WHI Perspectives:  
A Look Back at the History of WHI

Back in 1993, medical researchers across the country began doing what they’d never done before: taking a long, hard look at the most pressing health issues facing American women. That year, as you may recall, marked the beginning of WHI, a 12-year, $625-million study, sponsored by the National Institutes of Health (NIH) and designed to look at the causes of disease and death in midlife and older women.

Calling it "the mother of all trials," then NIH Director Dr. Bernadine Healy, said it would be the largest clinical study ever conducted in the United States. "Big problems call for big solutions," Dr. Healy said in announcing the initiative, "and that's exactly what the Women's Health Initiative is."

The action came after several tough years for health research, in which the nation's leading research centers were being widely criticized for historically excluding women from medical research. As a result, critics pointed out, medical treatments were routinely prescribed for women today that were never clinically tested as being safe or effective for women. "Men's hormones set the standards for us all," explained Dr. Healy.

Around the same time that the lack of information about disease prevention in women was becoming clear, Dr. Healy was appointed the first woman to head NIH. Her appointment was also timely since the baby boom generation was soon to enter menopause, and the medical community had little information on how to prevent major diseases as women grew older. Dr. Healy moved quickly to support a comprehensive study of women's health, which became WHI. In 1991, she lobbied for funding from Congress, and initial planning for the program got underway with involvement from scientists across NIH.

NIH has many institutes, each focusing on a different aspect of health. WHI involved many of the institutes, reflecting the huge

What's Inside ...

5 The Women of the WHI Clinical Trials
   - Who are the women of the Clinical Trials?.............. 5
   - What are your families like?.......................... 6
   - What are your health and lifestyle habits?............. 7
   - How is your health?.................................. 8
   - What have you contributed to WHI?..................... 9

10 Focus on WHI Findings
   - Major findings from the E+P Hormone Program ...... 10
   - Findings from the E-Alone Hormone Program......... 12
   - Findings from the Dietary Study....................... 12
   - Findings from the Calcium/Vitamin D Program...... 14
   - WHI findings from the Observational Study........... 14

16 What's Next?
The very magnitude of the study sent a signal to the best institutions in the country that women’s health was the place to be. Researchers flocked to the field, and a virtual army of women stepped forward to make the initiative work.

— Dr. Healy

their personal commitment to the success of this landmark study.

“The very magnitude of the study sent a signal to the best institutions in the country that women’s health was the place to be,” said Dr. Healy. “Researchers flocked to the field, and a virtual army of women stepped forward to make the initiative work.”

Initially, volunteers were recruited for 16 “Vanguard Clinical Centers,” the first of 40 Clinical Centers to carry out the study. To reach a wide cross-section of women, 10 centers focused on recruiting mainly African American, Latina, Asian American/Pacific, or Native American participants. Once all 40 Clinical Centers were on board, the number of women who volunteered to be part of WHI was staggering: 93,676 in the Observational Study, 48,835 in the Dietary Study, 27,347 in the Hormone Program, and 36,282 in the Calcium/Vitamin D Program.

“These women, drawn from all walks of life and from varied ethnic and racial backgrounds, are sharing their health experiences and donating blood samples to be stored for future use,” noted Dr. Healy. “Together they are already broadening our understanding of women’s well-being—and they will continue to expand our knowledge as scientists link their medical histories with our ever-growing insights into the genetic and environmental basis of disease.”

Dietary Study: 20 Years in the Making

Some women in the WHI Dietary Study have been faithfully participating in study activities for as long as 10 years, and all participants have been a part of WHI for at least five years. That’s a long commitment to a research study! But did you know some WHI staff and scientists have been working toward the Dietary Study for 20 years?

Back in 1984, about 150 women in Seattle, Cincinnati, and Houston gave up many of their favorite high-fat foods to begin trying to answer the question: Will a low-fat diet decrease the risk of breast cancer? They changed their eating patterns to limit their fat intake to 20 percent of their total calories, while a similar number of women in the study ate their usual diet.

This project, sponsored by the National Cancer Institute (NCI), was a small study to see if the participants could make a major change in their fat intake and stick with it—and they did! With that success, the program—the Women’s Health Trial (WHT)—began recruiting more women. However, WHT was canceled two years later mainly because it was felt the plan to enroll 30,000 women and the $130 million cost was too much. Critics wondered if those women could really stay on a diet for 10 years.

