The Women of the Observational Study

The first woman was enrolled in the Observational Study of the Women's Health Initiative (WHI) in September 1994. By the end of enrollment in December 1998, a total of 93,676 women across the U.S. had joined the OS, making it one of the largest observational studies ever done. This is a tremendous achievement and we have YOU to thank!

The Observational Study (OS), the largest component of WHI, was designed to describe factors contributing to health and disease in postmenopausal women. The OS is different from the WHI Clinical Trials (CT) in that it does not involve an intervention, such as a special dietary program or taking study pills. The CT will answer important questions about the effects of specific interventions on health and disease in postmenopausal women. The OS will answer important questions about other (and possibly new) risk factors for health and disease in women. This information may have an impact on healthcare for postmenopausal women like you in the future and on the design of new interventions to help reduce disability and disease.

Now that we're nearing the end of the study, we'd like to share with you a summary of some of the data you've provided over the years. First, we'll use that information to create a “picture” of the OS women as a group. Then we'll share some of the WHI study findings so far, including those from women in the OS, as well as from the Hormone Program.

Who are the women of the Observational Study?

Women between the ages of 50-79 were asked to join the WHI. Women over the age of 65 were especially encouraged to join. Since more chronic diseases tend to occur as women age, it is especially important to study women in their later years. As shown in the chart on the next page, 47% of our

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OS participants were aged 65 or over when they joined the study. The average age of OS participants was 63.6 years. Women in the OS were slightly older than women in the CT components, where the average age was 62.7 years.

As shown below, women in the OS come from a variety of marital and educational backgrounds, as reported when they joined the study. At that time, most were married and had completed some education beyond high school.

Forty WHI clinics located at major academic and research institutions nationwide ensured that the WHI findings would reflect the regional diversity of women in the United States.

Nearly 28,000 minority women (17% of all participants) joined the WHI CT and OS, giving this study the unprecedented opportunity to learn more about minority women's health. WHI aims to represent all women in our society, so it was important to seek out and include women from diverse cultures. Researchers hope to learn more about how different cultural factors might affect long-term health and well being. The chart below shows the racial/ethnic diversity of OS participants.

<table>
<thead>
<tr>
<th>Ethnicity of Participants in the OS</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian or Alaskan Native</td>
<td>422</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>2,671</td>
</tr>
<tr>
<td>Black or African-American</td>
<td>7,639</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3,623</td>
</tr>
<tr>
<td>White</td>
<td>78,013</td>
</tr>
<tr>
<td>Unknown</td>
<td>1,308</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>93,676</td>
</tr>
</tbody>
</table>

It's great for the mind and body to stay active. WHI participants like to join in group activities. At least once a month, 65.8% attend religious services and 55.5% attend club meetings.

What are your families like?

Collectively, the 93,676 women of the OS have raised over 246,068 children! The chart on the following page shows the number of births participants reported.
Exercise: At the start of the study, nearly 28% of OS participants reported getting strenuous exercise at least one day per week, over 42% reported moderate exercise weekly, and 28% reported getting mild exercise weekly. About 61% of you reported that you walked for exercise at least once a week for 20 minutes or more.

Diet: You provided a lot of dietary information when you joined the study. From that information, we learned that our OS participants on average get 31% of their calories from fat and eat about 4½ servings of fruits and vegetables per day. This is close to national recommendations to eat 30% or fewer calories from fat and 5+ fruit/vegetable servings per day.

Smoking habits: Nearly 51% of you have never smoked and an additional 43% managed to successfully kick the habit. Congratulations!

Alcohol consumption: Nearly 70% of OS women have an alcoholic beverage at least once a month, while 30% choose to abstain entirely. Of those who drink, most prefer wine over beer or other types of liquor.

What are your health and lifestyle habits?

