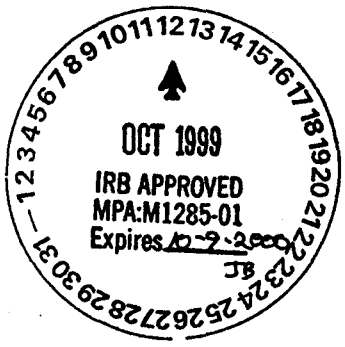
# INITIAL CONSENT TO TAKE PART IN THE WOMEN'S HEALTH INITIATIVE (WHI)




**WHI Coordinating Center**
**Fred Hutchinson Cancer Research Center**
**Seattle, Washington**

**WHI Clinical Center**
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[redacted]
**Principal Investigator**

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**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

# HORMONE REPLACEMENT THERAPY: RISKS AND BENEFITS

## (FOR WOMEN WHO HAVE A UTERUS)

# SUMMARY OF POSSIBLE BENEFITS AND RISKS OF BEING IN THE HORMONE REPLACEMENT PART OF THE WHI DURING THE NEXT 8 TO 12 YEARS

**(for women with a uterus)**

The hormone pills ESTROGEN and PROGESTERONE are used by millions of women. These pills are most often used to help with hot flashes and other symptoms that come with menopause ("change of life"). These hormone pills are also used to prevent osteoporosis (weakening of the bones) which can lead to fractures (broken bones). Whether these pills protect women against heart disease and broken bones has been suggested but not proven by past studies. The Women's Health Initiative (WHI) is specially designed to find out whether taking these hormone pills will prevent heart disease and fractures (broken bones). The WHI will also see if there are other benefits and risks from taking hormone pills.

In order for you to decide whether or not to join the WHI, it is important that you know the benefits and risks of hormone pills. There are two different pills that will be used in the WHI for women who have a uterus (i.e., have never had a hysterectomy): ESTROGEN and PROGESTERONE combined, or a PLACEBO (an inactive pill). In the study, the computer will choose randomly (like the flip of a coin) which one of the two types of pills you will take.

The table below is a brief summary of the possible benefits and risks of taking these pills. See the informed consent form for more details. The numbers in the table are our best guesses about how much the different pills will increase or decrease your chances of getting certain health problems. These numbers are based on past studies of women who have used female hormone pills. The WHI trial is different from these studies and should be able to find out what the real benefits and risks are.

| **STUDY GROUP** (women with a uterus) | **POSSIBLE BENEFITS** (good effects) | **POSSIBLE RISKS** (bad effects) |
|---|---|---|
| ESTROGEN and PROGESTERONE<br><br>(Note: Very little is known about benefits and risks.) | Out of every 1,000 women who take estrogen and progesterone:<br>• 5-10 fewer may have heart attacks.<br>• 8 fewer may break their hips.<br>• Bladder problems may decrease.<br>• Menopause symptoms may decrease. | Out of every 1,000 women who take estrogen and progesterone:<br>• 4-8 more may get breast cancer.<br>• Blood clots in the legs or lungs may increase.<br>• Symptoms like a period may increase. |
| PLACEBO<br><br>(inactive pill) | No known benefits from taking inactive pills. | No possible bad effects from taking inactive pills. |

# CONSENT FORM FOR THE HORMONE REPLACEMENT THERAPY PART OF THE WOMEN'S HEALTH INITIATIVE (WHI) CLINICAL TRIAL FOR WOMEN WHO HAVE A UTERUS

**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 Hormone Replacement Therapy 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. We expect thousands of women across the United States to be in the WHI. If you are also eligible for the Dietary part of the WHI, the WHI staff will give you a separate consent form for that part.

## Purpose of the Hormone Replacement Therapy Part of the WHI

The main purpose of the Hormone Replacement Therapy part of the WHI Clinical Trial is to find out whether taking the female hormones, estrogen alone, or estrogen with progesterone, will lower the risk of heart disease and bone fractures (breaks), and will improve the quality of life for women.

## Reasons for the Hormone Replacement Therapy Part of the WHI

There are several major diseases that women may get as they become older. Heart disease is the most common cause of death in women age 50 to 79. Hip fractures occur in about 150 out of every 1,000 women 50 and over. If we could prevent these diseases, women could expect to live longer and healthier lives.