Surprise, though—nearly six years later, most of the original participants were still on the low-fat eating plan, despite the study’s end. Those volunteers didn’t know it then, but sticking to the eating pattern helped to finally launch WHI. Their dedication helped get the attention of NIH.

“If they hadn’t done that, WHI may never have happened,” said Dr. Maureen Henderson, an investigator in both WHT and WHI. “It sort
of brought home the fact that once they make a change, many stay with it.”

“NCI received proposals for a full-scale study of a low-fat eating pattern and continued to fund related feasibility studies during the late 1980s and early 1990s,” says Dr. Ross Prentice, who headed the Statistical Coordinating Center for these feasibility studies, and is Principal Investigator for the WHI Clinical Coordinating Center. “However, it is quite unclear whether a full-scale dietary modification study would have ever arisen without Dr. Healy’s resolve and leadership.”

He continues, “The scientific literature was, and is, divided as to whether undertaking a low-fat eating pattern in the middle and later decades of a woman’s life will reduce the risk of cancer and other diseases. It is a tribute to the 48,835 Dietary Study participants, each of whom has given much time and effort for many years, that we will soon have reliable information on these important topics. This is a wonderful contribution to women’s health, for the present and for future generations.”

**Hormone Program: Changing Views and Practices**

Heart disease is the leading cause of death in women overall. A woman’s chance of having a heart attack rises quickly with age after menopause.

When WHI began, scientists believed that hormone therapy protected post-menopausal women from heart disease, as well as from fractures related to osteoporosis. However, those beliefs came from observational studies. Those studies use information about whether women did or didn’t take certain medications. But they can’t tell us if the women who took those medicines were different to begin with—maybe healthier or more likely to have good health habits—than women who didn’t use them. Did hormones keep women healthier, or did healthier women take hormones? A clinical trial like the WHI Hormone Program is the gold standard for dealing with such concerns. Also, did hormone therapy affect other diseases, such as stroke, breast cancer, dementia, or colon cancer? Clearly, there were many questions begging for answers.

During the early 1990s, there was increased use of hormones to prevent heart disease and other chronic diseases, and women began using the hormones for many years at a time. The belief that hormone use was beneficial to women’s health was not based on proof. When NIH looked at the most important women’s health issues, it realized that those diseases which may be affected by hormones, such as heart disease, stroke, breast cancer, and hip fractures, occurred often in women. It became an important priority to prove once and for all whether hormones prevented heart disease, and whether hormones improved overall health.

“If the hormone trials had been positive, the WHI findings would have led to an even greater use of hormones by older women. The question would have been, ‘Why not go on hormones?’ rather than ‘Should I take hormones?’” explains Dr. Jacques Rossouw, WHI Project Officer at the National Heart, Lung, and Blood Institute. “As it turned out, hormones did not prevent heart disease, and increased the risk for stroke. There were benefits, like fewer hip fractures. Estrogen combined with progestin increased the risk for breast cancer. All in all, the findings did not favor the widespread use of hormones to promote better health.”

The result? Hormone use dropped dramatically, and now these drugs are used mainly for their original purpose: to treat the symptoms of menopause. Seldom in the history of medicine has a single study had such a marked effect on medical practice.

“These important findings, and the effect they had on women’s health, were made possible by the contribution of each participant in the
study. WHI women truly provided answers for their children and grandchildren,” says Dr. Rossouw.

Calcium/Vitamin D Program
More than 350,000 people suffer a hip fracture each year in the U.S. Nearly all these fractures occur in people age 65 and older. Women over age 65 have a 20% chance of suffering a hip fracture during their lifetime, which can result in decreases in quality of life, disability, and death. Women with thinner hip bones have a greater chance of breaking a hip, so finding ways to build stronger bones or stop bone loss is important. Observational studies showed a link between taking calcium and vitamin D supplements and a lower risk of hip and other fractures. Also, some studies found that men who had a lot of calcium in their diets had much lower rates of colon cancer. Was the same true for women? Would these supplements hold up to a clinical trial? WHI wanted to find out.

“Although many health experts were already recommending calcium and vitamin D for bone health, it was clear in 1991 that few women or men were taking that advice,” according to Dr. Joan McGowan, WHI Project Officer at the National Heart, Lung, and Blood Institute. “It is important to have hard evidence that the supplements will prevent bone fractures in order to justify and implement a large public health effort to change individual behavior and clinical practice.”

