(s):

- ___ HRT
- ___ DM

___ Provide participant with copy of signed consent form(s)

___ Update *Form 6 - Final Eligibility Assessment*

___ Complete *Form 11 - Consent Status* for HRT/DM

FORMS REVIEW

___ Review *Form 30 - Medical History Questionnaire*

___ Review *Form 31 - Reproductive History Questionnaire*

CLINICAL PROCEDURES

___ Draw participant's fasting blood (if not completed at SV1) (*Form 100 - Blood Collection and Processing*)

___ Give participant a light snack after blood draw

___ Perform ECG (*Form 86 - ECG)*

___ Perform clinical breast exam (*Form 84 - Clinical Breast Exam*)

___ Instruct participant in breast self-exam

___ Schedule mammogram (*Form 85 - Mammogram*)

___ **or** request mammogram report if ≤ 12 months (*Form 85 - Mammogram*)

HRT Only:

___ Perform pelvic exam (*Form 81 - Pelvic Exam/Pap Smear*)

___ Perform Pap smear (*Form 81 - Pelvic Exam/Pap Smear*)

___ **or** request Pap smear report if performed within the previous 12 months

___ Perform endometrial aspiration (*Form 82 - Endometrial Aspiration*)

___ **or** request endometrial aspiration report if performed within the previous 12 months

___ Schedule transvaginal uterine ultrasound if unable to attain entry to uterus (*Form 83 - Transvaginal Uterine Ultrasound*)

___ Provide post-procedure information sheet for endometrial aspiration

DISPENSING ENROLLMENT MEDICATIONS - HRT ONLY

___ Review instructions for enrollment medications

___ Provide HRT Symptoms Brochure

___ Provide HRT Study Pill Instructions sheet

___ Give participant a WHI pill dispenser

___ Dispense HRT enrollment medications

___ Provide *Form 53 - HRT Calendar* with instruction

DIETARY INSTRUCTION - DM and DM + HRT Only

___ Distribute *Form 62 - Four-Day Food Record (4DFR)* and *Form 69 - Keeping Track of What You Eat*

___ View video and provide instructions for completing *4DFR*

___ Assign days for *4DFR*

END OF VISIT

___ Discuss current experience and future plans with the participant

CT Only:

___ Ensure participant has a signed copy of appropriate CT consent form(s)

___ Schedule Screening Visit 3 (SV3)

___ Distribute CT forms:

___ *Form 32 - Family History Questionnaire*

___ *Form 34 - Personal Habits Questionnaire*

___ *Form 37 - Thoughts and Feelings*

OS Only:

___ Provide detailed description of OS and obtain signed consent

___ Ensure participant has a signed copy of OS Consent Form

___ Distribute additional baseline forms

___ *Form 32 - Family History Questionnaire*

___ *Form 34 - Personal Habits Questionnaire*

___ *Form 37 - Thoughts and Feelings*

___ *Form 42 - OS Questionnaire*

___ Provide WHI memento, Exercise Brochure, and health education materials

POST VISIT

___ Key-enter/scan forms

___ Determine eligibility for HRT & DM

Figure E.4.4
Model SV3 Checklist

Date Begun: ____ - ____ - ____ (M/D/Y) Date Completed: ____ - ____ - ____ (M/D/Y) Final Review: ____ - ____ - ____ (M/D/Y)	**- Affix label here-** Clinical Center/ID: __ __ __ __ - ___ ___ ___ - __ First Name _____M.I._____ Last Name _____

Initial each activity when completed or write "NA" if not applicable.

SV3

PRE-VISIT PREPARATION

___ Review results:

- ___ *Form 85 - Mammogram*
- ___ *Form 81 - Pelvic Exam/Pap Smear* - HRT only
- ___ *Form 82 - Endometrial Aspiration* or *Form 83 - Transvaginal Uterine Ultrasound* - HRT only

___ Key-enter *Forms 81 - 83, 85*

___ Review tasks from SV1 and SV2 Checklists that were not completed. Add uncompleted tasks to SV3 Checklist

___ Run eligibility determination for HRT and DM, as appropriate

COMPLETION AND FORMS REVIEW

___ Complete *Form 6 - Final Eligibility Assessment*

___ Review *Form 32 - Family History Questionnaire*

___ Review *Form 34 - Personal Habits Questionnaire*

___ Review *Form 37 - Thoughts and Feelings*

___ Review *Form 62 - 4DFR* - DM only

___ Review *Form 53 - HRT Calendar* - HRT only

ENROLLMENT PILL ADHERENCE - HRT ONLY

___ Collect all HRT enrollment bottles

___ Count HRT enrollment pills

___ Key-enter pill count into the database

MEDICATIONS REVIEW

___ Review any medications that have changed since SV1 and enter in Current Medications (*Task 44*)

VERIFICATION OF ELIGIBILITY

___ Review all information on DM Eligibility Checklist (DM)

___ Review *Form 2/3 - Eligibility Screen* with participant for changes

___ Review all study forms for completion

___ Review all study procedures for completion

___ Scan *Form 32 - Family History Questionnaire* and *Form 34 - Personal Habits Questionnaire*

___ Key-enter *Form 6 - Final Eligibility Assessment*

___ Perform final eligibility determination in the database for each applicable component

- ___ HRT
- ___ DM

RANDOMIZATION

___ Randomize participant

___ Provide a confirmation of randomization/enrollment report to the participant

BASELINE PROCEDURES

___ Complete *Form 90 - Functional Status* (subsample)

___ Complete *Form 39 - Cognitive Function* (subsample)

END OF VISIT

All Participants:

- ___ Discuss current experiences and future plans with participant
- ___ WHI memento, Exercise Brochure, and health information materials
- ___ Complete *Form 11 - Consent Status*, if participant is not interested in study participation

HRT Only:

- ___ Dispense study pills
- ___ Provide HRT Study Pill instruction sheet
- ___ Provide new *Form 53 - HRT Calendar*, if necessary
- ___ Schedule six-month follow-up CC visit

DM Only:

- ___ Make assignment to intervention groups
- ___ Inform participant of target date for six-month follow-up contact

OS Only:

- ___ Provide detailed description of OS and obtain signed consent
- ___ Ensure participant has a signed copy of OS Consent Form
- ___ Distribute *Form 42 - OS Questionnaire*

POST VISIT

___ Key-enter/scan remaining forms

Figure E.4.5.
Model OS Checklist

[To Follow.]

Figure E.4.6.
Model Semi-Annual Checklist (CT)

Date Begun: ____ - ____ - ____ (M/D/Y) Date Completed: ____ - ____ - ____ (M/D/Y) Final Review: ____ - ____ - ____ (M/D/Y)	**- Affix label here-** Clinical Center/ID: __ __ __ __ - ___ ___ ___ - __ First Name _____M.I._____ Last Name _____

Model Semi-Annual Contact Checklist (CT)

Initial each activity when completed or write "NA" if not needed for this visit or component. An overview of required follow-up activities is in *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection*. Required activities for individual participants at specified contacts are listed on *WHIP0144 - Tasks Required at Visit*.

PRE-CONTACT PREPARATION

___ Print out a semi-annual visit plan *(WHIP0144 - Tasks Required at Visit)*
___ Send first-class packet two weeks before target date, containing:
- ___ Appointment reminder letter
- ___ *WHIP0441 - Personal Information Update*
- ___ *Form 33 - Medical History Update*
- ___ WHI logo bag for returning study pills *(HRT, CaD)*
- ___ map to CC
- ___ parking validation

___ Make a reminder phone call to participant two days before semi-annual visit

CONTACT PROCEDURES

___ Obtain signatures on General Medical Release forms
___ Review/complete *WHIP0441 - Personal Information Update*
___ Review/complete *Form 33 - Medical History Update*
___ Review/complete *Form 33D - Medical History Update (Detail)*, if appropriate
___ Review/complete *Form 53 - HRT Calendar (HRT participants w/uterus at SAV1 only)*
___ Assess adherence to study pills *(HRT, CaD)*
___ Complete *Form 10 - HRT Management and Safety Interview (HRT)*
___ Complete *Form 17 - CaD Management and Safety Interview (CaD)*
___ Dispense HRT study pills *(HRT)*
___ Offer new *HRT Handbook (HRT)*
___ Dispense CaD study pills *(CaD)*
___ Offer new *CaD Information Sheet (CaD)*
___ Offer new pill organizer *(HRT, CaD)*
___ Provide new *Form 53 - HRT Calendar (HRT participants w/uterus at SAV1 only)*
___ Provide appointment card with next AV date

Figure E.4.7.
Model Annual (CT) or Third-Year (OS) Visit Checklist

Date Begun: ____ - ____ - ____ (M/D/Y) Date Completed: ____ - ____ - ____ (M/D/Y) Final Review: ____ - ____ - ____ (M/D/Y)	**- Affix label here-** Clinical Center/ID: __ __ __ __ - ___ ___ ___ - __ First Name _____M.I._____ Last Name _____

Model Annual (CT) or Third-Year (OS) Visit Checklist

Initial each activity when completed or write "NA" if not needed for this visit or component. An overview of required follow-up activities is in *Vol. 1 - Study Protocol and Policies, Table 1-A1.2 - Frequency of Collection*. Required activities for individual participants at specified contacts are listed on *WHIP0144 - Tasks Required at Visit*.

