Women’s Health Initiative
Baseline Monograph: HRT Chapter

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WHI CT Sample Size, Outcomes, Follow-up
Women, aged 50-79
Total CT = 68,133

Diet Modification (DM) Trial
Primary Outcomes:
Breast & Colorectal Cancer
Secondary Outcome:
Coronary Heart Disease (CHD)

Hormone (HRT) Trial
Primary Outcome: CHD
Secondary Outcomes:
Hip Fracture, Breast Cancer
Ancillary Study: Memory

DM
48,836

HRT
27,347

Average Follow-up
DM: 8.5 years
HRT: 8.4 years
11.8% Overlap
### Background for HRT/CHD hypothesis

#### Observational Studies

- **LRC Prevalence Study** (‘83,’87)
- **Nurses’ Health Study** (‘85, ‘91)
- **Framingham Study** (‘85)-reversed
- **Nurses’ Health Study** (‘97) **PERT**
  - Survival benefit diminishes with longer duration use; is lower for women at low risk for CHD - NEJM ‘97: 336; 1769
- Many Observational Studies
  - HRT users vs nonusers (generally): less likely to smoke, leaner, more physically active, healthier, more educated, higher SES, visit MDs more often, at lower CVD risk
- **WHI (2005)**

#### Clinical Trials

- **PEPI** (‘95) healthy, aged 45-64.
  - HRT improved HDL-C (ERT > PERT) & LDL-C + fibrinogen; incr TG, CRP.
- **HERS** (‘98) prior CHD (+ uterus), aged<80.
  - PERT for MI: No benefit @ 4 yrs; incr. 1st yr, decre. 4-5 yrs; incr VTE (DVT&PE), Gallbladder D.
- **ERA** (‘00) angiographic CHD. No ERT or PERT benefit, aver 3.2 yr
- **PHASE (‘00)**; [WAVE?; WELL-HART?]
- **EPAT** LDL≥ 130; if >160, lipid-lowering-**No**
- **WEST** (‘01) recent stroke or TIA - **No**
- **WHI (2005)** women aged 50-79
WHI HRT Sample Size, Outcomes, Follow-up
Women, aged 50-79    Total HRT = 27,347

Hormone (HRT) Trial
Primary Outcome:    Coronary Heart Disease
Secondary Outcomes:
   Hip Fracture; Other Fractures
   Breast & Endometrial Cancers
WHI Memory Study (WHIMS)
   - for women 65+ - Memory

PERT 16,608
Average Follow-up 8.4 years

ERT 10,739
Average 8.4 years
WHI HRT Trial (N=27,347): Treatments
Adherence < 80% activates Intensive Adherence Program

<table>
<thead>
<tr>
<th>Women with a Uterus (55% by design): Actual = 60.7% (N=16,608)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Estrogen with Progestin (50%)</strong></td>
</tr>
<tr>
<td>Conjugated Equine Estrogen (CEE) - 0.625 mg/day +</td>
</tr>
<tr>
<td>Medroxyprogesterone Acetate - 2.5 mg/day (daily MPA)</td>
</tr>
<tr>
<td>or</td>
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<tr>
<td><strong>Placebo (50%)</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Women with a Hysterectomy (45%): Actual = 39.3% (N=10,739)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Estrogen only (50%)</strong></td>
</tr>
<tr>
<td>Conjugated Equine Estrogen (CEE) - 0.625 mg/day</td>
</tr>
<tr>
<td>or</td>
</tr>
<tr>
<td><strong>Placebo (50%)</strong></td>
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</tbody>
</table>
WHI HRT: Baseline Age Distribution

Goal: 50-54 = 10%; 55-59 = 20%; 60-69 = 45%; 70-79 = 25%

Mean ± SD: HystX-ERT = 63.6 ± 7.3; Uterus-PERT = 63.3 ± 7.1
WHI HRT: Minority Distribution

HystX: 2657/10,739 (24.7%)  Uterus: N = 2663/16,608 (16.0%)
Total HRT: N = 5320/27,347 (19.5%)

<table>
<thead>
<tr>
<th>Minority Group</th>
<th>Total Numbers of Minority Women in HRT Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blacks</td>
<td>N = 2741</td>
</tr>
<tr>
<td>Hispanic</td>
<td>N = 1543</td>
</tr>
<tr>
<td>Asian/PI</td>
<td>N = 527</td>
</tr>
<tr>
<td>Nat. Amer.</td>
<td>N = 131</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

