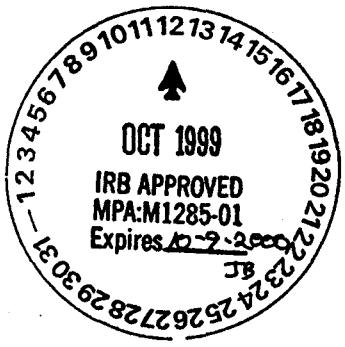
INITIAL CONSENT TO TAKE PART IN THE WOMEN'S HEALTH INITIATIVE (WHI)



WHI Coordinating Center
Fred Hutchinson Cancer Research Center
Seattle, Washington

WHI Clinical Center
University of Wisconsin
Madison, Wisconsin

[redacted]
Principal Investigator

[redacted]
Clinic Manager

Consent to Participate in First Screening Clinic Visit

This form is to tell you about the activities that will occur during your first WHI clinic visit.

Reason for the Study

There are several major diseases that women may get as they get older. Heart disease is the most common cause of death in women age 50 to 79. Breast cancer is the most commonly occurring major cancer in women. Cancers of the colon and rectum are the third most common major cancers in women. Hip fractures (breaks) occur commonly in about 150 out of 1,000 women age 50 and over.

If we could prevent these diseases, women could expect to live longer and healthier lives.

Purpose of the Study

The Women's Health Initiative (WHI), funded by the National Institutes of Health (NIH), is a study of ways to prevent breast cancer, colon and rectum cancer, heart disease, and bone fractures (breaks). About 160,000 women from approximately 40 centers in the United States will take part in this study. The WHI will investigate the possibility of improving the health of women age 50 to 79. Women will be followed in the study for 8-12 years. (How long you are in the study will depend on when you join. Women who enter the study in 1993 will be followed for up to 12 years, while women who join later will be followed for less time.)

Study Parts

There are two major parts to the WHI: a Clinical Trial and an Observational Study. The Clinical Trial will try to find out if there is a benefit to taking hormone replacement therapy,

or to changing one's diet to a low-fat, high fruit and vegetable, and high grain eating pattern, or to taking daily calcium and vitamin D. By joining this part of the study, you may help to answer the question of whether these various changes will improve health. You may choose to take part in one, two or three parts of the Clinical Trial.

The Observational Study part of the WHI will include women who do not join the Clinical Trial, but who are examined and followed for 8-12 years to provide more information about women's health, and to learn more about causes of disease in older women.

What Will You Be Doing?

Activities of the First Clinic Visit

The results of your first clinic visit will help to determine if you are able to join in the WHI. All of the activities are to see if you will be able to join either the Hormone Replacement part or the Dietary part of the study, or both. The WHI staff will be able to give you an idea of whether you might be able to join toward the end of the visit.

At this visit, Clinic Staff will:

1. Review the questionnaires you completed before or at the clinic visit.
2. Record the names (and possibly dosages) of medications you are currently taking.
3. Measure your pulse, blood pressure, height, weight and the distance around your hips and waist.
4. Give you some questionnaires about your personal qualities and lifestyle to complete either in the clinic or at home.
5. Briefly interview you about female hormones you may have used.
6. Draw about three tablespoons of blood for laboratory tests. For 12 hours prior to the blood test, you will not be able to exercise vigorously, eat, or drink anything except water and your regular medications. For 1 hour prior to the test, you will not be able to smoke.

This first clinic visit should take approximately 2 hours to complete.

Abnormal findings of the following clinic tests will be reported to you, your doctor or your clinic: e.g., high blood pressure or blood test for anemia done at your Clinical Center.

Some of the blood drawn will be stored for tests at a later date, including possible genetic studies. This stored blood will be used whether you are in the Clinical Trial or the Observational Study. These blood tests will not replace your usual medical care and results will not be available for you medical care (for example, your cholesterol level will not be reported to you or your doctor). Research studies require only looking at all lab results together and individual results will not be available.

Benefits and Risks

By taking part in this study, you will help increase scientific knowledge about the prevention of breast cancer, colon and rectum cancer, heart disease, and bone fractures (breaks) in women. Also, we will learn ways to prevent disease and promote the health of women from all backgrounds and lifestyles.

Pulse, blood pressure and height, weight, hip, and waist measures

There should be minimal risks with these tests.