PRE-VISIT PREPARATION

___ Print out an annual visit plan *(WHIP0144 - Tasks Required at Visit)*

___ Run a preliminary CaD eligibility determination *(CT at AV1 only)*

___ Obtain and review mammogram results *(CT - if needed)*

___ Obtain and review Pap smear results *(HRT participants w/uterus - if needed and performed by personal physician)*

___ Send first-class packet two weeks before target date, containing:

- ___ Appointment reminder letter
- ___ *WHIP0441 - Personal Information Update*
- ___ *Form 33 - Medical History Update*
- ___ *Form 38 - Daily Life (if needed)*
- ___ *OS Follow-Up Questionnaire (OS - if needed)*
- ___ *Form 60 - Food Frequency Questionnaire* and *Form 61 - How to Fill Out the Food Questionnaire (DM, OS - if needed)*
- ___ #2 pencil for completing mark-sense forms *(if needed)*
- ___ *Form 62 - Four-Day Food Record* (with completion dates assigned) and *Form 69 - Keeping Track of What You Eat (DM - if needed)*
- ___ *CaD Invitation* and consent form (eligible CT participants at AV1)
- ___ WHI logo bag for returning study pills or bringing in medications and supplements *(if needed)*
- ___ 30 ml urine container with *Urine Home Collection* instruction sheet *(BD sites only-if needed)*
- ___ map to CC
- ___ parking validation

Figure E.4.7 (continued)

VISIT PROCEDURES

Blood Collection (*Form 100 - Blood Collection and Processing (if needed)*

___ Draw participant's fasting blood

___ Give participant a light snack

___ Process blood sample

___ Send serum to local lab for triglycerides if lipemic *(HRT)* or for CBC *(OS)*

Urine Collection *(Form 101 - Urine Collection & Processing) (BD sites only-if needed)*

___ Collect urine sample

___ Process urine sample

CaD Screening and Randomization (eligible CT participants at AV1)

___ Discuss CaD consent with participant

___ Obtain signatures on CaD consent form

___ Complete *Form 11 - Consent Status*

___ Complete *Form 16 - CaD Eligibility Assessment*

___ Run final CaD eligibility determination and randomize to CaD

___ Provide participant with copy of CaD consent form

Forms Completion and Review

___ Obtain signatures on General Medical Release forms

___ Review changes to *WHIP0441 - Personal Information Update*

___ Review *Form 33 - Medical History Update*

___ Review/complete *Form 33D - Medical History Update (Detail)*, if appropriate

___ Review *Form 38 - Daily Life (if needed)*

___ Review *Form 53 - HRT Calendar (HRT participants w/uterus at AV1 only)*

___ Review *Form 60 - Food Frequency Questionnaire (DM, OS - if needed)*

___ Review and document *Form 62 - 4DFR* (w/completion dates assigned) *(DM - if needed)*

___ Review *OS Follow-Up Questionnaire (OS - if needed)*

___ Assess adherence to study pills *(HRT, CaD)*

___ Complete *Form 10 - HRT Management and Safety Interview (HRT)*

___ Complete *Form 17 - CaD Management and Safety Interview (CaD)*

___ Complete entry of current medications *(Task 44 - if needed)*

___ Complete entry of current supplements *(Task 45 - if needed)*

Figure E.4.7 (continued)

Clinical Measurements

___ Complete *Form 80 - Physical Measurements*

- ___ Resting pulse
- ___ Blood pressure measurement
- ___ Height measurement
- ___ Weight measurement
- ___ Waist measurement
- ___ Hip measurement

___ Complete *Form 39 - Cognitive Assessment (HRT - if needed)*

Clinical Measurements (cont.)

___ Complete *Form 90 - Functional Status (CT - if needed)*

- ___ Grip strength measurement
- ___ Chair stand
- ___ Six-meter walk

___ Perform ECG *(Form 86) (CT - if needed)*

___ Perform clinical breast exam *(Form 84) (CT - if needed)*

___ Perform pelvic exam *(Form 81) (HRT participants w/uterus)*

___ Perform Pap smear (*Form 92) (HRT participants w/uterus - if needed)*

___ Perform endometrial aspiration *(Form 82) (HRT participants w/uterus - if needed)*

Dispensing Study Pills *(HRT, CaD)*

___ Dispense HRT study pills *(HRT)*

___ Offer new *HRT Handbook (HRT)*

___ Dispense CaD study pills *(CaD)*

___ Offer new *CaD Information Sheet (CaD)*

___ Offer new pill organizer *(HRT, CaD)*

END-OF-VISIT PROCEDURES

___ Provide appropriate study-wide annual retention item

___ Schedule next semi-annual contact

POST-VISIT PROCEDURES

___ Review mammogram report and complete *Form 85 (CT - if needed)*

___ Review lab results *(HRT, OS - if needed)*

___ Review Pap smear results and complete *Form 92 (HRT participants w/uterus - if needed)*

___ Review endometrial aspiration results and complete *Form 82 (HRT participants w/uterus - if needed)*

___ Forward forms to data entry

3

E.5

E.6 Participant Handouts

Figure E.5.1
Model General Medical Release Form

Office use only.	- Affix label here- Clinical Center/ID: __ __ __ __ - ___ ___ ___ - __ First Name _____M.I._____ Last Name _____

1. **Explanation:**

   This consent is for release of medical and health care information from your doctor, clinic, or other health care provider.

2. **Consent:**

   I hereby give my consent for: _____ (Name of Doctor, Clinic, or Health Care Provider)

   _____ Address

   _____ City State Zip

   to provide copies of my medical records to: _____ CC Name

   _____ Address

   _____ City State Zip

   Phone: _____

   Medical records to include: _____

   _____

   _____

3. Approximate date of last medical treatment, condition, or service: __ __/__ __/__ __

4. **Purpose:** The medical information that is released will only be used for research purposes by the Women's Health Initiative (WHI) research staff.

5. **Duration:** This consent is effective upon signing and shall remain valid for the duration of the WHI study (1993-2008).

6. **Restrictions:** I understand this information will be used only for research purposes and will not be released by the WHI staff without my consent.

7. Signed: _____ _____
   (Study Participant/Spouse/Responsible Party) (Date)

   If signed by other than participant, indicate relationship: _____

   Printed name of study participant: _____

   Witness: _____
   Signature

   Spanish Translator: ☐ Yes _____ ☐ No

Signature

Figure E.5.2
Model HRT Endometrial Aspiration

HRT - ENDOMETRIAL ASPIRATION

As part of the HRT study, you have been asked to have an **ENDOMETRIAL ASPIRATION**. During this very common test, a specially trained clinic practitioner will take a small sample from inside your uterus (your womb) and send it to a laboratory to check for any abnormal cells. The results will let us know if it is safe for you to start or continue your study pills.

Generally, this procedure is simple and takes no more than 15 to 20 minutes. While you might feel some cramping, it is usually brief and not severe. Your clinic practitioner may offer you some medication to help decrease the amount of discomfort you have, if you do not have any health problems that prevent you from taking this type of medicine.

First, you will be helped into the pelvic exam position. The clinic practitioner will insert a speculum into your vagina, and cleanse the opening to your womb (your cervix) with an iodine solution. An injection, much like your dentist might use, might be given to you at this time to numb this same opening.

The practitioner will then use a "sampling aspirator." This aspirator tool is thin (about 1/8" wide) and very flexible. It will be used to suction out about 1/2 teaspoon or less of tissue lining the uterus.

After the procedure, you might have a slight amount of spotting and cramping. This should decrease and be gone within a day's time. Otherwise, you should be able to leave the clinic and enjoy your usual activities.

Figure E.5.3
Model HRT - After Your Endometrial Aspiration

HRT - AFTER YOUR ENDOMETRIAL ASPIRATION

After your endometrial aspiration, there will probably be a small amount of bleeding or spotting and maybe even a little cramping. Although other problems are rare, there is always the small chance that they might happen. We have listed a few symptoms that we would like you to watch for. Please call your Clinical Center if you have . . .

1. A temperature greater than 100 degrees F.

2. Vaginal bleeding heavier than what was a normal period for you, bleeding for more than 5 days, or an unusual discharge that has a bad smell.

3. Abdominal or pelvic pain that does not get better with over-the-counter medicines such as Tylenol® or Advil® (take only if you do not have health problems that prevent you from taking this type of medicine) or if the pain lasts more than a day.

4. Other symptoms that may be worrisome to you.

We also recommend that you do not put anything in your vagina (such as tampons and lubricants) or have intercourse until the bleeding stops.

Figure E.5.4
Model HRT Study Pills Instruction Sheet

HRT STUDY PILLS INSTRUCTIONS

1. **Take 1 pill every day**. Try to find a place to keep your pills that will work into your routine. If you take your pills at night time, keep them on your bedside table with your HRT Calendar. Then you can take your pill and record in your diary at the same time.

2. Use the WHI pill organizer if you find it hard to remember to take your pill every day (ask your Clinical Center staff for one).

3. Call the Clinical Center if you have heavy bleeding (heavier than a normal period flow) at any time, or if you have been on the pills for more than six months and have any bleeding at all.

4. Call the Clinical Center if your regular doctor prescribes any of the following medicines:

   Heparin

   Warfarin or Coumadin

   Hormones

5. Bring your pill bottle and pill organizer, if you use one, to your next visit.

6. Avoid exposing your pills to extreme heat.

Figure E.5.5
Model HRT Symptoms Brochure

REPLACED BY THE HRT HANDBOOK (APPENDIX F, FIGURE F.3.2) 9/95

Figure E.5.6
Model CaD Study Pill Instruction Sheet

REPLACED BY FIGURE IN *VOL. 2 - APPENDIX F, FIGURE F.2.5, CAD INFORMATION SHEET*

Figure E.5.7.
Model Request for Medical Information

[Date]

[Medical Institution]
[Address]
[City, State Zip]

RE: [Participant's Name]
[DOB]
[SS#]
[Dates of medical care]

Dear _____ :

The [Name of your institution] is involved in the Women's Health Initiative (WHI), a study of ways to prevent breast cancer, colon and rectal cancer, heart disease, and fractures in women ages 50 to 79. About 160,000 women from 40 centers in the United States will take part in this study which is funded by the National Institutes of Health. The Principal Investigator for this study at our institution is [PIs' Name].

As part of our study we are tracking all participants who develop certain events, such as cancer, heart disease, fracture, any hospitalization or death. We understand the above participant may have been treated for _____ on or about [Date of diagnosis on *Form 33 - Medical History Update*]. We would appreciate any medical records related to this event for confirmation of the diagnosis. Attached is a release of medical records form signed by the participant indicating the documents needed.

Please forward this information to:

[Your address]

[Attention whoever]

Thank you for your prompt attention to this matter. If you have any questions or concerns please feel free to call [Outcomes Specialist or PI] at [phone number] for further information.