Over 58.3% of you reported that you were in “Very good or excellent health” when you joined the study. Below we describe the health and lifestyle habits of OS women like you at the time the study started.
Coffee and tea consumption: Over 71% of you reported drinking at least one cup of coffee each day, with most of you preferring regular coffee to decaf. The chart below shows the average number of cups of regular coffee OS participants drink per day. Coffee is not necessarily the drink of choice for all of you. About 26% of OS participants reported drinking at least one cup of tea each day.

Average Number of Cups of Coffee Per Day

- 4-5 cups: 10.6%
- 2-3 cups: 41.2%
- 1 cup: 24.7%
- None: 20.6%
- 6 or more cups: 2.9%

Sleep habits: As shown below, the sleeping habits of OS women vary greatly, with some reporting less than 4 hours per night and others getting 12 or more!

Use of hormone therapy: When you joined the study, you were asked if you had ever used estrogen or estrogen plus progestin. Almost 41% of you had never used these hormones, 15% were previous users, and close to 45% were current users. At the clinic visit three years later, 56% of you reported hormone use in the previous two years. This was before the WHI Estrogen plus Progestin study findings were released.

How is your health?

A number of women deal with ongoing health problems, particularly as they grow older. Below are the numbers of OS participants who have experienced some of the more common health issues:

<table>
<thead>
<tr>
<th>Health Issue</th>
<th>Had prior to joining WHI</th>
<th>Occurred since joining WHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>High blood pressure (treated with pills)</td>
<td>23,464</td>
<td>17,180</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>5,298</td>
<td>3,166</td>
</tr>
<tr>
<td>Diabetes (treated with pills/shots)</td>
<td>3,902</td>
<td>3,884</td>
</tr>
<tr>
<td>Heart Attack</td>
<td>2,306</td>
<td>1,336</td>
</tr>
<tr>
<td>Endometrial (uterine) cancer</td>
<td>1,578</td>
<td>422</td>
</tr>
<tr>
<td>Stroke</td>
<td>1,415</td>
<td>1,351</td>
</tr>
<tr>
<td>Broken hip</td>
<td>887</td>
<td>702</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>857</td>
<td>656</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>644</td>
<td>267</td>
</tr>
</tbody>
</table>
Sadly, over 3,900 OS participants have passed away since joining the study and we honor their contributions to women’s health. The majority of these deaths were due to cancer and cardiovascular disease.

**Weight changes:** At the beginning of the study, the average OS participant weighed 158 pounds and was 5 ft-3 1/2 inches tall. OS women aged 60-64 years when they joined the study had an average weight of 162 pounds. The average weight for those aged 85 years was 131 pounds. When asked about weight changes during your adulthood, 33% of you reported that your weight had stayed the same, 31% had gained weight, 3% had lost weight, and 33% of you said that your weight went up and down. The chart below shows how weight is reported to have changed between ages 18 and 50 for the group as a whole.

![Weight Changes Chart]

The body weight and height measurements taken at clinic visits are used to calculate the Body Mass Index (BMI), an index that relates weight to height to identify specific weight categories. The chart below summarizes this information for OS women. To use the Internet to calculate your own BMI, go to: www.nhlbisupport.com/bmi.

<table>
<thead>
<tr>
<th>BMI Category</th>
<th># of pts</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (BMI &lt; 18.5)</td>
<td>1,107</td>
<td>1.2</td>
</tr>
<tr>
<td>Normal (18.5 - 24.9)</td>
<td>36,687</td>
<td>39.6</td>
</tr>
<tr>
<td>Overweight (25.0 - 29.9)</td>
<td>31,461</td>
<td>34.0</td>
</tr>
<tr>
<td>Obese(&gt; = 30.0)</td>
<td>14,580</td>
<td>25.2</td>
</tr>
</tbody>
</table>

What have you contributed to WHI?