The Power of the Observational Study
While the three studies described above will help answer many important questions about women’s health, WHI included an Observational Study (OS) to find answers to additional questions. The OS is different from the other WHI studies in that it does not involve an intervention, such as a special eating pattern or taking study pills.

The OS has two major purposes. One is to look at other important health problems not being studied in the WHI Clinical Trial. The OS can provide valuable information on less common diseases like ovarian cancer; age and ethnic differences in diet, weight, and economic status; and everyday experiences that affect quality of life. The second purpose of the OS is to provide a comparison group that may help us interpret the Clinical Trials. Lots of things change in our society over 10 years: new foods and diet recommendations emerge, new treatments become available, exercise fads come and go. Women in the OS reflect those trends and, like those in the Clinical Trials, provide information annually about their health. Having information from both groups helps researchers get additional value out of both types of studies. Information from the OS will have an impact on healthcare for women in the future and on the design of new interventions to improve long-term health.

“The OS has an amazing variety of information. It can help us learn about the full range of women’s health, from the most important and frightening diseases, to the nagging everyday problems, to things that might predict healthy aging,” says Dr. Robert Langer, Principal Investigator, La Jolla WHI Clinical Center. “It is a powerful resource that will point the way to tests of new treatments to help keep women healthy.”

Our Thanks to You
The hope and promise of WHI would have been fruitless without the dedicated efforts of you and every WHI participant. Only by so many women stepping up to give their time and effort to the future of women’s health has WHI met its goals. While we don’t yet know most of the study results, there is no doubt that the commitment of our participants will result in more knowledge and understanding.

As Dr. Healy said in 1993, “The women of the ‘90s have spoken out, prodded, pressed, participated, marched and raced to claim what is rightfully ours. The ‘revolutionaries’—people from every walk of life and every corner of the land—share a passion to make life better for their daughters and granddaughters as well as themselves. And they’re succeeding.”
The Women of the WHI Clinical Trials

The very first woman joined the Women's Health Initiative (WHI) in October, 1993. By the end of enrollment in December, 1998, a total of 161,900 women across the U.S. had joined the WHI. Of those, 68,132 were enrolled in one or more of the three Clinical Trials (CT): the Hormone Program, the Dietary Study, or the Calcium/Vitamin D Program. An additional 93,676 had joined the WHI Observational Study, making WHI one of the largest studies ever done. This is a tremendous achievement and we have you to thank!

Each WHI participant has answered hundreds of questions about her health and lifestyle habits. These data have become a major resource that adds to what we know about women's health. Now that we’re near the end of the study, we’d like to share with you some of the data you’ve provided over the years.

First, we'll use that information to create a "picture" of the CT women as a group, and then we’ll share some of the WHI study findings so far.

Who are the women of the WHI Clinical Trials?

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 chronic diseases tend to occur more as women age, it is particularly important to study women in their later years. As shown in the chart below, 40% of our CT participants were aged 65 or over when they joined the study. The average age of CT participants was 62.7 years. Women in the CT were slightly younger than women in the OS component, where the average age was 63.6 years.

<table>
<thead>
<tr>
<th>Age at Enrollment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-74</td>
<td>13.6%</td>
</tr>
<tr>
<td>75-79</td>
<td>5.3%</td>
</tr>
<tr>
<td>50-54</td>
<td>13.5%</td>
</tr>
<tr>
<td>65-69</td>
<td>21.3%</td>
</tr>
<tr>
<td>60-64</td>
<td>24.7%</td>
</tr>
<tr>
<td>55-59</td>
<td>21.5%</td>
</tr>
</tbody>
</table>

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 affect long-term health and well being. The chart below shows the racial/ethnic diversity of CT participants.

<table>
<thead>
<tr>
<th>Ethnicity of Participants in the CT</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian or Alaskan Native</td>
<td>293</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>1,521</td>
</tr>
<tr>
<td>Black or African-American</td>
<td>6,988</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2,889</td>
</tr>
<tr>
<td>White</td>
<td>55,521</td>
</tr>
<tr>
<td>Unknown</td>
<td>921</td>
</tr>
<tr>
<td>Total</td>
<td>68,133</td>
</tr>
</tbody>
</table>
As shown below, women in the CT 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.

---

**What are your families like?**

Collectively, the 68,132 women of the CT have had over 195,152 children! The chart on the following page shows the number of births participants reported.

When the study began, about 41% (28,125) of our participants reported that they cared for an ailing family member or friend. For those of you who provided care, 22% did so less than once a week, while 25% provided care 5 or more times per week.

