The Women’s Health Initiative: Hormone Therapy Trials

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WHI Webinar
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Women’s Health Initiative (WHI), Ages 50-79
Hormone Program Design

**Hysterectomy**

Women who had prior hysterectomy at start of study

**YES**

Conjugated equine estrogens (CEE) 0.625 mg/d

Placebo

N = 10,739

Women who had an intact uterus at start of study

**NO**

CEE 0.625 mg/d + medroxyprogesterone acetate (MPA) 2.5 mg/d

Placebo

N = 16,608
WHI Estrogen+Progestin Trial Findings, July 2002 (N=16,608; mean age 63 yrs; mean follow-up 5.2 yrs)

**Risks**

- Coronary Heart Disease 29% ↑
- Stroke 41% ↑
- Pulmonary Embolism 113% ↑
- Breast Cancer 26% ↑

**Benefits**

- Hip Fracture 34% ↓
- Colorectal Cancer 34% ↓

STOPPED Early, Clear Harm

Stopped 3.3 years early

Threshold Level

↑ Dementia (Age ≥65)

Adapted from data in: Writing Group for the Women’s Health Initiative. *JAMA* 2002;288:321.
WHI Estrogen-Alone and Health Outcomes (N=10,739; mean age 63.6 yrs; mean follow-up 6.8 yrs)

Risks

- Stroke 39% ↑

Null

- CHD (0.91)
- Pulm Emb (1.34)
- Breast Cancer (0.77)
- Colorectal Cancer (1.08)
- Total Mortality (1.04)
- Global Index (1.01)

Benefits

- Hip Fracture 39% ↓

STOPPED Early

Threshold Level

Stopped 1 year early

WHI Hormone Therapy Trials: Absolute Risks (cases per 10,000 person-years) for Outcomes in the Estrogen-Progestin and Estrogen-Alone Trials, by Age Group

<table>
<thead>
<tr>
<th>Major Endpoints</th>
<th>Intervention</th>
<th>Post-Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CEE+MPA</td>
<td>CEE</td>
</tr>
<tr>
<td>CHD</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Stroke</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>PE</td>
<td>↑</td>
<td>0</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>↓</td>
<td>0</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Global index</td>
<td>↑</td>
<td>0</td>
</tr>
</tbody>
</table>

### Estrogen+Progestin Therapy and Risk of Heart Attack in WHI: Results According to Time Since Menopause

<table>
<thead>
<tr>
<th>Time since Menopause Onset</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 yrs</td>
<td>Neutral</td>
</tr>
<tr>
<td>10-19 yrs</td>
<td>Slightly ↑</td>
</tr>
<tr>
<td>≥20 yrs</td>
<td>2x ↑</td>
</tr>
</tbody>
</table>

P, interaction = 0.01

### WHI Estrogen-Alone Trial: Results for Heart Attack by Age Group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>↓</td>
</tr>
<tr>
<td>60-69</td>
<td>↔</td>
</tr>
<tr>
<td>70-79</td>
<td>↑</td>
</tr>
</tbody>
</table>

\[ P, \text{ interaction} = 0.02^+ \]

<table>
<thead>
<tr>
<th></th>
<th>E+P Trial</th>
<th>E-Alone Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total mortality</strong></td>
<td>-5 +2 +2</td>
<td>-6 0 +13</td>
</tr>
<tr>
<td><strong>Global Index†</strong></td>
<td>+6 +11 +19</td>
<td>-10 -1 +25</td>
</tr>
</tbody>
</table>

†Global index is a composite outcome of CHD, stroke, pulm embolism, breast cancer, colorectal cancer, endometrial cancer, hip fracture, and mortality.

Conclusions

- Current evidence does not support the use of HT for the prevention of cardiovascular disease or other chronic diseases (due to increased risk of venous blood clots and stroke/breast CA [E+P] in all age groups).
- A personalized approach to decision making is recommended for women with menopausal symptoms.
- The best candidates for systemic HT are recently menopausal and symptomatic women in generally good health (low absolute risks and greater quality-of-life benefits).
- Additional studies of different HT formulations, doses, routes of delivery, and of non-hormonal options are needed.
Thanks to the Participants, Investigators, and Staff of WHI and other Research Studies

Thank you!