Sincerely,

PI or Designee
Title

Figure E.5.8
Model Antibiotic and Medication Allergies Questionnaire (HRT Participants with Uteri)

		No	Yes
1.	Has your doctor ever recommended that you take antibiotics prior to a dental, office, or surgical procedure?	☐	☐
2.	Have you ever had a heart valve replaced?	☐	☐
3.	Have you ever been told you had rheumatic heart disease?	☐	☐
4.	Have you ever had an infection of the valves or lining of your heart (bacterial endocarditis)?	☐	☐
5.	Have you ever had any joint surgically replaced (example - hip or knee)?	☐	☐
6.	Have you ever had chest surgery to shift blood flow away from your lungs (pulmonary shunt or conduit)?	☐	☐
7.	Are you allergic to any of the following medications?	☐	☐
	Penicillin	☐	☐
	Ampicillin	☐	☐
	Amoxicillin	☐	☐
	Erythromycin	☐	☐
	Other Antibiotics: **(Specify)** _____	☐	☐
	Aspirin	☐	☐
	Any anti-inflammatory medications (example - Ibuprofen, Advil, Motrin, Indocin, Naprosyn, Feldene)	☐	☐
	Tylenol	☐	☐

Figure E.5.9
Model Statement for Non-Child-Resistant Cap

RECEIPT OF NON-CHILD RESISTANT CAP(S) FOR STUDY MEDICATION

I, _____, have requested and received a non-child resistant cap(s) for my study drug bottle(s) as part of the Women's Health Initiative.

I have been advised of precautions to prevent accidental overdose.

_____ _____
Participant Date

_____ _____
Witness Date

Figure E.5.10
Model Summary of Changes in the Dietary Part of the WHI and in the Dietary Part Consent Form

Several changes have been made in the Dietary Part of the WHI since you joined and last signed a consent form.

- The biggest change is the mammogram requirement. When the Dietary Part was planned, yearly mammograms were required. Most expert groups, like the American Cancer Society, agreed with this. Since then, the need for yearly mammograms has been reconsidered. Now, many experts think that mammograms every 2 years are enough for women over 50 years old. So, WHI is changing this requirement for women who are only in the Dietary Part of the study. We would like you to have a mammogram at least every 2 years while you are in the program. Women who are also in the Hormone Replacement Part of the WHI will still get yearly mammograms because of the possibility that hormones may increase the risk of breast cancer. Of course, you can still have a mammogram every year if you and your doctor decide that is best for you. But we will only help you pay for a mammogram (if you need assistance) every other year.

- Another change is that you only need to come to a clinic visit once a year, not every 6 months *[tailored to clinic specifications]*. We know that it can be hard to come to the clinic often, so we will call you on the phone or contact you by mail between visits if we need information from you.

- There is a chance that you will be asked to complete additional Four-Day Food Records. This means writing down the foods you eat for four days. These food records would be completed four times over the course of the study.

- A small number of participants will be asked to talk on the telephone with a nutritionist about what you ate the day before (a 24-hour recall). This would only happen once or twice during the study and would take about 30 minutes of your time.

- If you are part of the Dietary Change Program, you will be doing activities at home in addition to coming to group instructional sessions with a nutritionist. These home activities include keeping food diaries and practicing what you learned during the nutrition sessions. Home activities could take up to one hour per day.

I have read the above information and understand the changes listed.

_____ _____

Signature of Participant Date

Figure E.5.11
Model Invitation to Join the Calcium and Vitamin D Program of the WHI!

Figure E.5.12
Privacy Act Notification Statement

_____(name of CC) is one of 40 clinics across the U.S. that have been funded by the National Institutes of Health Women's Health Initiative to study the prevention of heart disease, cancer, and other diseases in women between 50 and 79 years of age. We would like some information about you and your interest in the study. The WHI is authorized under the Privacy Act 42 USC 241. Your decision to join in this is voluntary and you may refuse to answer any questions. All information will be kept confidential and your privacy will be protected to the extent required by law. No personal identifiers will be revealed in any publication or release of results. WHI authorized staff will have access to your name, address, and social security number only for the purpose of study wide mailings and for maintaining and updating your study records. Whether or not you choose to join the study will not affect your personal medical or medical insurance coverage.

Figure E.5.13
Model Summary of Changes for Participants in the 4DFR Subsample

We have made some changes to the WHI since you joined and last signed a consent form. In your last informed consent, you agreed to complete four Food Records during the study. We are now asking you to:

- Complete one Food Record for your first annual visit.
- Complete two telephone interviews near the time of your third, sixth, and ninth annual visit.

An interviewer from the WHI Coordinating Center in Seattle will call you and ask about the foods you eat. Each interview will take about 20 minutes. You do not need to do anything special to prepare for these calls.

- There are no other changes to the study.

We appreciate your continued interest in the Women's Health Initiative. This is an important study and the information you provide you provide will help us learn more about how diet affects women's health.

E.5.14 – Model Better Balance in Eating Patterns

Potential Ideas to Provide Better Balance in Eating Patterns

Food Choices:

- o Increase use of poultry (turkey, chicken, Cornish game hen).
- o Increase use of fish.
- o Have a meatless meal using beans or legumes at least once/week.
- o Increase use of low-fat dairy foods, if tolerated.
- o Encourage use of whole grain choices of cereals, pasta, rice, or other grains.
- o Decrease use of fat-free or low-fat baked goods.
- o Increase use of vegetables.
- o Increase variety of vegetables eaten.
- o Increase use of fruit (canned, fresh, frozen or dried).
- o Use 100% juices (fruit or vegetable) vs. fruit drinks or blends.
- o Use small amounts of vegetable oils, nuts/seeds, occasional use of low-fat salad dressings or mayonnaise (instead of fat-free versions).
- o Decrease use of high-sugar sweets such as candy, sugar and sodas if gaining weight or if low on servings of F/V or whole grains.
- o Increase water intake.
- o Decrease use of alcohol if overused in relation to other nutrient-dense foods (e.g., fruits, vegetables, lean protein, low-fat dairy and whole grains).
- o Other:_____

Eating Behaviors:

- o Reduce meals eaten alone by asking friends or family to share meals once or twice a week.
- o Make the place you eat more friendly and inviting (flowers, nice tablecloth, music, etc.).
- o Reduce difficulties chewing or swallowing by looking for "softer" food sources (e.g., canned foods), softer protein sources (e.g. cottage cheese, eggs, tofu, beans), etc.
- o Identify time-saving ingredients, foods, and recipes to have on hand.
- o Have a list of low-fat frozen dinners (homemade or commercial) for alternative quick and easy meals.

Other:_____

E. 5.15 – Model Fact Sheet – Learning about Fat

- Fact Sheet - Learning about Fat

Is there a minimal amount of fat that I should be eating?

There is no ideal level of dietary fat that applies to everyone. In the WHI Dietary Study, participants are encouraged to eat about 20% of their calories from fat. This percentage represents an amount that is well above minimal nutritional needs for fat.

Have other low-fat studies been safely conducted with postmenopausal women?

Yes, there are a couple of studies where postmenopausal women have followed low-fat eating patterns. The Women's Health Trial Vanguard Study and the Women's Intervention Nutrition Study had participants who followed dietary programs that contained between 15 and 20% calories from fat. These studies show that average nutrient intake is adequate at this level of fat intake.

How is safety of the WHI Dietary Study monitored study wide?

There is an independent board appointed by the National Institutes of Health (NIH) to monitor study progress, outcomes, and participant safety. This board (Data and Safety Monitoring Board) meets twice a year. It reviews study data and makes recommendations, when appropriate.

Would dry skin and hair loss be caused by a low-fat eating pattern?

No, not likely. To date, only hospitalized patients receiving liquid diets for long periods of time (more than 6 mos.) have reported these symptoms. Symptoms, such as dry skin, are often the result of other factors, for example, from changes in the environment, such as weather, air conditioning, and heating. Changes in detergents, bath products, and cosmetics can also cause dryness to occur. Even new medications, a lack of water intake, and stress can create similar results. In addition, dry skin and hair loss are more likely to occur as a woman ages and goes through menopause. If you have questions about your low-fat food choices, talk with your nutritionist about the variety and balance in your own eating pattern.

Do changes in my fingernails, such as vertical ridges or brittleness, indicate that I am deficient in fat or some other nutrient?

Probably not. In 99 out of 100 cases, vertical ridges occur as a normal part of aging. The ridges develop as a result of changes over time in the nail matrix—the group of nail-producing cells that lie beneath the skin at the base of the fingernail. In addition, nails tend to become increasingly brittle with age.

I like to save my fat grams for red meats, desserts, and baked goods. Is this a problem?

Yes, this can be a problem. It's important to eat a mixture of animal and plant foods because each of these foods provide different types of fat. Saturated fats are mostly found in animal foods. Unsaturated fats (monounsaturated and polyunsaturated) are mostly found in plant foods and some seafoods.

Unsaturated fat provides some important nutrients that are not available in saturated fat. So, if most of your fat grams are saved for foods that contain a lot of saturated fat (e.g., red meats, high-fat baked goods, etc.), you may be missing foods that contain unsaturated fats (e.g., beans, whole grains, vegetable oils, nuts/seeds, etc.).

Consider rotating some of your higher-fat choices, such as meat and baked goods with fish, beans, and vegetable oils. The amounts you use do not have to be large, nor do they need to be eaten every day. The point is to get a healthy balance in your food choices.

What is the difference among the types of fats: saturated, monounsaturated, and polyunsaturated?

There are three main classes of fats found in foods: saturated, monounsaturated and polyunsaturated fats. Saturated fats are found in large proportions in animal-based foods, including whole milk, cream, cheese, butter, meat and poultry. They are also found in some plant-based foods, including coconut, palm and palm kernel oils, and in hydrogenated oils. Saturated fat is generally more solid than other types of fats at room temperature.

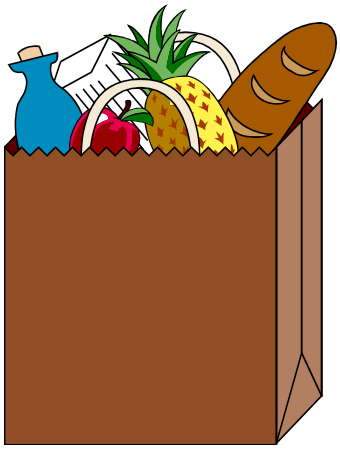
Monounsaturated fat is found in foods from both plants and animals. Olive, canola, and peanut oil all have large proportions of monounsaturated fat. Polyunsaturated fat is found in large proportions in many foods from plants, including corn, soybean, and safflower oils, walnuts and sunflower seeds. Some varieties of fish also contain polyunsaturated fat.

I hear that too much trans fatty acids are bad. What are they and where are they found?