Taken together, the data described above help us understand the health and lifestyle habits of postmenopausal women. Over the past 10 years, you have been contributing to these data by filling out questionnaires each year and providing physical measures and blood samples at your screening and Year 3 visits. Here are some amazing facts showing all you’ve given over the years:

- OS women have completed over 2,750,000 forms to date (and up to another 180,000 when the forms from this packet are returned)!
- OS women have completed 246,932 WHI clinic visits, counting screening and Year 3 visits. In addition, participants at the three bone density centers have attended another 4,500 visits.
- As of this mailing, around 94% have completed at least one form in the past year. That is an incredible accomplishment!

As you can see, you and your OS sisters form a diverse, fascinating group of women. This information and much more will be analyzed by scientists over the next several years to help find answers to many questions about women’s health. Major findings from WHI have already been released and will continue to be published in the months and years to come.

On the next several pages we describe findings from papers published on Observational Study participants, as well as the major findings reported on women in the hormone part of WHI. Every single participant like you has helped make WHI a success. Thank you again for your role in this tremendous achievement!
Focus on WHI Findings

As you probably remember, the Women's Health Initiative consists of the Observational Study and three Clinical Trial programs: Hormone, Dietary, and Calcium/Vitamin D. For the past several years, participants in the Hormone and Calcium/Vitamin D Programs have taken study pills, while women in the Dietary Program have followed either a low fat eating pattern or their usual eating habits. Each WHI participant has answered hundreds of questions about her health and lifestyle habits. These data will contribute to what we know about women's health. Information provided by women in the Estrogen plus Progestin part of the Hormone Program has already led to important breakthroughs in the health care of postmenopausal women.

Major results from the Dietary and Calcium/Vitamin D Programs, as well as additional results from the Hormone Program, will be released early in 2006. In spring 2006, a newsletter highlighting the major findings from all study components, including the OS, will be mailed to all WHI participants.

In the pages that follow, we summarize some of the important findings on hormone use in postmenopausal women. Then we highlight just a few of the many findings on OS women that have been published in the past several years.

WHI Findings from the Hormone Program

As reported in previous issues of WHI Matters and in newspapers and magazines around the world in July 2002, estrogen plus progestin hormone treatment—long believed to help postmenopausal women maintain good health—was actually shown to increase risk for several life-threatening diseases. This information was based on data collected from women in the Estrogen plus Progestin (E+P) part of the WHI Hormone Program, but did not reflect findings in the Estrogen-alone study.

In trying to understand the overall balance of health risks and benefits of taking estrogen plus progestin, WHI scientists reviewed information on many health conditions. Heart attacks, breast cancer, strokes, and blood clots occurred in more women on E+P than in those taking placebo. Fewer women on these hormones had colorectal cancer and hip fractures, and there were no differences in the number of women who had endometrial cancer or in the number of deaths. Overall, more women taking E+P had a serious health event than did women taking placebo, and scientists concluded that the benefits from taking E+P do not outweigh the risks.

Since the release of these findings, WHI investigators have continued to analyze health data of women in the E+P in much more detail, taking into account additional health conditions that these women reported before they stopped their study pills. These analyses confirmed that

For additional information on WHI study findings as they are released, an updated and complete list of published articles, and other news on WHI as it happens, please visit the WHI website at www.whi.org.
more women taking active E+P hormones developed heart attacks, strokes, and breast cancer than did those taking placebo (inactive) pills. Other reports on the effects of E+P included:

- Breast cancer tumors in the E+P group tended to be larger and at a later stage than those in the placebo group. Also, more women in the E+P group had abnormal mammograms compared to the placebo group.

- Taking E+P offered no clear improvement in quality of life, including perceptions of general health, energy, social functioning, mental health, depression, and sexual satisfaction.

- There were 24% fewer fractures (broken bones) and 33% fewer hip fractures in women assigned to E+P compared to placebo. In addition, hip bone density increased 3.7% after 3 years of taking E+P compared to only a 0.14% increase in the placebo group.

- Women taking E+P had 19% fewer endometrial (uterine) cancers, compared to placebo.

Women in the E+P group also had increased ovarian cancer rates compared with those in the placebo group. However, the small number of ovarian cancers in E+P participants overall (only 32), means that this may be a chance finding.