Blood draw

There is a small risk with drawing blood. You may feel a little discomfort as the needle goes through the skin. There may be some bruising at the site where blood is drawn. Pressing hard on the spot for one or two minutes after the needle is removed will help to prevent a bruise. Very rarely, the arm may become infected. Occasionally a woman may feel lightheaded or even faint when her blood is drawn. If you feel faint, tell the person drawing your blood and she or he will have you lie down until the feeling goes away.

Alternate Treatments

This clinic visit is only to find out if you are eligible to be in these studies.

Costs

The tests, procedures, medications and visits that are a part of this study will cost only your time and travel. Any test or procedure that would normally be billed to your insurance company, Medicare, or Medicaid will be billed to those sources. If these sources do not pay for tests and procedures, the study will pay these costs. Pelvic exams and Pap smears done at the WHI clinic are free of charge to you. The WHI study has not set aside funds to pay for pelvic exams and Pap smears done by your own doctor.

The study and Clinical Center have not set aside funds to pay for any health conditions that you may develop, and will not pay for any health problems or conditions or injuries that might occur during the course of this study. These might be covered in whole or in part 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.

In the event that physical injury occurs as a result of this research, the University does not automatically provide reimbursement for medical care or other compensation. If physical injury is suffered in the course of research, or for more information, please notify [redacted]. [redacted] Principal Investigator at [redacted]

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. If a health condition is detected during this examination, you will be told about it and the information will be given to your doctor or clinic. Only WHI staff at the University of Wisconsin WHI Clinical Center in Madison, Wisconsin, 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 43 United States Code 241.

Right to Withdraw

Your decision to join in this study is voluntary. You may quit at any time, for any reason, without notice. Even if you decide to stop taking part in the study, you will still be asked to come for clinic visits so we can know what happens to you until the end of the study but you can decide for yourself whether to agree. We hope you will take part for the entire time of the study because we will use all of this information to draw correct conclusions. If you decide to leave the study, we hope to be able to contact you yearly to see how you are doing. If you decide to leave the study, it will not affect your regular 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 be on hand to answer them before you sign this consent form. Also, if you have any questions about your rights as a participant in this study, please call the Patients' Rights Representative at the University of Wisconsin at [redacted] If you have any questions at any time, you may call: WHI Clinical Center at the University of Wisconsin-Madison at [redacted], 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 unclear to you.

Other Information

Your joining is important to the success of this study. Unless many volunteers like you agree to join, this study will not be possible. If, as a result, we learn that a low fat diet reduces the risk of breast cancer, colon or rectum cancer, or coronary heart disease, or that hormone replacement therapy reduces the risk of heart disease or broken bones, many women may benefit. We also expect to discover risks which may be associated with these treatments.

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 and others to join this study.

In order for this study to be valid, you should not join other health studies where you would be assigned at random (like the flip of a coin) to receive a medication, special test, or special treatment. There may be reasonable exceptions to this rule. We therefore ask you to discuss with clinic staff any plans you may have to join other studies before doing so.

If any study test suggests that a health problem needs further follow-up, you will be sent back to your doctor or clinic, who will evaluate the need for further study. Copies of reports and hospital records of your doctor's follow-up may be requested by the WHI and become part of your study record at the University of Wisconsin Clinical Center in Madison, Wisconsin. If you are unable to complete follow-up forms, the WHI clinic staff may contact your spouse, close relative, or friend for updated information about your health. 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. Whether or not you choose to join any part of the study will not directly affect your personal medical care or your medical insurance coverage.

The study does not replace your usual medical care.

An independent committee of experts in medical research will be reviewing study results regularly to see if there are clear benefits or harmful side effects. You will be informed if definite benefits or harmful results are found during the study.

INVESTIGATOR'S STATEMENT

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

_____ _____

Signature of Principal Investigator or Designee Date

PARTICIPANT STATEMENT

I certify that I have read the WHI study description and I voluntarily consent to join in this study. I understand that I may quit the study at any time. I have had a chance to ask questions. I understand that I may ask further questions at any time and that I will receive a signed copy of this consent form for my records. I have had an opportunity to carefully review the Initial Informed Consent form and ask questions about it.

_____ _____

Signature of Participant Date

CONSENT FORM FOR THE DIETARY PART OF THE WOMEN'S HEALTH INITIATIVE (WHI) CLINICAL TRIAL

WHI Coordinating Center
Fred Hutchinson Cancer Research Center
Seattle, Washington

[Clinical Center]

[Principal Investigator]

[24-Hour Contact]

This form is to tell you about the Dietary part of the Women's Health Initiative (WHI) Clinical Trial. If you are able, you may choose to be in this part of the study. If you also are eligible for the Hormone Replacement Therapy part of the WHI, you'll get another consent form. We expect thousands of women across the United States to be in the WHI.