Trans fats are unsaturated fatty acids formed when vegetable oils are processed and made more solid. This processing is done to promote freshness and better texture, and for product quality. These fats also occur naturally, mainly in meat and dairy products, which account for about one-fifth of the trans fats in our diets. Trans fats are also present in some processed foods that are made with hydrogenated vegetable oils.

Trans fats have been compared with saturated fats in terms of their effect on blood cholesterol levels. A few studies suggest that trans fats may raise LDL (bad) blood cholesterol much like saturated fat does. Other studies have indicated trans fats have lesser effects on total blood cholesterol than do saturated fats. Currently the Nutrition Facts panel on food products does not contain information about the amount of trans fats in the food.

Tips



- Reduce your use of highly saturated food sources (e.g., meat and high-fat dairy foods, such as cheese and ice cream) and commercially processed foods that contain 'hydrogenated' fats (higher in trans fats).
- Eat plenty of beans and green leafy vegetables.
- Eat fish at least once a week.
- Once or twice a week use one of the following ideas to obtain a better balance of unsaturated essential fats in your diet.
  - Garnish salads with 1-tablespoon of toasted sunflower seeds or walnuts.

    OR
  - Use small amounts of vegetable oil (1-2 tsp.) to sauté vegetables or other foods. (Canola™, olive, safflower, sunflower, or corn).

    OR
  - Use small amounts (1-2 tsp.) of low-fat salad dressings and/or low-fat mayonnaise instead of fat-free.

Figure E.16
Participant Certificate of Appreciation

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E.7 OS Participant Contact Materials

Figure E.6.1
Model Contact Letter for Women Ineligible for CT Between Screening Visits

WOMEN'S HEALTH INITIATIVE
[CLINIC NAME AND ADDRESS]

[Date]

[Participant's Name and Address]

Dear [Participant Name]:

Thank you for your interest in taking part in the Women's Health Initiative, a study sponsored by the National Institutes of Health. We have reviewed the forms and results of the tests you recently completed during your visit to our Clinical Center. Based on these results, we would like to invite you to join the health tracking or "Observational" part of the study. The purpose of the Observational Study is to learn more about women's health in general and about the causes of disease in women. The information we collect will be used to study the relation between lifestyle factors and disease, and may also be used in related research by other scientists interested in women's health. We plan to enroll a total of 100,000 women from all over the U.S. into the study. We want the results of this study to represent all women, so your participation is very important to us!

Here is what we would like you to do:

1) Please read "Welcome to the Observational Study of the Women's Health Initiative" (enclosed) to learn more about the study.

2) Please read the "Consent Form for the Observational Study Part of the Women's Health Initiative (WHI) Study" (enclosed). We have sent you two copies: one for your records and one to return to us. If you decide to take part in the Observational Study, sign both copies of the consent form.

3) Then, complete the enclosed health questionnaires as soon as possible. We have included a sheet describing all of the questionnaires for the Observational Study and have circled the ones we've included here. It is very important that you use the enclosed pencil to complete the questionnaires, so that our machines can read your answers.

4) Finally, return one copy of the consent form and the health questionnaires in the postage-paid envelope. That's all you need to do for now.

Each year for the next 8-12 years you will receive a packet of health questionnaires to complete and mail back to the Clinical Center. You will also receive a copy of the WHI newsletter that will help keep you informed about the progress of the study. Once you have decided to join, we would like you stay with the

study until it is over. It is very important that we have complete follow-up information on all participants to make sure that the results of the WHI are accurate and scientific.

Participation in this study is voluntary and you may refuse to answer any question on the questionnaires. The information you provide will be kept confidential and your name will not be linked with data given to anyone other than the researchers of this study. This study is authorized under Privacy Act 42 USC 241. If you have any questions about the consent form or the health questionnaires, or need any help in filling out the questionnaires, please call _____ at _____. During the next 8-12 years, we need to know where to send your newsletter and health updates, so it is also important that you call the Clinical Center if you move to a different address.

We appreciate your interest in the Women's Health Initiative. As a small "thank you," we have included a WHI magnet with the WHI clinic's phone number and some pamphlets about ways to improve your health. This is the first study designed to examine the health of a large number of women over a long period of time. By being a part of this project, you will help provide information that may improve the health of women for generations to come. We hope you'll join us.

Enclosures ***(suggested order)***:

- Welcome to the Observational Study
- OS Consent Forms (2)
- Questionnaire Description
- Health Questionnaires
- Health Pamphlets
- WHI Magnet
- Pencil
- Return Envelope

Figure E.6.2
Model Follow-Up Thank You/Reminder Postcard

Sent at one week post-mailing or post-clinic visit to all women given OS questionnaires to return.

[Date]

Last week a packet of questionnaires was mailed to you from the Women's Health Initiative. If you have already completed and returned the questionnaires to us, thank you very much for your quick response. If not, could you return them right away? We cannot officially enroll you in the study until we have received all of your forms. It is very important that we have complete information on all participants, so that the results of the Women's Health Initiative accurately represent the health of U.S. women.

If you did not receive the questionnaires, or if they have been misplaced, please call me collect today and we will mail you another set right away.

Sincerely,

[WHI logo]

[signature]
[typed name]
Clinic Manager *(or other signee)*
(*xxx-xxx-xxxx*)

Figure E.6.3
Model Contact Letter for Women Screened Before September 1, 1994

WOMEN'S HEALTH INITIATIVE
[CLINIC NAME AND ADDRESS]

[Date]

[Participant's Name and Address]

Dear [Participant Name]:

Thank you for your interest in taking part in the Women's Health Initiative, a study sponsored by the National Institutes of Health. We have reviewed the forms and results of the tests you completed several months ago during your visit to our Clinical Center. Your results indicated that you were not eligible or did not choose to join the parts of the study going on at that time. Since that time, we have started the health tracking or "Observational" part of the study, and would like to invite you to join. The purpose of the Observational Study is to learn more about women's health in general and about the causes of disease in women. The information we collect will be used to study the relation between lifestyle factors and disease, and may also be used in related research by other scientists interested in women's health. We plan to enroll a total of 100,000 women from all over the U.S. in this part of the study. We want the results to represent all women, so your participation is very important to us!

Here is what we would like you to do:

1) Please read "Welcome to the Observational Study of the Women's Health Initiative" (enclosed) to learn more about the study.

2) Please read the "Consent Form for the Observational Study Part of the Women's Health Initiative (WHI) Study" (enclosed). We have sent you two copies: one for your records and one to return to us. If you decide to take part in the Observational Study, sign both copies of the consent form.

3) Then, complete the enclosed health questionnaires as soon as possible. We have included a sheet describing all of the questionnaires filled out by women in the Observational Study and have circled the ones we've included here. It is very important that you use the enclosed pencil to complete the questionnaires, so that our machines can read your answers.

4) In addition to filling out the new questionnaires, please review the questionnaires you have already completed and update them if any changes have occurred since you filled them out. Use the enclosed red pen to mark these changes in the margins next to your previous answers.

5) Finally, return one copy of the consent form and all of the health questionnaires in the postage-paid envelope. That's all you need to do for now.

Each year for the next 8-12 years you will receive a packet of health updates to complete and mail back to the Clinical Center. You will also receive a copy of the WHI newsletter that will help keep you informed

about the progress of the study. Once you have decided to join, we would like you stay with the study until it is over. It is very important that we have complete follow-up information on all participants to make sure that the results of the WHI are accurate and scientific.

Participation in this study is voluntary and you may refuse to answer any question on the questionnaires if you choose. The information you provide will be kept confidential and your name will not be linked with data given to anyone other than the researchers of this study. This study is authorized under Privacy Act 42 USC 241. If you have any questions about the consent form or the health questionnaires, or need any help in filling out the questionnaires, please call _____ at _____. During the next 8-12 years, we need to know where to send your newsletter and updates, so it is also important that you call the Clinical Center if you move to a different address.

We appreciate your interest in the Women's Health Initiative. As a small "thank you," we have included a WHI magnet with the WHI clinic's phone number and some pamphlets about ways to improve your health. This is the first study designed to examine the health of a large number of women over a long period of time. By being a part of this project, you will help provide information that may improve the health of women for generations to come. We hope you'll join us.

Enclosures ***(suggested order)***:

- Welcome to the Observational Study
- OS Consent Forms (2)
- Questionnaire Description
- Health Questionnaires already completed
- New Health Questionnaires
- Health Pamphlets
- WHI Magnet
- Pencil
- Red Pen
- Return Envelope

Figure E.6.4
List of Questionnaire Descriptions for Inclusion with OS Contact Letters

The following is a list and brief description of each of the forms and questionnaires that you are asked to fill out as a participant in the Observational Study.

- **OS Consent Form:** This form contains a description of the Observational Study and explains the benefits and risks. By signing this form, you are agreeing to participate in the study.
- **Form 20 - Personal Information:** This form asks for information about where you can be contacted, personal information such as your age, education, and occupation, and health information, such as the name of your health care provider.
- **Form 30 - Medical History:** This form requests information about your history of hospitalization and medical conditions.
- **Form 31 - Reproductive History:** This form requests information about your pregnancies, menstrual periods, and menopause.
- **Form 32 - Family History:** This form contains questions about members of your family and diseases that your relatives may have had.
- **Form 34 - Personal Habits:** This form asks questions about your health habits, such as smoking, alcohol use, and exercise.
- **Form 37 - Your Thoughts and Feelings:** This form asks about your social relationships and quality of life.
- **Form 42 - OS Questionnaire:** This form includes questions about your habits and lifestyle, such as work history.
- **Form 60 - Food Frequency Questionnaire:** This form asks for information about the foods you usually eat.

E.8 Close-out Materials

Figure E.7.1
Model Close-out Visit Appointment Reminder Letter

Dear _____:

Congratulations! Your **final** WHI clinic visit is scheduled at _____ on _____. It's hard to believe we have come so far together! We are so proud and thankful that we've been able to reach this milestone with you. We hope to make this visit a special celebration of your commitment to the WHI, while we continue to collect your important health information.