As women go through menopause ("change of life"), their bodies stop making some female hormones. Some past studies have suggested that taking female hormone pills may decrease the chances of getting heart disease or fractures.

In the past few years, many doctors have commonly given estrogen with progesterone to women who have their uterus (womb), because women who take only estrogen have an increased chance of developing cancer of the endometrium (lining of the uterus). Progesterone prevents this increased chance of cancer of the endometrium. However, it may be that the progesterone hormone takes away from the good effects of estrogen in reducing heart attacks which are much more common than endometrial cancer.

The problem with these studies is that women who were taking female hormones may have been different from those who are not. Doctors don't really know whether taking female hormones after menopause is helpful or not.

The Women's Health Initiative is specially set up to find out whether or not female hormone pills improve women's health by protecting against heart disease and fractures and will give us information about harmful effects, as well.

**What Will You Be Doing?**

If you decide to join in the hormone replacement part of the WHI, you will be asked to fill out some health forms and have some tests to see if you are able to join the study. These tests will include:

- mammogram
- pelvic exam and Pap smear
- tests of your uterus

If you have had any of these tests in the past year, you may not need to have these tests repeated before entering the study. These tests are described in more detail below.

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 hormone replacement 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.

If you are eligible to join the hormone replacement part, and you want to join, a computer will assign you at random (like the flip of a coin) into one of the following two groups:

1) a group given pills with estrogen + progesterone combined; or
2) a group given inactive pills containing no real medicine (a placebo).

You will have an equal chance of being placed in either group.

The estrogen to be used is Conjugated Equine Estrogen. The amount is 0.625 mg each day. The progesterone to be used is Medroxyprogesterone, 2.5 mg each day. The types and amounts of estrogen and progesterone to be used in this study have been used for several years in hundreds of thousands of women in the U.S.

The placebo (inactive) pills are necessary because you, the clinic staff and doctors won't know whether you're taking estrogen and progesterone, or the placebo. All the pills look the same. While you are in the study, you will not be able to take any additional female hormones other than those prescribed by WHI clinic doctors for symptoms or for vaginal bleeding.

If you have a hysterectomy during the study, your study medications will either be changed or stopped. If your hysterectomy is for cancer, your study pills will be stopped. If your hysterectomy is for any other reason, your study pills will be either estrogen alone or placebo.

If you join in the hormone replacement part of the study, you may be asked to have clinic contact every 6 months for 8–12 years. (The length of time you will be in the study depends on the year you join. For example, women joining in 1994 will be followed for up to 12 years. Women joining in 1997 will be followed for about 8 years.) You will also be asked to phone the clinic if you have problems and to keep a calendar of symptoms and vaginal bleeding while you are taking the study pills. In the beginning years of the study, clinic staff may call you between visits to make sure you are not having any problems.

Before you are enrolled in the hormone replacement part of the study, you will be given study medication for 4 weeks to see if taking medication fits into your daily life.

The amount of time asked of you to join in the hormone replacement part of the study will be about:

| Activity | Total Time |
|---|---|
| • 3 or more screening visits to start | 4 to 8 hours altogether, plus travel to clinic |
| • Recording any bleeding in your calendar (during the 1st year) and taking study pills | Less than 5 minutes each day |
| • Clinic visits: As often as every 6 months | 3 hours each year, plus travel to clinic |
| • Completing questionnaires before or at each clinic visit | 2 hours each year |
| • Talking with clinic staff by phone between clinic visits | ½ hour each year |

If you decide to join the Dietary part of the study, you may be asked to spend an additional 30 hours in the first year and 8 hours per year throughout the rest of the study.

**Description of Procedures During HRT Study**

During the 8–12 years you are in the hormone replacement part of the WHI, you will have clinic contacts as often as every 6 months. You will also be advised to do moderate exercise, such as walking, for ½ hour each day.

**Six-month contacts**

At the 6-month contacts, the Clinic Staff will:

- Review your calendar record for any bleeding you had.
- Review the questionnaire you completed before the clinic contact.

**Yearly Visits**

At each yearly visit, Clinic Staff will:

- Review your calendar record for any bleeding you had.
- Collect your remaining study pills and give you a new bottle of your pills.