- E+P does not protect women from normal declines in cognitive function when compared with placebo. In addition, women in the E+P group were at higher risk for developing dementia than those in the placebo group, although the number of actual dementia cases overall was small.

Taken together, these findings indicate that the overall risks of estrogen plus progestin hormone therapy outweigh the benefits. These results apply only to women who take combined estrogen plus progestin hormones. Results from the Estrogen-Alone part of the Hormone Program and other study components will be reported as they become available.

The time and effort of women in the Hormone Program have already made it possible to answer one of the many important questions for postmenopausal women. We expect WHI to provide many more answers in the years to come.
WHI Findings from the Observational Study

The estrogen plus progestin findings described above captivated the public and scientific communities. At times, it may have seemed that hormones and women's health was all that WHI is about. However, as you know, WHI is that and so much more! WHI scientists are well aware of the importance of the information participants are sharing for the future of women's health. In fact, many other scientific papers have been published over the last few years based on analyses of the Observational Study data. These findings, some of which are summarized on the following pages, greatly extend our knowledge about women's health.

Physical Activity in Women
How do activity levels change throughout a woman's life? WHI investigators studied differences in women's vigorous physical activity over time. Vigorous activity was defined as strenuous exercise at least three days per week, including aerobics, jogging, tennis, and swimming laps. Investigators also assessed whether past activity was predictive of current activity. OS women answered questions about their activity levels at ages 18, 35, 50, and present day. Researchers found that women's current participation in vigorous activity was around 13-16% and did not differ by racial/ethnic group. Not surprisingly, vigorous activity decreased with age for women of all racial/ethnic groups after age 50. Researchers also found that women's vigorous activity at age 50 was better at predicting their current vigorous activity than was their activity at age 18 or 35. These findings suggest that establishing and maintaining vigorous physical activities is possible in mid-life, but women may want to think about finding help to stay active as they grow older.

Insurance Coverage and Cancer Screening
Although having screening tests to detect cancer is important for all women, not everyone carries health insurance that covers the costs of these screenings. WHI investigators looked at health insurance coverage and screening for breast, cervical, and colorectal cancer among groups of OS participants. The data showed that women with prepaid health insurance were more likely to have mammograms, Pap smears, and colorectal cancer screening than were women without prepaid health insurance. The good news about OS participants: overall more than 80 percent of you reported having a mammogram within the last two years and a Pap smear within the last three years. However, only about 60 percent reported having colorectal cancer screening within the last five years. Screening tests for colorectal cancer include having regular testing for blood in the stool and a flexible sigmoidoscopy. Please talk with your doctor if you want to know more about any of these important tests.

High Blood Pressure and Its Treatment

High blood pressure, or hypertension, is a major risk factor for stroke and heart disease, but fortunately there are many ways to get it lowered. We looked at blood pressure data from WHI participants to see how many had hypertension and how it was being treated and controlled. We found that 38% of WHI women had hypertension (equal to or above 140/90 mm HG) or were on medication for high blood pressure. Of those with hypertension, about two-thirds were being treated with medications, but only about one-third of hypertensive women had their blood pressure under control. Of those being treated with medication, about 70% had their blood pressure controlled with one type of drug and 20% had to use two or more types. African-American and Asian women were more likely to have hypertension than White or Hispanic women, but less likely to have their blood pressure under control. Twice as many women over age 70 had hypertension (53%) compared to women aged 50-59 years (27%). Older women, who are most at risk for stroke and other consequences of high blood pressure, were also less likely to have their blood pressure under control. The next time you have your blood pressure taken, ask what the measurement showed. If it was equal to or above 140/90, you may want to ask your healthcare provider how to control it better. There are many effective medications that can help control hypertension and potentially lower the risk for cardiovascular disease.