This is an important visit, so please allow at least 90 minutes for us to:

- **Collect all WHI study pills.** If you are in either the Hormone or Calcium Vitamin D (CaD) Programs and still have study pills or pill bottles, please bring them to this visit.
- **Review your WHI health forms.** Please complete the health forms included in this packet: a *Medical History Update, Thoughts and Feelings* form, and for some participants, an *Estrogen-Alone Survey*.
- **Tell you if you were assigned to active calcium and vitamin D or placebo study pills. If you are in the CaD Program,** this visit ends the study's intervention phase, so your study pill information will be available. We can also give you a letter with this information for your health care provider.
- **Provide you with current WHI results and general health recommendations.** The WHI has developed a special thank-you packet of information.
- **Talk with you about the WHI Extension Study.** We are now approved to collect health information by mail from WHI participants through 2010! For this extension study, you do not need to come into the clinic. We hope you will read the enclosed "WHI Extension Study Consent Form" and consider joining. We will have more details about this new opportunity and can answer any questions at your upcoming visit.
- **Talk with you about your stored WHI blood samples.** We are asking your permission to share these samples with non-WHI scientists who have the ability to make significant scientific advances in women's health. Please read the enclosed "Supplemental Consent Form" and let us know at your upcoming visit if you have any questions.
- **Finally, we want to celebrate with you the many contributions you have made over the years to the WHI and women's health!**

Close-out visit appt reminder.doc 8/1/04

CHECKLIST FOR YOUR FINAL WHI VISIT

Your final WHI visit is an exciting transition for all of us, so it is a little different from visits you have had in the past. You will not be having tests like an electrocardiogram (ECG) or your weight and height measured, but there are some other important activities to complete. The checklist below will help you remember what to bring to this final WHI visit.

This is truly a wonderful, but sad time for us all--we are so happy and thankful you have shared so much of your life with the WHI, but we will miss your visits in the future!

The appointment for your final WHI clinic visit is:

_____

Please remember to bring the following to your appointment:

- □ Your WHI study pill bottles and any unused pills
- □ *Form 33 - Medical History Update*
- □ *Form 37 – Thoughts and Feelings*
- □ *Form 21 – Personal Information Update*
- □ *Form 55 – Estrogen-Alone Survey* (your packet will include this form only if you were still taking study pills in the Estrogen-Alone study when it was stopped in March 2004)
- □ WHI Extension Study Consent Form
- □ Supplemental Consent Form

Please call us if there are any questions or problems with your appointment time. We look forward to seeing you!

Close-out visit appt reminder.doc 8/1/04

Figure E.7.2
Model Cover Letter – Extension Study Consent (Non-HT)

The WHI Extension Study

As a Very Important Participant in the Women's Health Initiative, we are pleased to invite you to join the **WHI Extension Study**. This new study is designed to update WHI participants' health information for five more years after the "close-out" contact. The WHI Extension Study will help us learn more about how women's health changes as they get older. Health care providers and women alike need this information for the important health decisions they will make in the future.

Women from all the WHI programs – Hormone, Dietary, Calcium/Vitamin D, and Observational Study – are being invited to join the WHI Extension Study. We expect over 100,000 current WHI participants from across the United States to continue in the WHI.

If you decide to join the WHI Extension Study:

- We will ask you to fill out health forms by mail once a year through 2010. These forms will be like the medical history updates you have completed in the past. They will be sent to you with a postage-paid reply envelope.
- We may ask you to sign a Medical Release form to get more medical details about health changes that you report on the forms.
- We will not ask you to come into the WHI clinic for extension study activities. If we have questions after receiving your forms, we will contact you by telephone.

Attached are two copies of the consent form for the WHI Extension Study. Please read the form carefully and write down any questions you might have. When you come to the clinic for your close-out visit, bring the form and your questions with you. A WHI staff person will tell you more about this new study and answer your questions. Finally, we will ask you to sign the consent form, if you are willing to join the WHI Extension Study.

We appreciate all of the time and effort you have shared with us over the years and hope you decide to continue with the Women's Health Initiative. You have given so much to the cause of women's health, and we hope you will be a part of finding these new answers as well.

Thank you for participating in the Women's Health Initiative. You are making a difference in women's health!

Cover Letter – CT Pre-visit (non HT) Extension Study Consent.doc 8/1/04

Figure E.7.3
Model Extension Study Consent – (Non-HT)

CONSENT FORM TO PARTICIPATE IN THE

WOMEN'S HEALTH INITIATIVE EXTENSION STUDY

WHI Clinical Coordinating Center
The Fred Hutchinson Cancer Research Center
Seattle, Washington

[*Clinical Center*]

[*Principal Investigator*]

[*Other Investigators, as appropriate*]

[*24-Hour Contact*]

This form is to tell you about the Women's Health Initiative (WHI) Extension Study. You are invited to join the WHI Extension Study because you were a participant in either the WHI Clinical Trial or the WHI Observational Study. The WHI Extension Study will extend your participation in the WHI study through 2010. All participants in the WHI Diet Modification, Hormone Program, and Calcium and Vitamin D Clinical Trials, regardless of their treatment assignments to control or placebo or active interventions, and those in the WHI Observational Study are invited to participate in the WHI Extension Study. We expect up to 150,000 participants across the United States to join and continue to contribute important information to women's health.

Purpose of the WHI Extension Study

The main purpose of the WHI Extension Study is to continue to learn about the health of postmenopausal women over an additional five years of follow-up. We hope to learn more about risks for heart disease, stroke, blood clots, breast cancer, colon cancer, other cancers, and osteoporotic fractures (broken bones), as well as quality of life. For women who were in the WHI Clinical Trials, we hope to learn if the risks or benefits for these health conditions continue or disappear after women have stopped taking their WHI study pills, are no longer in contact with the study nutritionists, or are continuing to follow their usual diet. We also hope to learn if these changes are different for women who were originally assigned to take active or placebo study pills or were in the Dietary Change or Comparison group. For women in the Clinical Trials and the Observational Study, we expect that five additional years of follow-up will help us to learn more about both common and more rare diseases of aging.

Reasons for the WHI Extension Study

Results from the WHI Clinical Trials and Observational Study have given health care providers important information about the effects of diet, hormones, and calcium/vitamin D supplements and initial health characteristics, including family and medical history and lifestyle factors, such as activity levels, on diseases of aging in postmenopausal women. As more and more women are

re-evaluating their diet, use of hormone therapy, and other factors, it is important to understand how maintaining or changing these factors affects disease over time. These questions have been asked by health care providers and the millions of women who are moving into the next decade of their lives. The WHI Extension Study can find answers by comparing changes in health status over the course of the initial WHI study period with those in the five-year follow-up period.

What Will You Be Doing?

If you decide to join the WHI Extension study, you will be asked to fill out health forms each year. You will not be asked to come into the WHI Clinical Center for these activities. The health forms will be similar to the medical history updates you were asked to complete regularly while you were in the WHI Clinical Trial or Observational Study. For the Extension Study, you will only be asked to complete the forms once a year through 2010. The form will be mailed to you, with a pre-paid mailing envelope, and you will be asked to return your completed form by mail. If the WHI staff has any questions after receiving your forms, they will contact you by telephone. We may also ask you to sign a Medical Release form to get more detailed information about health issues that you report on the form.

The amount of time asked of you to participate in the WHI Extension Study will be:

Activity	Total Time
• Completing health forms	About 30 minutes each year through 2010

Benefits and Risks

We cannot and do not guarantee or promise that you will receive any personal benefits from this study; however, there is also little risk. By taking part in the Extension Study, you will help advance scientific knowledge about postmenopausal women's health.

There are no risks to completing the health update forms for this study.

Costs

You will not be paid for being in the study. The WHI has not set aside funds to pay for any health conditions that you may develop, and will not pay for any health problems or conditions that might occur during the course of this study. These might be covered by your usual insurance, Medicare or Medicaid. You will not be paid back for any wages lost from taking part in this study. If you have questions about your costs, financial responsibilities, and/or medical insurance coverage for this activity, please contact [*CC financial office or other budgetary person and institutional department*] at [*phone number*].

Confidentiality

All of your study records will be kept confidential to the extent required by law. Your personal identity will not be revealed in any publication or release of results. Only WHI staff at the [*Name*] Clinical Center and the Clinical Coordinating Center at the Fred Hutchinson Cancer Research Center in Seattle, Washington, will have access to your study number, name, social security number and address for the purpose of study wide mailings, as well as maintaining and updating your study records. The Food and Drug Administration may be allowed to examine

your study records for safety reasons. Study records will be kept indefinitely for analysis and follow-up. This study is authorized by Privacy Act 42 United States Code 241.

You have the right to limit the use and sharing of your health information, and you have the right to see your medical records and know who else is seeing them. Everyone involved in this study respects your privacy. Any and all information about you obtained for this research study will be kept confidential and will not be released for any reason without your written permission unless compelled by law. In addition:

- staff are trained to protect your privacy and sign an agreement to do so;
- paper records are stored in locked files;
- computer records are password protected;
- your name or other personal information will not be included with any data shared with anyone who is not part of the WHI Study Research Staff.

USE AND DISCLOSURE OF YOUR MEDICAL INFORMATION

By signing this consent form, you are authorizing the use and disclosure of your health information collected in connection with your participation in this research study. Your information will only be used as we have described in this consent form and any applicable laws. If you decide to stop participating in the study, you may revoke your authorization, except to the extent that the law allows us to continue using your information.

What Information Will Be Used or Disclosed?

Health information related to this study may include, but is not limited to: demographic information, the results of physical exams, blood tests and related records, x-rays, and other diagnostic and medical procedures. This information may be used or disclosed in connection with this research study. We may request from your physician a copy of your medical record related to your diagnosis and treatment of cancer or other diseases if we have obtained from you a signed Medical Release form.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The [*CC*] WHI Research Staff
- The [*CC*] Administrative Panel on Human Subjects in Medical Research or Institutional Review Board (IRB) and any other unit of the [*CC*], as necessary
- The WHI Clinical Coordinating Center Staff at the Fred Hutchinson Cancer Research Center in Seattle, Washington

- The Institutional Review Board at the Fred Hutchinson Cancer Research Center

Who May Receive / Use the Information?
The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The Food and Drug Administration (FDA)

Your information may be redisclosed if the recipients described above are not required by law to protect the privacy of the information.

Expiration
Your authorization for the use and disclosure of your health information will continue indefinitely.

Right to Withdraw

Your decision to be in the study is voluntary. You may quit at any time, for any reason, without notice. We hope that you will take part for the entire time of the study because we need all of this information to draw correct conclusions. If you decide to leave the study, it will not affect your regular medical care.