- Review the questionnaire you completed before or at the clinic visit.
- Record the names (and possibly dosages) of any medications you are currently taking.
- Interview you briefly about female hormones you may have used.
- Give you a clinical breast exam and, at your first exam, teach you to examine your own breasts.
- Measure your pulse, blood pressure, and weight.
- You will be given a pelvic exam and Pap smear before being started on study pills. The pelvic exam and the Pap smear will be done at least every three years during follow-up. You will need to have a pelvic exam every year that you are in the study. This may be done either by your own doctor or at the WHI clinic. The pelvic exam and Pap smear will be the same as those done by gynecologists or other doctors you may have seen. During this exam, the clinic doctor, nurse practitioner, or physician assistant will insert a plastic or metal instrument in your vagina so that your cervix can be seen, take scrapings from your cervix for the Pap smear, and do an examination of your uterus, ovaries, and rectum with her/his gloved hands.
- You will also be given a test of the lining of your uterus (endometrial aspiration) before you start the study pills. You may be given an endometrial test during later years. The test includes taking a small sample of the lining of your uterus. This is called an "endometrial aspiration". After inserting an instrument into your vagina, the doctor, nurse practitioner, or physician assistant will insert a thin tube through your cervix and take samples from the lining of your uterus. You may feel cramping of your uterus during and after the test, which can be treated with medicine. If you find the test uncomfortable, a pain-killing injection can be given into your cervix.

  If after 2 different attempts, it is not possible to do an endometrial aspiration, an ultrasound exam of your uterus will be done. In this test, a probe (a little bigger than the size of a tampon) is put into your vagina, and a sound-wave picture of your uterus is taken. This test should be no more uncomfortable than a pelvic exam. If further tests are needed, you will be referred to your usual health care provider.
- You will be required to have a mammogram each year throughout the trial.
- You will be given 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.

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 one tablespoon) which will be stored for laboratory tests of bone health 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 test, you will not be able to smoke.
- 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 a test of your memory and thinking (this may also be done when you first join the study).
- Give you some questionnaires about your personal qualities and lifestyle to complete either in the clinic or at home.

Abnormal findings of the clinic tests will be reported to you or your doctor or clinic: blood pressure, blood test for anemia done at your Clinical Center; mammogram, pelvic exam, Pap smear, endometrial aspiration, uterine ultrasound and electrocardiogram (ECG). Some abnormal findings may exclude you from continuing the hormone replacement 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 the 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

### Hormone Replacement Therapy

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 increase scientific knowledge about the prevention of heart disease and of broken bones (fractures) in women. You will also help increase scientific knowledge about how female hormone replacement therapy affects the risk of breast cancer and endometrial cancer in women.

The Women's Health Initiative is being done to find out clearly whether the benefits of hormone replacement therapy are greater than the risks. At present, we simply do not know. Our knowledge of the possible benefits and risks are presented here. The possible benefits and risks presented are what we think will happen to women age 50-79 during the 8-12 years of the study.

Half of the women in the hormone replacement part of the WHI will receive inactive pills containing no real medicine (placebo). The others will receive actual female hormone pills (estrogen and progesterone).

1. Benefits and risks if you get the placebo (inactive pills):

   Women who receive the inactive pills (placebo) should have no direct effects from these pills. They may miss out on the possible protection from bone fractures (breaks) and heart disease that may occur with taking female hormones. On the other hand, they are not exposed to any of the possible risks of taking female hormones.

   Women who receive placebo pills will also not be getting hormone pills that might relieve hot flashes or prevent osteoporosis (weakening of the bones).

2. Possible benefits if you get the combination of estrogen and progesterone:

   The possible benefits of taking estrogen and progesterone are the same as those for estrogen alone, except that we really do not know whether adding progesterone changes the risk of getting heart disease. If progesterone does not change the effect of estrogens, the chance of developing heart disease may decrease from about 50 out of 1,000 women who do not take estrogen and progesterone to about 40 out of 1,000 for women who do take estrogen and progesterone. If progesterone does change the effect of estrogens, about 45 out of 1,000 women may get heart disease. Estrogen and progesterone together may decrease the chance of getting a broken hip from about 39 per 1,000 women to 31 per 1,000 women over the course of the WHI study.