Breast Cancer and Body Weight

Obesity has generally been associated with an increased risk of breast cancer among postmenopausal women. More recently, scientists have wondered if other weight-related factors, such as the amount of weight gained over one’s lifetime or the way body weight is distributed, might be even more important in predicting this risk. WHI investigators looked at weight, weight distribution, and weight gain in OS participants who did and did not develop breast cancer in the two to four years after menopause. Because of recent WHI findings on hormone use, they analyzed the data separately for those who used hormone therapy (HT) and those who did not. Among women who had never used HT, heavier women had a greater risk of getting breast cancer than slimmer women. The amount of weight gained over a woman’s lifetime also predicted risk, in that greater weight gains resulted in greater risk. Weight distribution, which is the measure of waist to hip circumference, was not related to breast cancer risk in this study. For women who had used HT, none of these factors (weight, weight gain, or weight distribution) appeared to affect breast cancer risk. This study confirms that for women who never used HT, current weight is an important and potentially controllable risk factor in the prevention of postmenopausal breast cancer.

Walking may be as beneficial as more strenuous exercise in helping protect the heart.

Exercising to Protect the Heart
Regular physical activity is known to protect the heart, but scientists have been uncertain whether the benefits of walking are similar to more vigorous exercise. Research on this subject has been limited, particularly among women of color. WHI researchers looked at data from OS participants to study the links between total physical activity, walking, and vigorous exercise and risk of heart disease. They found that increased physical activity was strongly related to a lower risk of heart disease. White and black women both had similar decreases in heart disease risk (30-40 percent) with increasing activity. Strenuous exercise and walking were associated with similar decreases in risk. Ethnicity, age, or body mass index did not affect this relationship. This research suggests that walking may be as beneficial as more strenuous exercise in helping protect the heart.


Predicting Mammogram Use
Even though mammography (an X-ray exam of the breasts) is an effective method for detecting breast cancer in women ages 50 and older, many women do not get mammograms. In this study, scientists looked at factors that might predict mammography use. Their analyses showed the following factors were strongly associated with whether or not women had regular mammograms: having health insurance, a regular medical provider, an annual household income greater than $20,000, a high school diploma, and being 65 years or older. The most significant factor was having a medical provider. For WHI participants and all women, these results underscore the importance of having a regular medical provider and getting routine exams.

Bush RA and Langer RD. The effects of insurance coverage and ethnicity on mammography utilization in a postmenopausal population. Western Journal of Medicine 1998;168:236-240

Sleep Habits
Being well-rested can enhance the overall quality of your life. Looking at data provided by OS and CT participants at the beginning of the study, investigators found that white women reported an average of 6.9 hours of sleep each night, while minorities reported less sleep. For example, Hispanic women reported an average of only 6.5 hours of sleep each night. Only 27 percent of women overall reported sleeping 8 hours or more each night. Women who reported that they were retired or unemployed slept only 6 to 12 minutes more than those who were employed. Waking up several times a night and waking up earlier than planned was reported by the majority of participants. Napping increased dramatically in postmenopausal women from age 50-54 to age 75-79, but other sleep symptoms were not strongly age-related. Those sleeping 9 or 10 hours and those sleeping 6 hours or less were more obese and more depressed than those sleeping 7 or 8 hours. These interesting results suggest that sleeping longer may be associated with some of the same health issues as not getting enough sleep.

Inflammatory Biomarkers and Heart Disease

Postmenopausal hormone therapy (HT) has been shown to raise the level of a certain protein in the blood called C-reactive protein (CRP). CRP is an inflammatory biomarker, which is a sign of some sort of reaction that resembles inflammation. This protein, along with other inflammatory biomarkers, has been shown to be predictive of risk for heart disease in other studies. WHI scientists were interested to look at the effect of HT on CRP and cardiovascular risk in WHI OS women. They looked at 304 OS women who had developed coronary heart disease (CHD) and compared them to 304 women matched by age, smoking status, ethnicity, and follow-up time who had not developed heart disease. Researchers found that levels of CRP were higher among women with heart disease than women without heart disease. As expected, current use of hormone therapy was associated with higher CRP levels. However, they found that the baseline level of CRP in the blood at the time the women joined the study was a predictor of heart disease risk, whether or not the women used hormone therapy. Since exercise, a healthy diet, and smoking cessation lower CRP levels, the researchers conclude that making these types of lifestyle changes continue to be the most important ways to prevent heart disease.