Other Information

Your joining is important to the success of this study. You may join the WHI Extension Study whether or not you were in the active or placebo group of the WHI Hormone or Calcium and Vitamin D Clinical Trials, in the Dietary Change or Comparison group, or in the WHI Observational Study. You may also join even if you have started taking hormones prescribed by your health care provider or have made any changes to your diet or use of calcium supplements. We have tried to make joining the study as easy as possible for you. Please let us know if there are ways you think it would be easier for you to join this study.

At the beginning of this study, the WHI staff will ask for your permission to contact your spouse, close relative, or friend for updated information about your health in case you are unable to complete the health update forms. If you move, and we are not able to find you, we may try to locate you through nationally available records, such as social security. If you choose not to join the WHI Extension Study, it will not affect your personal medical care or your medical insurance coverage. The study does not replace your usual medical care.

Voluntary Consent

If you have any questions about any part of the study or your rights as a volunteer, a WHI staff person will answer them before you sign this consent form. Also, if you are not satisfied with the manner in which this study is being conducted, or if you have any questions about your rights as a study participant, please call [*IRB Official's Name*] in the Institutional Review Board Office of [*Clinical*

Center's Institution] at [*phone number*]. If you have any questions at any time, you may call: [*Clinical Center name and phone number*] or any of the investigators listed at the beginning of this form. Before you sign this form, please ask any questions on any part of this study that is not clear to you.

Investigator's Statement

I have provided an explanation of the above research program. The participant was given an opportunity to discuss the procedures, including risks, and to ask any additional questions. A signed and dated copy of the consent form has been given to the participant.

_____ _____

Signature of Principal Investigator or Designee Date

PARTICIPANT'S STATEMENT

I certify that I have read, or had read to me the description of the WHI Extension Study. I understand this information and voluntarily consent to join. I understand that I may quit the study at any time. I have had a chance to ask questions about the study and my participation and about the need for access to my medical records. They have been answered to my satisfaction. I understand that future questions I may have about the research will be answered by one of the investigators listed above and that any questions I have about my rights as a research subject will be answered by the person identified above. I acknowledge that I will receive a signed copy of this consent form for my records.

_____ _____

Signature of Participant Date

_____ _____

Signature of Witness Date

Figure E.7.4
Model Cover Letter – Extension Study Consent (HT)

The WHI Extension Study

As a Very Important Participant in the Women's Health Initiative, we are pleased to invite you to join the **WHI Extension Study**. This new study is designed to update WHI participants' health information for five more years after the "close-out" contact. The WHI Extension Study will help us learn more about how women's health changes as they get older. Health care providers and women need this information for the important health decisions they will make in the future.

Women from all the WHI programs – Hormone, Dietary, Calcium/Vitamin D, and Observational Study – are being invited to join the WHI Extension Study. We expect over 100,000 WHI current participants from across the United States to continue in the WHI.

If you decide to join the WHI Extension Study:

- We will ask you to fill out health forms by mail once a year through 2010. These forms will be like the medical history updates you have completed in the past. They will be sent to you with a postage-paid reply envelope.
- We may ask you to sign a Medical Release form to get more medical details about health changes that you report on the forms.
- We will ask you to have a mammogram each year for the next two years and to give us permission to review the report.
- We will not ask you to come into the WHI clinic for extension study activities. If we have questions after receiving your forms, we will contact you by telephone.

Attached are two copies of the consent form for the WHI Extension Study. Please read the form carefully and write down any questions you might have. When you come to the clinic for your close-out visit, bring the form and your questions with you. A WHI staff person will tell you more about this new study and answer your questions. Finally, we will ask you to sign the consent form, if you are willing to join the WHI Extension Study.

We appreciate all of the time and effort you have shared over the years and hope you decide to continue with the Women's Health Initiative. You have given so much to the cause of women's health, and we hope you will be a part of finding these new answers as well.

Thank you for participating in the Women's Health Initiative. You are making a difference in women's health!

Cover letter – CT Pre-visit (HT) Extension Study Consent.doc 8/1/04

Figure E.7.5
Model Extension Study Consent (HT)

CONSENT FORM TO PARTICIPATE IN THE WOMEN'S HEALTH INITIATIVE HORMONE PROGRAM EXTENSION STUDY

WHI Clinical Coordinating Center
The Fred Hutchinson Cancer Research Center
Seattle, Washington

[*Clinical Center*]

[*Principal Investigator*]

[*Other Investigators, as appropriate*]

[*24-Hour Contact*]

This form is to tell you about the Women's Health Initiative (WHI) Hormone Program Extension Study. You are invited to join the WHI Hormone Program Extension Study because you were a participant in either the WHI Estrogen plus Progestin Trial or the WHI Estrogen-Alone Trial. The WHI Hormone Program Extension Study will extend your participation in the WHI study through 2010. All participants in the WHI Hormone Clinical Trials—those who were in the active hormones and in the placebo groups—may join this research study. We expect thousands of Hormone Program participants across the United States to join and continue to contribute important information to women's health.

Purpose of the Hormone Program Extension Study

The main purpose of the WHI Hormone Program Extension Study is to continue to learn about the health of women after they have stopped the WHI Hormone Clinical Trials study pills. We hope to learn whether hormone-related health risks and benefits for heart disease, stroke, blood clots, breast cancer, colon cancer, other cancers, and osteoporotic fractures (broken bones), as well as quality of life, change after women have stopped taking the WHI study pills. We also hope to learn whether these changes are different for women who were originally assigned to take active hormone pills and those assigned to take placebo pills. This study will help us to find out if the risks and benefits related to hormone pills continue or disappear over time.

Reasons for the Hormone Program Extension Study

Results from the WHI Hormone Clinical Trials have given health care providers important information about the effects of hormones on diseases of aging in postmenopausal women. As more and more women are re-evaluating their use of hormone therapy, it is important to understand how stopping hormones changes these hormone-related effects on disease over time. This question has been asked by health care providers and the millions of women who were taking and continue to take estrogen pills, with or without progestins. The WHI Hormone Extension Program can find answers to the question by comparing the health changes in women who stopped taking hormone study pills with changes in women who stopped taking placebo pills.

What Will You Be Doing?

If you decide to join the WHI Hormone Program Extension study, you will be asked to fill out annual health forms during the next five years and to have annual mammograms during the first two years. You will not be asked to come into the WHI Clinical Center for these activities. The health forms will be similar to the medical history and hormone use updates you were asked to complete every 6 months while you were in the WHI Hormone Clinical Trial. However, for this Extension Study, you will only be asked to complete the forms once a year through 2010. The forms will be mailed to you, with a pre-paid mailing envelope, and you will be asked to return your completed form by mail. If the WHI staff has any questions after receiving your forms, they will contact you by telephone. We may also ask you to sign a Medical Release form to get more detailed information about health issues that you report on the form. During the first two years, the WHI staff will also remind you to have an annual mammogram and will ask your permission to obtain a copy of the mammogram report, just as when you were in the Hormone Clinical Trial.

The amount of time asked of you to participate in the Hormone Program Extension Study will be:

Activity	Total Time
• Completing health forms	About 30 minutes each year through 2010
• Releasing a copy of your annual mammogram report to the WHI staff	Less than 15 minutes each year during the first two years

Benefits and Risks

We cannot and do not guarantee or promise that you will receive any personal benefits from this study; however, there is also little risk. You may find that the yearly mammogram report requested by the WHI staff helps you remember to have this important breast cancer screening test that is recommended by many health care providers. By taking part in the Hormone Program Extension Study, you will help advance scientific knowledge about postmenopausal women's health. Specifically, you will help scientists learn about health changes after participants stop their study pills in the WHI Hormone Clinical Trial.

There are no risks to completing the health update forms for this study. The annual mammogram that you are asked to obtain during the first two years does use radiation, which may slightly increase the risk of developing breast cancer. Scientists of the WHI and the National Cancer Institute believe that this small risk is outweighed by the benefit of finding breast cancer early in women. Mammograms are recommended for all women in your age group every 1-2 years.

Costs

The procedures that are a part of this study will cost only your time and travel to obtain an annual screening mammogram during the first two years. You will bill your insurance company, Medicare, or Medicaid for the cost for these screening mammograms as usual. If you do not have sources to pay for these screening mammograms during the first two years, the study will pay these costs. However, additional diagnostic studies will not be covered by the study. The WHI has not set aside funds to pay

for any health conditions that you may develop, and will not pay for any health problems or conditions that might occur during the course of this study. These

might be covered by your usual insurance, Medicare or Medicaid. You will not be paid back for any wages lost from taking part in this study. You will not be paid for being in the study. If you have questions about your costs, financial responsibilities, and/or medical insurance coverage for this activity, please contact [*CC financial office or other budgetary person and institutional department*] at [*phone number*].

Confidentiality

All of your study records will be kept confidential to the extent required by law. Your personal identity will not be revealed in any publication or release of results. Only WHI staff at the [*Name*] Clinical Center and the Clinical Coordinating Center at the Fred Hutchinson Cancer Research Center in Seattle, Washington, will have access to your study number, name, social security number and address for the purpose of study wide mailings, as well as maintaining and updating your study records. The Food and Drug Administration may be allowed to examine your study records for safety reasons. Study records will be kept indefinitely for analysis and follow-up. This study is authorized by Privacy Act 42 United States Code 241.

ACCESS TO YOUR INFORMATION

You have the right to limit the use and sharing of your health information, and you have the right to see your medical records and know who else is seeing them. Everyone involved in this study respects your privacy. Any and all information about you obtained for this research study will be kept confidential and will not be released for any reason without your written permission unless compelled by law. In addition:

- staff are trained to protect your privacy and sign an agreement to do so;
- paper records are stored in locked files;
- computer records are password protected;
- your name or other personal information will not be included with any data shared with anyone who is not part of the WHI Study Research Staff.

USE AND DISCLOSURE OF YOUR MEDICAL INFORMATION

By signing this consent form, you are authorizing the use and disclosure of your health information collected in connection with your participation in this research study. Your information will only be used as we have described in this consent form and any applicable laws. If you decide to stop participating in the study, you may revoke your authorization, except to the extent that the law allows us to continue using your information.

What Information Will Be Used or Disclosed?

Health information related to this study may include, but is not limited to: demographic information, the results of physical exams, blood tests and related records, x-rays, and other diagnostic and medical procedures. This information may be used or disclosed in connection with this research study. We may request from your physician a copy of your medical record related to your diagnosis and treatment of cancer or other diseases if we have obtained from you a signed Medical Release form.