In terms of your living arrangement when the study started, 28% of you were living alone and 68% with a husband or partner. Almost 17% of you lived with your children and 18% with other relatives, friends, or roommates. CT participants also have plenty of animal companionship – over 44% have at least one pet. For those of you who have a pet, as you might guess, dogs and cats are most common.

---

It's great for the mind and body to stay active. WHI participants like to join in group activities. At least once a month, 67.4% attended religious services and 55.7% attended club meetings.
What are your health and lifestyle habits?

Over half 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 WHI women like you at the time they joined the study.

Exercise: At the start of the study, over 21% of CT participants reported getting strenuous exercise at least one day per week, over 42% reported moderate exercise weekly, and 27% reported getting mild exercise weekly. About half 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 CT participants on average got 37% of their calories from fat and are nearly 4 servings of fruits and vegetables per day. National recommendations are to eat 30% or fewer calories from fat and 5 or more fruit/vegetable servings per day.

Smoking habits: Nearly 51% of you have never smoked and an additional 41% managed to successfully kick the habit. Congratulations!

Alcohol: About 71% of CT women had an alcoholic beverage at least once a month, while 29% chose not to drink at all. Of those who did drink, most preferred wine over beer or other types of liquor.

Coffee and tea: Nearly 62% of you report 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 CT participants drink per day.

Average Number of Cups of Coffee Per Day

- 6 or more cups: 3.2%
- 4-5 cups: 10.3%
- 2-3 cups: 33.6%
- 1 cup: 15.2%
- None: 37.7%
Sleep habits: As shown below, the sleeping habits of CT women vary greatly, with some reporting less than 5 hours per night and others getting 9 or more!

<table>
<thead>
<tr>
<th>Hours</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 or less</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
</tr>
<tr>
<td>9 or more</td>
<td></td>
</tr>
</tbody>
</table>

Use of supplements: When you joined WHI, we asked if you were taking vitamin or mineral supplements. Nearly half of you — 48% — responded yes. About 32% of you took multivitamins with minerals. Among single supplement preparations, Vitamin E was the most commonly taken, with 25% of you reporting its use. Vitamin C was close behind, with 23% reporting its use.

Weight changes: At the beginning of the study, the average CT participant weighed 168 pounds and was 5 ft-4 inches tall. The average weight was higher for women in the younger age groups. When asked about weight changes during adulthood, 25% of you reported that your weight had stayed the same, 37% had gained weight, 2% had lost weight, and 37% of you said that your weight went up and down.

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 CT women when they joined the study. To use the Internet to calculate your own BMI, go to: www.nhlbisupport.com/bmi.

<table>
<thead>
<tr>
<th>BMI Category</th>
<th># of ppts</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (BMI &lt; 18.5)</td>
<td>290</td>
<td>0.4</td>
</tr>
<tr>
<td>Normal (18.5 - 24.9)</td>
<td>18,247</td>
<td>26.9</td>
</tr>
<tr>
<td>Overweight (25.0 - 29.9)</td>
<td>24,205</td>
<td>35.7</td>
</tr>
<tr>
<td>Obese (&gt; =30.0)</td>
<td>25,054</td>
<td>37.0</td>
</tr>
</tbody>
</table>
How is your health?
A number of women deal with ongoing health problems, particularly as they grow older. Below are the numbers of CT participants who have had some of the more common health issues. Keep in mind that generally healthy women joined WHI, so the rates of health issues might be lower in WHI than in the general population. Sadly, over 2,800 CT 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.

<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>16,188</td>
<td>15,639</td>
</tr>
<tr>
<td>Diabetes (treated with pills/shots)</td>
<td>3,265</td>
<td>4,476</td>
</tr>
<tr>
<td>Heart Attack</td>
<td>1,397</td>
<td>1,348</td>
</tr>
<tr>
<td>Stroke</td>
<td>750</td>
<td>1,288</td>
</tr>
<tr>
<td>Broken hip</td>
<td>517</td>
<td>584</td>
</tr>
<tr>
<td>Endometrial (uterine) cancer</td>
<td>460</td>
<td>301</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>246</td>
<td>197</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>106</td>
<td>616</td>
</tr>
</tbody>
</table>

What have you contributed to WHI?
Taken together, the data described above help us to understand the health and lifestyle habits of postmenopausal women. Over the past several years, you have been contributing data by filling out questionnaires, providing physical measures and blood samples at your clinic visits, and having screening tests like mammograms and pap smears. Here are some amazing facts showing all you’ve given over the years:

- CT women have completed over 4,822,500 forms to date
- CT women have completed over 750,000 total clinic visits, including screening, semi-annual, and annual visits
- CT women have had 336,228 mammograms, 89,855 pap smears, and over 140,000 blood draws
- In the Hormone Program, over 750,000 bottles of pills were dispensed, which is over 215 million pills
- Dietary Study participants have completed nearly 175,000 food frequency questionnaires and over 50,000 Four Day Food Records

- In the Calcium/Vitamin D Program, nearly 500,000 bottles of pills were dispensed — almost 160 million pills
- Combined, CT and OS participants attended over 1,000,000 clinic visits and completed over 7,500,000 forms.

As you can see, you and your WHI sisters form a diverse, fascinating group of women who have accomplished something truly incredible. All of this information 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. 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

The information you have provided over the years will 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. Information provided by women in the Hormone Program has already led to important breakthroughs in the healthcare of postmenopausal women.

In the pages that follow, we summarize some of the important findings on hormone use in postmenopausal women. We will also discuss some of the questions we hope to answer when the findings of the other programs are released in 2006. Finally, we include brief summaries of just a few of the many findings on OS women that have been published in the past several years.

Major findings from the E+P Hormone Program

As reported in previous issues of your newsletter, 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.

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 taking active E+P than in those taking placebo. Fewer women on these combined 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 active 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 study in much more detail, taking into account additional health conditions that these women reported before they stopped their study pills. These analyses confirmed the earlier findings and provided additional information, including:

- Breast cancer tumors in the E+P group tended to be larger and at a more advanced stage than those in the placebo group. Also, more women in the E+P group had abnormal mammograms compared to the placebo group.
- Taking active E+P offered no clear improvement in quality of life, such as perceptions of general health, energy, social functioning, mental health, depression, and sexual satisfaction.

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.
... findings indicate that the overall risks of estrogen plus progestin hormone therapy outweigh the benefits.

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

- Women taking active E+P had 19% fewer endometrial (uterine) cancers, compared to placebo. This made their risk similar to or slightly lower than national rates of endometrial cancer. 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 difference may be due to chance.

- E+P does not protect women from normal declines in cognitive function when compared with placebo. In addition, women in the active 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.

- Fewer women taking active E+P had colorectal cancer than those taking placebo. Because of E+P use, there were 6 fewer cases of colorectal cancer for every 10,000 women per year. Overall, there was a 44% decrease in the risk for colorectal cancer due to E+P.

Taken together, these findings indicate that the overall risks of estrogen plus progestin hormone therapy outweigh the benefits. Results from the Estrogen-Alone part of the Hormone Program, which included women who had already had a hysterectomy at the time they joined the study, were analyzed and published separately.
Focus on Findings

Findings from the E-Alone Hormone Program

In March 2004, participants in the Estrogen-Alone (E-Alone) part of the Hormone Program were also asked to stop taking their study pills and to enter the follow-up phase of the study. Data provided by these participants showed that there were both benefits and risks to taking estrogen alone. Specifically, the E-Alone study showed that estrogen alone does not appear to affect the risk of heart disease or increase the risk of breast cancer. At the same time, estrogen alone appears to increase the risk of stroke and to decrease the risk of hip fracture. After nearly 7 years of study, the NIH felt that enough data had been obtained to provide an overall assessment of the risks and benefits of estrogen alone and that these results were not likely to change if study pills were continued for another year. The NIH believes that an increased risk of stroke is not acceptable in healthy women in a research study, especially since it appears that estrogen alone does not prevent heart disease.

WHI researchers published these results in the spring of 2004. Additional analyses and findings—for example looking at the effect of estrogen on quality of life and cognitive decline—will be published in the months to come. All participants will receive a summary of these findings in a newsletter in 2006.

The time and effort of women in both parts of 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.

Findings from the Dietary Study

The Dietary Study was designed to help us learn if a low-fat eating pattern high in fruits, vegetables, and grains reduces the risk of breast cancer, colorectal cancer, and heart disease in postmenopausal women. By 1998, a total of 48,835 women had joined the Dietary Study to help answer this question.

Sixty percent of these women were randomly assigned to participate in the Comparison part of the study and were asked to eat as usual. The Comparison group is very important to the study. Without this group of women who continued to eat as usual, scientists cannot tell if differences in disease risk are due to the dietary changes that are part of the Dietary Study or other unrelated changes.