Breast Cancer and Nonsteroidal Anti-inflammatory Drugs

Can use of certain types of anti-inflammatory drugs help reduce breast cancer risk? WHI Investigators looked at the effects of regular use of aspirin, ibuprofen, and other nonsteroidal anti-inflammatory drugs (NSAIDs) on breast cancer risk in WHI participants. They found that women who reported regular NSAID use (two or more tablets per week) for 5-9 years had a 21% reduction in the incidence of breast cancer, while those taking NSAIDs for 10 or more years had a 28% reduction. As duration of NSAID use increased, breast cancer incidence decreased. The risk reduction for long-term use of ibuprofen was greater than for aspirin. Regular use of acetaminophen or low-dose aspirin (<100 mg), which do not have the same anti-inflammatory effect, did not show a similar reduction in breast cancer risk. While these results are promising, they do not suggest that women should start taking NSAIDs to reduce breast cancer risk. There are many risks associated with NSAID use, so further research is needed before any sort of recommendation regarding NSAID use can be made.


Statin Use, Broken Bones, and Bone Density

Can cholesterol lowering drugs impact bone density and fractures (broken bones)? Recent laboratory studies have shown that cholesterol-lowering drugs called statins may help stimulate bone formation, which caused scientists to wonder if statins might help prevent bone fractures. WHI researchers examined data on statin use, bone density, and broken bones provided by OS participants to see if this might be the case. Specifically, they looked at the association of statin use with levels of bone density and rates of hip, arm/wrist, and other
fractures. They found that the rates of these types of broken bones were similar between statin users and nonusers, regardless of how long statins had been used. Bone density levels also did not differ between statin users and nonusers. Their conclusion was that statin use did not improve fracture risk or bone density in OS participants. Therefore, using statins to prevent osteoporosis is not recommended.


Physical Activity and Risk of Breast Cancer
Can participating in moderate physical activity (e.g., brisk walking) help reduce the risk for breast cancer? Women who engage in regular exercise have been shown to have a lower risk for breast cancer, but it was not clear whether life-long, strenuous physical activity was necessary. After examining reported physical activity and breast cancer rates in OS women, WHI scientists confirmed that breast cancer risk was lower in women who were more active. Women who currently engaged in 1.25 to 2.5 hours per week of brisk walking had an 18% lower risk of breast cancer compared with inactive women. The risk was even lower for women who walked briskly for 10 hours or more per week. This study suggests that increased physical activity is related to reduced breast cancer risk, that longer duration of exercise provides more benefit, and that the activity itself need not be strenuous.


We have provided a very brief peek at just a few of the many articles that have been published about Observational Study participants. For years to come, scientists will be busy studying and analyzing the OS data, and study results will continue to be published in scientific journals. Check the WHI participant website (www.whi.org) from time to time for an updated list of publications. You can expect to receive a newsletter highlighting major study findings from all WHI components in the spring of 2006. If your address changes in the next few years, be sure to notify your local clinical center so that we can keep you on our mailing list.

Because the contributions that you are making to women's health through the WHI are so important, WHI scientists have made a strong case to continue parts of the study until 2010. We feel this is valuable because longer-term information can help us answer questions about less common diseases like ovarian cancer and specific types of heart disease and breast cancer. At press time, this plan was still being reviewed. If a follow-up study is funded we would invite you to continue providing information about your health by mail.

The data you provide today is just as important as the data you've provided over the years, because scientists are looking at changes in women's health over time. So, thank you in advance for completing the current set of forms. We extend an even bigger thank you from the WHI staff and investigators, and from women everywhere, for all you've done over the years. WHI would not have been possible without each and every one of you! You are all part of the answer!