Who May Use or Disclose the Information?
The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The [*CC*] WHI Research Staff
- The [*CC*] Administrative Panel on Human Subjects in Medical Research or Institutional Review Board (IRB) and any other unit of the [*CC*], as necessary
- The WHI Clinical Coordinating Center Staff at the Fred Hutchinson Cancer Research Center in Seattle, Washington
- The Institutional Review Board at the Fred Hutchinson Cancer Research Center

Who May Receive / Use the Information?
The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The Food and Drug Administration (FDA)

Your information may be redisclosed if the recipients described above are not required by law to protect the privacy of the information.

Expiration
Your authorization for the use and disclosure of your health information will continue indefinitely.

Right to Withdraw

Your decision to be in the study is voluntary. You may quit at any time, for any reason, without notice. We hope that you will take part for the entire time of the study because we need all of this information to draw correct conclusions. If you decide to leave the study, it will not affect your regular medical care.

Other Information

Your joining is important to the success of this study. You may join the WHI Hormone Program Extension Study whether or not you were in the active hormone or placebo group of the WHI Hormone Clinical Trials. You may also join even if you have started taking hormones prescribed by your health care provider. Unless many volunteers like you agree to join, this study will not be successful in meeting its goal of finding out the long-term health risks and benefits of recent hormone use. We have tried to make joining the study as easy as possible for you. Please let us know if there are ways you think it would be easier for you to join this study.

If your mammogram suggests a possible health problem, we will ask you to go back to your doctor or

clinic to evaluate the need for further tests. Copies of reports and hospital records of your doctor's follow-up may be requested by the WHI and become part of your WHI study record.

At the beginning of this study, the WHI staff will ask for your permission to contact your spouse, close relative, or friend for updated information about your health in case you are unable to

complete the health update forms. If you move, and we are not able to find you, we may try to locate you through nationally available records, such as social security. If you choose not to join the Hormone Program Extension Study, it will not affect your personal medical care or your medical insurance coverage. The study does not replace your usual medical care.

Voluntary Consent

If you have any questions about any part of the study or your rights as a volunteer, a WHI staff person will answer them before you sign this consent form. Also, if you are not satisfied with the manner in which this study is being conducted, or if you have any questions about your rights as a study participant, please call [*IRB Official's Name*] in the Institutional Review Board Office of [*Clinical Center's Institution*] at [*phone number*]. If you have any questions at any time, you may call: [*Clinical Center name and phone number*] or any of the investigators listed at the beginning of this form. Before you sign this form, please ask any questions on any part of this study that is not clear to you.

Investigator's Statement

I have provided an explanation of the above research program. The participant was given an opportunity to discuss the procedures, including risks, and to ask any additional questions. A signed and dated copy of the consent form has been given to the participant.

_____ _____

Signature of Principal Investigator or Designee Date

PARTICIPANT'S STATEMENT

I certify that I have read, or had read to me the description of the WHI Hormone Program Extension Study. I understand this information and voluntarily consent to join. I understand that I may quit the study at any time. I have had a chance to ask questions about the study and my participation and about the need for access to my medical records. They have been answered to my satisfaction. I understand that future questions I may have about the research will be answered by one of the investigators listed above and that any questions I have about my rights as a research subject will be answered by the person identified above. I acknowledge that I will receive a signed copy of this consent form for my records.

_____ _____

Signature of Participant Date

_____ _____

Signature of Witness Date

Figure E.7.6
Model Cover Letter – Supplemental Consent

The WHI Supplemental Consent for Use of Stored Specimens

Recently, there have been important breakthroughs in health care because women like you have been a part of the WHI and provided valuable information for answering questions about women's health. The blood samples you have provided are also precious resources for women's health research. For example, WHI scientists are learning how proteins and DNA (the genetic building block of life) affect certain health conditions.

Since you joined the WHI, medical science and technology have grown in ways we never thought possible. Some of the new techniques for analyzing blood are so specialized or expensive that they can only be done by scientists at a select few private non-profit or for-profit research centers or companies. We would like to partner with these non-WHI scientists in the hopes that there will be even more breakthroughs in women's health. The blood samples and DNA you have provided in the past are an important link in that partnership, and we are asking your permission to share them with other scientists. Your gifts to women's health research can then go even further.

The attached consent form explains the ways we are planning to use WHI blood samples and DNA. Please keep the following in mind as you read the form:

- Your blood samples will be shared with non-WHI scientists only if you sign the consent.
- We are not asking for more blood, only to share stored samples you have already given.
- Your personal identity will always be kept confidential, away from the samples, and it will never be shared with other scientists, private companies, your doctor, or your insurance company.
- Neither you nor the WHI will profit from studies that use your blood samples.
- There are no costs to you or your insurance for any of the blood or DNA studies.
- You may withdraw your consent to share these samples at any time, and it will not affect your participation in other parts of the WHI.
- You will not be given individual results of any blood or DNA studies.

Please read the consent form carefully and write down any questions you might have. When you come to the clinic for your final visit, bring the form and your questions with you. A WHI staff person will go over supplemental use of blood and answer your questions. Finally, we will ask you if you want to sign the consent and agree to this supplemental use of your stored blood samples.

Thank you for being a part of the Women's Health Initiative and its legacy of health for generations of women to come!

Cover letter – CT Pre-visit Supplemental Consent.doc 8/1/04

E.7.7
Model Supplemental Consent

SUPPLEMENTAL CONSENT FOR USE OF STORED SPECIMENS BY RESEARCHERS AT PRIVATE OR NON-PROFIT ORGANIZATIONS

THE WOMEN'S HEALTH INITIATIVE (WHI)

[Clinical Center]
[CC Principal Investigator, Tel #]
[CC Study Coordinator, Tel #]

WHI Clinical Coordinating Center
Fred Hutchinson Cancer Research Center
Seattle, Washington
[CCC Principal Investigator, Tel #]
[CCC Study Coordinator, Tel #]

Study Sponsor: National Heart, Lung, and Blood Institute (NHLBI)

1. Introduction

When you joined the study, you and all participants in the Women's Health Initiative were asked to sign a consent allowing research on your stored blood samples by WHI researchers. That research includes studies of genetic (inherited or DNA) differences that may affect disease or disease outcome. Much has already been learned from this research, and the blood samples provided by WHI women continue to be a very valuable scientific resource. Because of its scientific value, research on the blood samples has been expanded so that even more can be learned.

Up until now, all research on your samples has been done by WHI researchers and their colleagues at academic institutions. Every use of your samples is reviewed by study committees, by the NHLBI, and by an independent Institutional Review Board (IRB). An IRB is a board of experts at the research institution that carefully reviews proposed studies to make sure they do not violate the rights or safety of study participants. When you joined the study, you signed a consent allowing use of your samples. **The use of your samples by WHI researchers can continue under your existing consent. However, you are free to withdraw your existing consent at any time.**

Since the time WHI started, there have been many advances in the ways in which DNA and proteins in the blood can be studied. These new ways are now beginning to be used for predicting risk of diseases such as cancer and heart disease. Some of these new ways of studying DNA and proteins can only be done by private or non-profit organizations, because they have some of the most advanced technologies. **We are asking your permission to allow your DNA and blood samples to be shared with researchers at private (including for-profit companies) or non-profit organizations when that is the best way to advance scientific knowledge and public health. This consent would supplement (be in addition to) your existing consent for use of your samples by WHI researchers.**

2. Purpose of genetic and blood studies

Genetic (inheritance or DNA) studies look at DNA in blood cells to find genes that may cause or protect people from the health conditions affecting older women, e.g., heart disease, stroke,

dementia, blood clots, cancers, fractures, and diabetes. Also, new ways of studying proteins in the blood are being developed to find patterns linked to health conditions in older women. Other health conditions affecting women, beyond those currently considered in WHI, may be studied in the future as we gain new knowledge.

3. What am I being asked to do?

You are being asked to allow your genetic and blood samples to be shared with researchers at private or non-profit organizations. Your samples have already been collected and stored, so you will not be asked to give new blood or tissue samples. From the samples you have already provided, your white blood cells were obtained and frozen. The white blood cells are not alive and cannot be reproduced. In genetic studies, DNA is extracted from the white blood cells and differences in health conditions are examined. In the future, the DNA samples may be copied to produce DNA samples for the types of studies discussed above. Your DNA cannot be used for cloning.

If you agree, researchers at WHI or NHLBI may work with scientists in private for-profit and non-profit organizations in the future. There is value in bringing together scientists at WHI and NHLBI with other scientists who have special knowledge or skills. We believe working together makes the best possible use of the samples you have given. Working with scientists at private for-profit or non-profit organizations may lead to the development of new tests to diagnose or predict disease. It may also lead to the development of new medicines. The scientists from outside organizations will be given the blood or DNA only after the NHLBI and the Institutional Review Board have carefully reviewed their research proposals, and only after your name and all identifying information have been removed.
All results in the WHI will be kept confidential and no results of genetic or blood studies done on your samples will be provided to you, your family, or your doctor. You will not be able to retrieve your samples or information about them. The genetic studies done in this study are for research only. The results of research studies like WHI apply to groups as a whole and we will not know what they mean for your personal health.

Participation in a genetic study does not mean that you have had genetic testing. Genetic testing means having a specific type of test performed and the results provided to you and your doctor. If you are interested in having genetic testing performed, you should consult your healthcare provider.

5. Will I get anything from the sharing of my samples?

You will not benefit directly from these genetic and blood studies. These studies may, one day, result in new tests and treatments or may help to prevent or cure disease. Scientific knowledge often advances slowly, but it may benefit future generations. Neither you nor your heirs will benefit financially from studies of these samples. Neither your blood nor DNA will be sold to anyone. The WHI program and the NHLBI will not profit from these studies.

6. Will this cost me anything?

There are no costs to you or your insurance carrier for any of the blood or genetic research studies.

7. What will happen to my samples?

Blood, urine, genetic samples, tissue samples, and/or other materials taken from you will be considered donated by you to medical research and will be under the control of the NHLBI. The WHI Clinical Coordinating Center provides these samples to NHLBI without personal identifying information, such as your name, address, or Social Security number. The WHI or NHLBI may share your data and samples with other scientists who meet their requirements. All research on your samples will be done only by individuals and organizations that meet NHLBI standards and procedures. This means that research proposals will undergo careful review by WHI and NHLBI, or by an NHLBI review group, and by Institutional Review Boards. Organizations will be required to treat the data or samples as strictly confidential, and agree not to share data or samples with other parties.