   If you have hot flashes or other menopausal symptoms, these may be relieved by estrogen and progesterone. Some women seem to have fewer bladder problems if they take estrogen and progesterone.

Possible risks if you get the combination of estrogen and progesterone:

There also are some risks to taking estrogen and progesterone after menopause. Women who have used estrogen alone in the past have been found to have an increased chance of getting cancer of the lining of the uterus (endometrial cancer). However, women taking progesterone with the estrogen do not seem to have an increased risk of endometrial cancer compared with women who do not take any female hormones after menopause. In this study, the lining of your uterus may be tested to see if changes that might indicate a future cancer are occurring. If such changes are found, your study pills will be changed. Women who develop endometrial cancer will need to have a hysterectomy (have their womb removed). With early detection of problems, we believe that there should be no increased risk of endometrial cancer with the estrogen and progesterone study pills.

The long-term use of estrogen and progesterone may cause an increase in the risk of breast cancer. About 30 out of 1,000 women in the study may develop breast cancer without estrogen therapy. For those who take estrogen and progesterone, this may increase to about 34 women out of 1,000 or possibly 38 out of 1,000 women. It is possible that women who are at high risk for breast cancer (for example, women with a family history of breast cancer, and possibly women who have used diethylstilbestrol (DES) in the past) may have a somewhat greater risk of breast cancer from the use of estrogen and progesterone than other women.

Your breasts will be examined regularly, including the use of mammograms, to help find any cancer of the breast at an early stage.

The use of estrogen and progesterone after menopause may also cause a small increase in the risk of getting a blood clot in the legs or lungs, or getting gallstones.

3. Other possible effects of estrogen and progesterone:

The use of estrogen and progesterone may have other effects like having a period. These include vaginal bleeding, breast tenderness, bloating, changes in weight, irritability, and depression. Usually, these effects are minor and often stop being a problem within several months.

If you have vaginal bleeding or spotting, you may need to have an extra endometrial aspiration test, and may have to stop taking your study pills and take different hormones. If bleeding continues or if the endometrial test is abnormal, you may need further tests, which will be done by your doctor, not by WHI doctors. Occasionally a woman may need a hysterectomy for bleeding or for pre-cancerous conditions of the uterus.

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

There should be minimal risks with 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 he or she will have you lie down until the feeling goes away.

**Pelvic exam, Pap smear and ultrasound exam of your uterus**

There should be no risks with these examinations, but some women may find them unpleasant or uncomfortable. Any small discomfort is outweighed by the benefit of early detection of any abnormality.

**Endometrial aspiration (Testing the lining of the uterus)**

This procedure has few risks. Some women feel cramps. In rare cases, tearing of the uterus, bleeding from the vagina, infection or an allergic reaction to the solution used to clean your cervix or to the pain killer injection can occur.

**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 are recommended for all women in your age group every 1-2 years.

**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 heart disease and fractures (broken bones) in women.

## Other Treatments to Prevent Heart Disease or Fractures

### 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.

### Prevention of fractures due to weakened bones

Estrogens, calcium and vitamin D supplements, and regular exercise help prevent osteoporosis (weakened bones). Some treatments, such as estrogen and calcium and vitamin D supplements are now also being tested to see if they will prevent fractures (broken bones). New medicines such as bisphosphonates (like alendronate or Fosamax) and intranasal calcitonin have been approved for the treatment of osteoporosis to strengthen weakened bones and fractures in postmenopausal women with osteoporosis. These medicines may be taken to maintain bone density.

## 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. 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.

**Right to Withdraw**

Your decision to be in the study is voluntary. You may quit at any time, for any reason, without notice. Even if you have to stop taking study pills, 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 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, 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 of 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 hormone replacement therapy reduces the risk of heart disease or fractures (broken bones) in women, 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 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 Hormone Replacement Therapy 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 review 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 the 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 Hormone Replacement Therapy 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 Hormone Replacement Therapy part of the study, and I have had an opportunity to carefully review the Hormone Replacement Therapy Informed Consent form. 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 watch the Hormone Replacement Therapy Informed Consent videotape, and read the handout called "Hormone Replacement Therapy: Benefits and Risks," and ask questions about them.

_____ _____

Signature of Participant Date

_____ _____

Signature of Witness Date