Purpose of the Dietary Part of the WHI

The main purpose of the Dietary part (also called Dietary Modification – DM part) of the WHI Clinical Trial is to see if greatly reducing the amount of fat and increasing the amount of grains, fruits, and vegetables in the diet will reduce the risk of breast cancer, colon and rectum cancer, and heart disease in women, and increase the quality and length of life.

Reasons for the Dietary Part of the WHI

There are several major diseases that women may get as they get older. Breast cancer is the most commonly occurring major cancer in women. Cancers of the colon and rectum are the third most common major cancers in women. Heart disease is the most common cause of death in women age 50 to 79. If we could prevent these diseases, women could expect to live longer and healthier lives.

Some past studies have found that having a diet that is high in fat may increase the chance of getting cancers of the breast, colon, or rectum, or of getting heart disease. Not all studies have found this, however and few of the heart disease studies have been conducted in women. The WHI has been specially set up to include a very large number of women, so that we will have clear answers about whether a low-fat diet with high fruits, vegetables and grains will increase the quality and length of women's lives by decreasing their chances of getting these cancers and heart disease.

What Will You Be Doing?

If you decide to join in the Dietary part of the WHI, you will be asked to fill out some health forms and have a mammogram to see if you are able to join the study. If you have had a mammogram in the past year, you may not need to have one repeated before entering the study.

A doctor, nurse, or physician assistant will review your health history and test results to see if there is any medical reason why you should not join in the Dietary part of the WHI. If you agree to join, you will be asked for the name of your doctor or clinic, so that he or she can be told that you are joining the WHI.

You will also be asked to write down the foods you eat for four days (Four-Day Food Record) to see if you are able to join this part of the study.

If you are found to be able to join the Dietary part, and want to join, you will be placed by chance into 1 of 2 groups:

1) A Dietary Change Group, where you will be taught ways to greatly reduce your daily dietary fat intake and to increase your intake of fruits, vegetables, and grains.

2) A Comparison Group, where no special dietary change teaching or effort will be required.

Your placement into one of these groups will occur by chance, and will be done by a computer, not by a WHI staff member. There will be a slightly greater chance of being assigned to the Comparison Group than to the Dietary Change Group.

Dietary Change Group

If you are placed in the Dietary Change Group, you will be taught how to lower the fat in your diet to approximately 20% of total calories and to increase your intake of fruits, vegetables, and grains. (In the average American diet, fat is about 36% of total calories.)

You will be asked to come to group instructional sessions led by a nutritionist. At the beginning, the groups will meet once a week for 6 weeks, once every two weeks for the next 6 weeks, and once a month for 9 months. After the first year they will meet 4 times a year until the study ends in about 8–12 years. If you cannot attend a group session, you will be asked to make it up. Each session lasts about 2 hours. During these sessions, the nutritionist will help you learn how to plan and shop for low-fat foods and to prepare low-fat meals. You will also be asked to keep careful records of the foods you eat throughout the 8-12 years of the study. You will spend about 36 to 40 hours of your time in sessions away from home in the Dietary Change Group sessions during the first year, and from 20 to 25 hours a year after that until the study ends. You will spend about 2-3 hours per week, especially during the first three months, doing home activities and recording the foods you eat in addition to the time spent away from home.

You will be asked to visit the clinic every year and to phone the clinic if you have problems. This visit will last about 1½ hours.

Comparison Group

If you are placed into the Comparison Group, you will not be asked to make any changes in what you normally eat. If you are in this group, you will spend less than 10 hours a year on the study.

Both Groups

The amount of time asked of you in the Dietary part will be about:

Activity	Total Time
• Three or more Clinic visits at the beginning for enrollment	4-8 hours, plus travel to clinic
• Clinic visits every year	1½ hours/year, plus travel to clinic
• Completing the questionnaires before (or at) each clinic visit	2 hours/year
• For women in the Dietary Change group only	36-40 hours, plus travel, in Year 1: 20-25 hours, plus travel, per year, Years 2-9
• For women in the Dietary Change group only	2-3 hours per week on home activities and review, especially during the first 3 months

If you decide to join the Dietary part of the WHI program, you will be asked to do several clinic activities and have tests to see if you are able to join the study, including a mammogram if you have not had one in the past year.