Your blood and DNA samples will be stored at a central site listed under a code number. The samples will be stored for as long as they are useful for research. Your DNA may be copied, so that an unlimited supply can be available for future use without the need to obtain more blood from you.

By signing this consent form, your DNA and blood may be used by private for-profit or non-profit organizations for research. Researchers may only use the blood for the specifically approved purpose. They may not keep any leftover samples for other purposes. They must either return any unused remaining sample to NHLBI or dispose of the sample if so instructed by NHLBI.

8. How can I be assured that my results will be kept confidential?

All information collected during this research will be kept confidential and results will not be given to anyone without your permission, except as described below. Data may be given to other researchers for scientific purposes, but only after removing your name and all other personal identifiers. To ensure confidentiality, a study code number has been assigned to you. Samples provided to laboratories are labeled with a different code number. Only a small number of scientists and staff at the WHI Clinical Coordinating Center at the Fred Hutchinson Cancer Research Center will be able to link the study code number with the laboratory code number. The link will be kept in a secure location.

Your study records may be reviewed by authorized representatives from the National Heart, Lung, and Blood Institute (NHLBI), the Food and Drug Administration (FDA), the Office of Human Research Protection (OHRP), and the Institutional Review Boards in charge of protecting research participants at the WHI Clinical Coordinating Center and your WHI Clinical Center. By signing this consent form, you agree to this access to your records for the current study and any further research that may be conducted in relation to it (even if you withdraw from WHI). Because of the need at times to release information to the authorized groups listed above, absolute confidentiality cannot be guaranteed.

Any publication or presentation of the data will not identify you by name or any other means. Your information will be grouped with that of all other persons taking part in the WHI and will only be used for statistical analysis to further medical knowledge. When results of this study are published or presented at medical or research meetings, only group findings will be presented.

U.S. FEDERAL CERTIFICATE OF CONFIDENTIALITY

WHI has been granted a Certificate of Confidentiality from the United States Federal Government to make sure that we can best protect your confidentiality. This certificate means that WHI researchers

cannot be forced to tell anyone not connected with the study about your participation, without your written consent. The researchers will only release information if you request it.

9. What if I decide to withdraw my consent to share my samples with private or non-profit organizations?

Your agreement to share your samples is completely voluntary and you may withdraw your consent for the use of your blood samples and DNA at any time. This will not affect your participation in the other parts of WHI. If you decide later that you don't want your blood or DNA to be used for future research at private or non-profit organizations, you may notify any of the people listed at the top of this document. They will make every effort to stop any additional studies with your samples and to return your samples to WHI. However, in some cases where the samples have already been shared or your DNA has been copied, it may not be possible to stop ongoing studies.

10. What if I have questions about the study?

If you have any questions about the use of your samples, you may contact the study researchers listed above. If you have any questions about your rights as a research subject, you may contact (IRB, number).

I agree to the sharing of my DNA and blood samples with researchers at private or non-profit organizations. By signing this form, I confirm that I have read the preceding consent information (or it has been read to me) and that I understand the contents. I will be given a copy of this consent form to keep.

I understand that samples and information collected from me will be used for research purposes only. My name or other information that could identify my family or me will not be released.

My signature below means that I have VOLUNTARILY agreed to release my genetic (DNA) samples and blood, for research purposes, to researchers from private or non-profit organizations who wish to develop tests to diagnose medical conditions, medications, or therapies that could benefit many people. (Note: Neither you nor your heirs will benefit financially from this, and neither your DNA nor your blood will be sold to anyone for profit.)

I understand that by signing this form I am not waiving any legal rights I may have.

_____ _____

Participant's signature Date

_____

Printed name of participant

_____ _____

Signature of person obtaining consent Date

_____

Printed name of person obtaining consent

Figure E.7.8
Model Thank You Packet Cover Letter

Dear Valued WHI Participant,

Thank you for being part of the answer! You have been an important participant in the Women's Health Initiative (WHI), and all of the WHI staff and investigators want to congratulate you on your historic contribution to women's health.

This special packet celebrates your extraordinary commitment to the WHI and all that you have helped us achieve. It includes:

- A letter to you from your WHI Principal Investigator.
- A newsletter that describes the WHI history we've shared, our remarkable participants, and some of the many answers about women's health that you have helped us find.
- A handy chart showing the important health screenings that women should continue to have.
- An official and personalized WHI Certificate of Appreciation.
- A small WHI "thank-you" gift.
- Further information about your specific program(s) in the WHI.

What's next?
After the last WHI clinic visits have ended, some important data analyses will begin. The results of these analyses will be published in late 2005 or early 2006, at which time we'll send you a newsletter about the findings. For many years to come, we will be analyzing the data you have provided to the WHI, and even more answers about women's health will be published. We will keep an up-to-date list of these reports on the WHI participant website at *www.whi.org*. We hope you'll check this site often for the latest WHI news.

Your contribution to the WHI is like a priceless treasure—a gift of women's health that's being passed on to future generations of women. You can help us extend that legacy by continuing to tell us about your health through 2010. This longer-term information can help us learn even more about how women's health changes as they get older and how risk for disease changes when interventions, like those studied in the WHI Clinical Trials, come to an end. If you decide to join the "**WHI Extension Study,**" we will mail you health update forms each year for the next five years. You will not need to come to a WHI clinic for visits. Your WHI staff has more details for you about this new opportunity.

Years ago, when you joined the Women's Health Initiative, we asked you to "*be part of the answer.*" Now it's time to celebrate your achievement and to thank you for being part of the WHI!

Best wishes,
The WHI Staff and Scientists

Cover letter – CT Thank you packet.doc 8/1/04

Figure E.7.9
Model PI Thank You Letter

Dear *(participant name)*,

I want to thank you on behalf of all of the WHI investigators and staff for your important role in the Women's Health Initiative. The WHI is a major accomplishment for all of us, but we would not have been able to complete this important study without participants like you, who made it all possible.

The Women's Health Initiative is a historic achievement. In the beginning, some people doubted that women would join such a long study. Your involvement in the WHI proved that there are dedicated women willing to provide long-term support to a study of women's health. We have already answered many important questions about women's health, including the recent news about the health risks and benefits of hormone use after menopause and with your help, we will be able to answer many more.

Now that the WHI Clinical Trial interventions have ended, your WHI staff will not be providing study pills or dietary classes, but the WHI investigators will continue to analyze the data you have contributed over these many years. We plan on publishing many of the main WHI findings at the end of 2005 and the beginning of 2006.

Research findings often raise new questions, so the answers we find today will help us ask important new questions tomorrow. Because of your efforts and all of the health information you have provided, we will be able to continue to analyze data and answer even more questions in the future.

Thank you again for being part of the WHI. I hope that it has been a good experience for you; you can certainly feel proud of your contribution to women's health. I wish you the best of health and happiness in the future.

Warmest regards,

Xxxxxxxx
Principal Investigator, *xxxxx* Clinical Center

Cover Letter PI Thank you.doc 8/1/04

Figure E.7.10
Model Cover Letter for Mailed Consent Packet

Dear Valued WHI Participant,

Thank you for being part of the Women's Health Initiative (WHI)! The WHI was created to learn more about women's health and the causes of disease in women. The information provided by WHI participants like you over the years has already changed medical practice and will continue to help women for generations to come.

Enclosed in this packet are two separate WHI consent forms for you to look over:

1) **The WHI Extension Study** – Because of your contributions to women's health over the years, we are pleased to tell you that WHI scientists have received funding to extend the WHI until 2010 to collect health information by mail. The **WHI Extension Study Consent Form** includes more details about this new opportunity.
2) **The Supplemental Consent for Use of Stored Specimens** – Since you joined the WHI, there have been amazing advances in the ways blood specimens can be studied. More details about the ways we are planning to use WHI samples are in the enclosed Supplemental Consent Form.

Please read through the enclosed consent forms and follow the instructions on the cover sheet for each form. The consent forms should be kept separate when you make your decisions about signing. That is, you may agree to sign one, both, or neither of the forms – the decision is yours.

Whether or not you sign the consent forms, we'd like to hear from you. After you read the forms over and decide on your future WHI plans, please fill out the enclosed "WHI Consent Summary Worksheet". We would also like you to review the Personal Information Sheet in this packet and make any corrections right on the sheet. Then, return the Consent Worksheet, Information Sheet, and one copy of each consent form that you sign in the postage-paid reply envelope. The second copy of each consent form is for you to keep.

Thank you in advance for reviewing this information. We are very excited about these new opportunities and hope you will join us for the years ahead. If you have any questions about the WHI Extension Study or the Supplemental Consent, please call the WHI staff at **xxx-xxx-xxxx**.

Warmest regards,

[WHI Staff Name or Investigator]

Cover letter – OS Mail Consent Packet.doc 8/1/04

Figure E.7.11
Model WHI Consent Summary Worksheet

WHI Consent Summary Worksheet

After reviewing the consent forms in this packet, please complete and mail this sheet back in the enclosed envelope. This sheet will help us understand your future plans for WHI.

WHI Extension Study Consent Form

Please check one:

☐ **Yes**, I want to join the **WHI Extension Study**.
*(Please sign and return one copy of the **WHI Extension Study Consent Form**. You may keep the second copy of the form.)*

☐ **No**, I do not want to join the **WHI Extension Study**.
*(Please return this worksheet. You do not need to return the **WHI Extension Study Consent Forms**.)*

WHI Supplemental Consent Form

Please check one:

☐ **Yes,** I consent to the sharing of my blood samples with researchers at private for-profit or non-profit organizations.
*(Please sign and return one copy of the **WHI Supplemental Consent Form**. You may keep the second copy of the form.)*

☐ **No,** I do not give consent for this use of my blood samples.
*(Please return this worksheet. You do not need to return the **WHI Supplemental Consent Forms**.)*

Thank you for taking the time to review these consent forms. We are very grateful for all you've contributed over the years and hope that you will continue to be a part of the WHI.

Thank you for all you have done for women's health. *You* are an important part of The Women's Health Initiative!

Consent Summary Worksheet.doc 8/1/04

Appendix E
Model CC Printed Materials
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