Forty percent of women in the Dietary Study were randomly assigned to the Dietary Change part of the study. These women were asked to lower their fat intake to 20% of energy (calories) and received individualized targets for the amount of fat (in grams) they could eat each day to achieve this goal. Another study goal was to have women reduce their intake of saturated fat to 7% of energy. Because people usually eat less saturated fat when they decrease total fat in their diet, women were not given a specific saturated fat goal. Women in the Dietary Change group were also given goals to eat five or more servings of fruit/vegetables daily, and to eat six or more servings of grain daily. To help make and maintain these changes, women in the Dietary Change group were asked to attend group sessions and to monitor their intake of fat, fruit/vegetables, and grains.

"...the E-Alone study showed that estrogen alone does not appear to affect the risk of heart disease or increase the risk of breast cancer. At the same time, estrogen alone appears to increase the risk of stroke and to decrease the risk of hip fractures."
At the start of the Dietary Study, before women made any changes to what they ate, they reported a fat intake of about 36% of energy, saturated fat about 13% of energy, fruit/vegetable servings about four daily, and grain servings about four daily. The table below shows dietary intake for women in both the Comparison and Dietary Change groups after the first year of the study and then toward the end of the study, in Years 6-8.

<table>
<thead>
<tr>
<th>Total Fat, Saturated Fat, Fruit/Vegetable, and Grain Intakes</th>
<th>Comparison Group</th>
<th>Dietary Change Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of energy from total fat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>36%</td>
<td>25%</td>
</tr>
<tr>
<td>Years 6-8</td>
<td>39%</td>
<td>30%</td>
</tr>
<tr>
<td>% of energy from saturated fat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>13%</td>
<td>9%</td>
</tr>
<tr>
<td>Years 6-8</td>
<td>14%</td>
<td>10%</td>
</tr>
<tr>
<td>Fruit/Vegetable servings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>4 servings</td>
<td>5 servings</td>
</tr>
<tr>
<td>Years 6-8</td>
<td>4 servings</td>
<td>5 servings</td>
</tr>
<tr>
<td>Grain servings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>4 servings</td>
<td>5 servings</td>
</tr>
<tr>
<td>Years 6-8</td>
<td>4 servings</td>
<td>4 servings</td>
</tr>
</tbody>
</table>

Unlike the Hormone studies, major results for the Dietary Study are not yet known. Nonetheless, some interesting findings from the Dietary Study have been published:

- Before joining WHI, women who were interested in participating in the Dietary Study reported a variety of low-fat eating practices. For example, 69% of the women reported that they rarely or never ate skin on chicken, 76% rarely or never ate fat on meat, 36% usually drank fat-free milk, and 59% ate low-fat snacks or chips.

- After one year in the Dietary Study, the major differences in dietary fat intake between Comparison and Dietary Change women were that the Dietary Change group ate fewer of the following: fats added to foods (such as spreads and salad dressings), meats, desserts, milk and cheese, mixed dishes and soups, and high fat breads and salty snacks.

- For women in the Dietary Change group:
  - 74% monitored their own intake of fat, fruit, vegetable, and grain servings during the first year of intervention, and many continued to use a variety of monitoring aids throughout the study.
  - Women who reported less physical pain and better physical functioning, general health, and mental health at the beginning of the study seemed to follow the low-fat diet more closely during the first year of the Dietary Study.
  - For women in general, attending dietary change group sessions and monitoring their diet improved their adherence to the low-fat eating pattern.

In early 2006, results of the Dietary Study are expected to be available. At that time, WHI participants and the world at-large will find out if a low-fat eating pattern helps reduce the risk of breast and colorectal cancers and heart disease in postmenopausal women.
Findings from the Calcium/Vitamin D Program

The Calcium and Vitamin D (CaD) Program will help us learn if taking daily supplements of calcium and vitamin D reduces the risk of hip and other fractures and cancers of the colon and rectum in postmenopausal women. A total of 36,282 women were enrolled in this program to help answer these questions. Half of the women were randomly assigned to take the “active” CaD supplement and half to take the “placebo”.