During the study, there is a chance that you will be asked to complete additional Four Day Food Records and 24-hour telephone recalls. If you are selected, these Food Records would be completed once as part of your first annual clinic visit and once again one year after the Four Day Food Record you complete as part of the screening activities. There is also a chance that you will be asked to talk on the telephone with a nutritionist interviewer about what you ate the day before (a 24-hour food recall). If you are selected for this telephone interview, it would happen between one and eight times during the study. You will also be advised to do moderate exercise, such as walking, for ½ hour each day.

If you decide to join the Hormone Replacement Therapy part of the study as well as the Dietary part, you will be asked to spend an additional 5 minutes a day for the first year recording in an Hormone Replacement Therapy calendar, plus an extra ½ hour per year throughout most of the study for the yearly physical examination needed for the Hormone Replacement Therapy part.

Description of Procedures During Dietary Study

During the 8–12 years you are in the Dietary part of the WHI study, you will have clinic visits every year, and will be asked to phone the clinic if problems occur. You will also be contacted by Clinic Staff six months after each clinic visit to ask you about your health.

Yearly Visits

At each yearly visit, Clinic Staff will:

- Review the questionnaires you completed before the clinic visit.
- Record the names (and possibly dosages) of any medications you are currently taking.
- Require you to have a mammogram every other year throughout the trial.
- Give you an electrocardiogram (ECG) heart examination when you first join the study and every 3 years. This consists of placing wires on your chest while you are lying down, and recording your heart's activity. If you smoke, you will not be able to have a cigarette for 1 hour prior to the test.
- Measure your pulse, blood pressure, and weight.

For Osteoporosis Substudy Clinical Centers only:

When you first join the study, and at your 1st, 3rd, 6th, and 9th yearly visits:

- You will be asked to provide a urine sample (about 1 tablespoon) which will be stored for laboratory tests at a later date.
- Your bone density will be measured in your hip, spine and in your whole body. The test is painless and takes about 30 minutes.

In addition, Clinic Staff may:

- Draw about 3 tablespoons of blood for laboratory tests. For 12 hours prior to the blood test, you will not be able to exercise vigorously, eat or drink anything but water and your regular medications. For 1 hour prior to the blood test, you will not be able to smoke.
- Give you a clinical breast exam and teach you how to examine your own breasts.
- Measure your height and the distance around your hips and waist.
- Measure your physical ability in 3 ways (this may also be done when you first join the study):
  1) You will be asked to squeeze 2 handles together in one hand, to measure the strength of your hand.
  2) You will be asked to stand up out of a chair several times from a sitting position to measure the strength of your legs.
  3) You will be asked to walk a distance of 18 feet and a Clinic Staff member will measure how long it takes you to walk that far. This will measure your walking ability.

- Give you some questionnaires about your personal qualities and lifestyle to complete either in the clinic or at home.

Abnormal findings of the following clinic tests will be reported to you, your doctor or your clinic: blood pressure, blood test for anemia done at your Clinical Center, mammogram, and electrocardiogram (ECG). Some abnormal findings may exclude you from continuing the Dietary part of the study. If this should occur, the reasons why you are not able to continue will be fully explained by the Clinic Staff.

Some of the blood drawn will be stored for tests at a later date, including possible genetic studies. This stored blood will be used whether you are in the Clinical Trial or Observational Study. These blood tests will not replace your usual medical care, and results will not be available for your medical care (for example, your cholesterol level will not be reported to you or your doctor). Research studies require only looking at all lab results together, and individual results will not be available.

Benefits and Risks

Every medical treatment has good effects (benefits) and bad effects (risks). There may be no direct benefit to you for participating in this study. By taking part in this study, you will help to increase scientific knowledge about the prevention of breast cancer, colon and rectum cancer, and heart disease in women. This study will provide stronger scientific evidence than currently exists about whether eating a low-fat, high fruit, vegetable and grain diet will change your risk of these diseases. The eating patterns of women in the Dietary Change Group will be monitored for nutritional balance.

Dietary Change

The dietary changes to be made by women in the Dietary Change Group have no known risks for health in women who keep a well-balanced diet. Changes in your diet may lead to minor discomforts: occasional diarrhea or constipation, or increased gas. You will be advised on ways to avoid these problems or to make the changes easier to tolerate. You may also experience a small amount of weight loss.

Pulse; blood pressure; height, weight, hip, waist and physical strength measures; and clinical breast exams

There should be minimal risks with any of these activities.

Blood draw

There is a small risk with the process of drawing blood. You may feel a little discomfort as the needle goes through the skin. There may be some bruising of the site where blood is drawn. Pressing hard on the spot for 1 or 2 minutes after the needle is removed will help to prevent a bruise. Very rarely, the arm may become infected. Occasionally, a woman may feel lightheaded or even faint when her blood is drawn. If you feel faint, tell the person drawing your blood and she or he will have you lie down until the feeling goes away.

