The estrogen-alone study of the WHI. The estrogen-alone study of the Women’s Health Initiative (WHI), conducted through the National Institutes of Health, was designed to investigate the long-term benefits and risks of estrogen therapy (estrogen therapy is generally prescribed to women who have had a hysterectomy). After 6.8 years of treatment, the study ended early, and patients were asked to enter the follow-up phase.

- After 7.1 years of follow-up, findings regarding the incidence of heart attack, breast cancer, stroke, and new thromboembolic events (VTE) have been published.
- The average age of women who took estrogen at the start of the WHI study was 63.3 years—approximately 12 years past the average age of menopause (51.4 years) and well past the age most women start hormone therapy.
- Because this was a long-term prevention study, the study was not designed to evaluate the risk of menopausal symptoms, such as hot flashes, night sweats, and vaginal dryness, or the prevention of postmenopausal osteoporosis—two reasons why women start hormone therapy.

Evaluating the results of the WHI estrogen-alone study in perspective.

Estrogen therapy is not indicated for any of the medical conditions listed in the following chart.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of events per 1,000 women taking estrogen therapy</th>
<th>Number of events per 1,000 women taking placebo</th>
<th>Difference in risk compared with placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Attack</td>
<td>5.6</td>
<td>5.3</td>
<td>0.3 more women experienced heart attacks</td>
</tr>
<tr>
<td>Breast Cancer*</td>
<td>3.4</td>
<td>2.8</td>
<td>0.6 more women had breast cancer</td>
</tr>
<tr>
<td>Stroke</td>
<td>3.3</td>
<td>4.5</td>
<td>1.2 more women experienced stroke</td>
</tr>
<tr>
<td>Venous Thromboembolisms (Blood Clots)</td>
<td>2.2</td>
<td>3.0</td>
<td>0.8 more women had blood clots</td>
</tr>
<tr>
<td>Hip Fracture</td>
<td>1.7</td>
<td>1.1</td>
<td>0.6 more women had hip fractures</td>
</tr>
<tr>
<td>Vertebral Fracture</td>
<td>1.7</td>
<td>1.7</td>
<td>0.6 more women had vertebral fractures</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>1.6</td>
<td>1.7</td>
<td>0.1 more women had colorectal cancer</td>
</tr>
</tbody>
</table>

Conclusions:

- Estrogen did not increase the risk of heart attack or breast cancer in postmenopausal women.
- Estrogens decreased the risk of fractures at the hip and spine.
- Compared with placebo, the risk of stroke and deep vein thrombosis (certain types of blood clots) was increased.

Please see reverse side for Important Safety Information.

Deciding if estrogen therapy is right for you

- Estrogen therapy is the most effective FDA-approved medicine proven to treat moderate to severe hot flashes.
- Estrogen therapy helps to improve and maintain vaginal health.
- Estrogen therapy is proven to help prevent postmenopausal osteoporosis.
- In general, an appropriate candidate for estrogen therapy is a healthy, symptomatic menopausal woman who has undergone a hysterectomy.
- Benefits and risks of therapy are weighed along with individual risk factors, such as family history of breast cancer or stroke, and therapeutic needs, such as security of hot flashes.

When considering estrogen therapy, talk with your health care professional about

The time since your menopause started

Your benefit-risk profile

Low-dose options

Your expected duration of use

If you decide to start estrogen therapy

- Take the lowest effective dose for as short a time as possible.
- Meet with your health care professional periodically to reexamine your need for continued treatment—goals and risks change over time.

Important safety information about estrogen therapy

- Estrogen therapy is used after menopause to reduce moderate to severe hot flashes to treat moderate to severe dryness, itching, and burning, and in and around the vagina, and to help reduce your chances of getting osteoporosis (thin, weak bones).
- Estrogen therapy isn’t right for all women. It doesn’t prevent heart disease or dementia and may increase your chance of heart attack, breast cancer, stroke, or blood clots. If you have a uterus, estrogen increases the risk of uterine cancer. Adding progesterone greatly reduces this risk. The use of estrogen should be reassessed regularly with your health care provider and should be taken for the shortest time based on your individual goals and risks. If you're still having menopausal symptoms, non-estrogen treatments should be considered before starting estrogen therapy to prevent bone loss.