You may remember that all WHI participants were given current dietary recommendations about getting at least 1200 mg of calcium in their diet each day. To be sure that CaD participants — even if they were taking placebo pills — were getting adequate calcium, they were told they could take their own supplements of calcium and vitamin D. Even with personal calcium use, the CaD Program will tell us a great deal about the effects of calcium and vitamin D on women’s health, because we will be able to compare health effects between the active and placebo groups of women. Neither the participants nor the staff at the Clinical Centers knew which group women were assigned to. This information was stored in the computer database and is being released to you as part of your close-out visit.

We have answers from WHI about the effects of hormones on postmenopausal women’s health; the interventions for the Hormone Program were stopped early. Women, health care providers, and scientists throughout the world still await answers about CaD and women’s health; that intervention is continuing through to the originally planned end of WHI. We eagerly await the results of this study in 2006.

WHI Findings from the Observational Study

In addition to the many findings from the three Clinical Trials, many scientific papers have been published over the last few years based on analyses of Observational Study (OS) data. These findings, a few of which are summarized below, greatly extend our knowledge about women’s health. Data collected from women in the OS will continue to be analyzed and should provide important information about women’s health in the years to come.

- **Exercising to protect the heart**: Regular physical activity is known to protect the heart, but scientists have not known whether the benefits of walking are similar to more vigorous exercise. Data collected from OS participants confirmed that increased physical activity was strongly related to a lower risk of heart disease. Both strenuous exercise and walking were associated with similar decreases in risk, which suggests that walking may be as beneficial in helping protect the heart.
- Physical activity and risk of breast cancer: Previous studies have shown that women who exercise regularly have a lower risk for breast cancer. However, it was not clear whether life-long, strenuous physical activity was necessary. Findings based on OS data suggest that women who did brisk walking 1.25 to 2.5 hours per week had a lower risk of breast cancer compared to women who were not active. The risk of breast cancer 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 and that the activity itself need not be strenuous.

- A predictor of heart disease: WHI researchers looked at the impact of hormone use on levels of a substance in the blood called C-reactive protein, which have predicted risk for heart disease in other studies. They found that baseline levels of this substance in the blood at the time the women joined the study did predict heart disease risk, whether or not the women used hormone therapy. Since exercise, a healthy diet, and stopping smoking will lower levels of C-reactive protein, researchers concluded that these types of lifestyle changes continue to be the most important ways to prevent heart disease.

- Breast cancer and body weight: Investigators were interested in the association between body weight factors and risk for breast cancer. They found that for women who had never used Hormone Therapy (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. For women who had used HT, weight and weight gain did not appear to affect breast cancer risk.

- Breast cancer and nonsteroidal anti-inflammatory drugs: Can use of certain types of anti-inflammatory drugs (NSAIDs) like aspirin or ibuprofen help reduce breast cancer risk? WHI investigators found that OS women who reported regular NSAID use (two or more tablets per week) for at least 5 years had a decreased risk of breast cancer compared to women who did not use these drugs. Long-term use of ibuprofen was associated with a greater risk reduction, compared to aspirin. While these results are interesting, they do not suggest that women should start taking these drugs to reduce breast cancer risk. There are many risks associated with NSAID use, so further research is needed before any sort of recommendation can be made.

"Since exercise, a healthy diet, and stopping smoking will lower levels of C-reactive protein, researchers concluded that these types of lifestyle changes continue to be the most important ways to prevent heart disease."
What’s Next for WHI?

ne have provided a very brief look at the evolution of WHI: the history, the women, and a few of the many reports that have been published about data provided by WHI participants. For years to come, scientists will be busy studying and analyzing the WHI 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 updates on published findings. You can expect to receive a newsletter highlighting major study findings from all the WHI components in the spring of 2006.

Because the contributions you are making to women’s health through the WHI are so important, WHI scientists made a strong case to continue to collect information about the health of WHI participants until 2010. We feel this is valuable because longer-term information can help us answer questions about how women’s health changes as they get older. This type of long-term follow-up can also tell us about how risk for disease changes when interventions, like those studied in the Clinical Trials, are stopped. In spring of 2004, we received the great news that the plan to continue WHI had been approved. You will be receiving additional information from your Clinical Center about joining the “WHI Extension Study”. If you decide to join the extension, we will ask you to continue providing information about your health by mail, but will not ask you to come to the Clinical Center for any exams or sessions. If you decide not to extend your participation, we understand. You have already contributed much to our understanding of the factors affecting the health of post-menopausal women. All women and the healthcare community owe you tremendous thanks for the contributions you’ve made over the years.

Our Thanks!

We extend a big 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!