Mammogram

A mammogram uses 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. Mammograms every 1 to 2 years are recommended for all women in your age group.

ECG (Electrocardiogram)

There should be no risk with this procedure.

Osteoporosis Substudy Clinical Centers only

Bone Density Measurement

The bone density measurement involves a small amount of radiation. Small amounts of radiation may have potential harm, but the risk is difficult to measure and is probably very small. The total radiation dose from the bone density measurements is less than 5% of the natural background radiation a person receives living in a typical American community for 1 year. You get about the same amount of radiation during 3 coast-to-coast airline flights.

Urine Sample

The urine sample involves no risk.

By taking part in this study, you will help increase scientific knowledge about the prevention of breast cancer, colon and rectum cancer, and heart disease in women.

Other Treatments to Prevent Breast Cancer, Colon and Rectum Cancer, or Heart Disease

Prevention of breast cancer

No treatment has been shown to prevent breast cancer. At the present time, the standard treatment would include routine physical exams, mammograms, and breast self-examination to find cancer early.

Prevention of colon and rectum cancer

No treatment has been shown to prevent colon or rectum cancer. At the present time, the standard treatment would include routine physical exams and yearly exams of your stool by your doctor for the presence of blood to find cancer early. Other ways of finding cancer early, such as screening with

flexible sigmoidoscopy (an internal examination of the bowel), are thought to reduce the risk of dying from these cancers.

Prevention of heart disease

At the present time, the standard treatment would include controlling blood cholesterol, blood pressure and weight, exercising regularly, and being a nonsmoker.

Costs

The tests, procedures, medications and visits that are a part of this study will cost only your time and travel. Any test or procedure that would normally be billed to your insurance company, Medicare, or Medicaid will be billed to those sources. If you do not have sources to pay for tests and procedures, the study will pay these costs.

The study and Clinical Center have 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.

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. If a health condition is detected during this examination, you will be told about it and the information will be given to your doctor or clinic. 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. Study records will be kept indefinitely for analysis and follow-up. This study is authorized by Privacy Act 42 United States Code 241.

Right to Withdraw

Your decision to join in this study is voluntary. You may quit at any time, for any reason, without notice. Even if you stop taking part in the Dietary part of the study, you will still be asked to come for clinic visits so we can know what happens to you until the end of the study. We hope 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, we hope to be able to contact you yearly to see how you are doing. If you decide to leave the study, it will not affect your regular 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 be on hand to answer them before you sign this consent form. Also, if you have any

questions about your rights as a participant in this study, please call _____ in the Institutional Review Board Office of [Clinical Center] 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 unclear to you.

Other Information

Your joining is important to the success of this study. Unless many volunteers like you agree to join, this study will not be possible. If we learn that a low-fat, high fruit, vegetable and grain diet reduces the risk of breast cancer, colon or rectum cancer, or heart disease, many women may benefit.

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 and others to join this study.

In order for this study to be valid, you should not join other health studies where you would be assigned at random (like the flip of a coin) to receive a medication, special test, or special treatment.

If any study test suggests that a health problem needs further study, you will be sent back to your doctor or clinic, who will evaluate the need for further study. Copies of reports and hospital records of your doctor's follow-up may be requested by the WHI and become part of your study record at the [Clinical Center]. If you are unable to complete the follow-up forms, the WHI clinic staff may contact your spouse, close relative, or friend for updated information about your health. 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. Whether or not you choose to join the Dietary part of the study will not affect your personal medical care or your medical insurance coverage. The study does not replace your usual medical care.

An independent committee of experts in medical research will be reviewing study results regularly to see if there are clear benefits or harmful side effects. You will be informed if definite benefits or harmful results are found during the study.

Investigator's Statement

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

_____ _____

Signature of Principal Investigator or Designee Date

PARTICIPANT STATEMENT

I certify that I have read, or had read to me, and that I understand the description of the Dietary part of the WHI. I voluntarily consent to join in this part of the study. I understand that I may quit the study at any time. I have had a chance to ask questions about the Dietary part of the study. I understand that I may ask further questions at any time and that I will receive a copy of this signed consent form for my records. I have also had an opportunity to carefully review the Dietary Informed Consent form, watch the Dietary Informed Consent videotape, and ask questions about them.

Signature of Participant	Date
Signature of Witness	Date