- HystX(75.3% White)
- Uterus (84.0%)
- HRT total (80.5%)
Total HRT Goal: 50-59=30% 60-69=45% 70-79=25%
WHI HRT: Differences among Minority Groups
Whites, N=22,027; Black, N = 2741; Hispanics, N = 1543; Asian/PI, N = 527

Total Percent with Hysterectomy by Ethnic Group

![Bar chart showing the percentage of hysterectomies by ethnic group for ERT and PERT.]
WHI HRT: Age by Uterine Status and Ethnicity
Whites, N=22,027; Black, N = 2741; Hispanics, N = 1543; Asian/PI, N = 527
WHI HRT: Body Mass Index (kg/m²) by Uterine Status
Whites, N=22,027; Black, N=2741; Hispanics, N=1543; Asian/PI, N=527

Mean BMI by Ethnic Group and Uterine Status

- Total
- White
- Black
- Hispanic
- Asian/PI

HystX - ERT
No HystX - PERT
WHI HRT: Education Level

- < H.S. Diploma Equiv.: 9.9% ERT; 6.8% PERT
- Some College: 67.4% ERT; 73.8% PERT

Bar chart showing:
- HysterX-ERT
- Uterus-PERT
- HRT Total

Education levels:
- Gr 0-8
- Gr 9-11
- HS/GED
- Some College
- ≥ Coll Degree

Percentages for each level and treatment option.
WHI HRT: Baseline Body Mass Index (kg/m²)

Mean BMI: ERT = 30.1 ± 6.2; PERT = 28.5 ± 5.9; HRT = 29.1 ± 6.1

Percent Normal Weight, Overweight and Obese

<table>
<thead>
<tr>
<th></th>
<th>Hyst-ERT</th>
<th>Uterus-PERT</th>
<th>HRT Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;19</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>19-24.9</td>
<td>22.7</td>
<td>22.7</td>
<td>22.7</td>
</tr>
<tr>
<td>25-29.9</td>
<td>35.1</td>
<td>35.1</td>
<td>35.1</td>
</tr>
<tr>
<td>30-34.9</td>
<td></td>
<td>35.1</td>
<td>35.1</td>
</tr>
<tr>
<td>≥35.39.9</td>
<td>10.3</td>
<td>10.3</td>
<td>10.3</td>
</tr>
<tr>
<td>≥40</td>
<td>5.2</td>
<td>5.2</td>
<td>5.2</td>
</tr>
</tbody>
</table>

% Overwt+Obese
ERT: 79.3 %
PERT: 69.4 %
HRT: 73.3 %
WHI HRT: Moderate & Strenuous Exercise
(≥ 20 minutes/bout)

No Activity or ≤1X/wk
63.7% of HRT

Recommended by CDC: 21%
WHI HRT: Alcohol Intake and Smoking

Alcohol Intake

- Non/Past: 32.1%
- <1 drink/wk: 33.5%
- 1-<7/wk: 23.1%
- 7+/wk: 11.2%

Smoking Status

- Never Smoked: 50.3%
- Past Smoker: 39.2%
- Current Smoker: 10.5%

Legend:
- HystX-ERT
- Uterus-PERT
- Total HRT
WHI HRT: Family Income

<table>
<thead>
<tr>
<th>Family Income</th>
<th>HysterX-ERT</th>
<th>Uterus-PERT</th>
<th>Total HRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; $20,000</td>
<td>6.7%</td>
<td>16.8%</td>
<td>28.3%</td>
</tr>
<tr>
<td>$10,000 - $19,999</td>
<td>20.5%</td>
<td>20.4%</td>
<td>16.4%</td>
</tr>
<tr>
<td>$20,000 - $34,999</td>
<td>28.2%</td>
<td>16.4%</td>
<td>22.9%</td>
</tr>
<tr>
<td>$35,000 - $49,999</td>
<td>20.4%</td>
<td>16.4%</td>
<td>22.9%</td>
</tr>
<tr>
<td>$50,000 - $74,999</td>
<td>20.4%</td>
<td>16.4%</td>
<td>30.9%</td>
</tr>
<tr>
<td>&gt; $75,000</td>
<td>11.4%</td>
<td>16.4%</td>
<td>22.9%</td>
</tr>
</tbody>
</table>
WHI HRT: Marital Status

Percent

Never Married 3.8
Divorced or Separated 17.7
Widowed 20
Marriage (like Relationship) 58.5

HystX-ERT Uterus-PERT Total HRT
WHI CaD: Outcomes, Relationship to CT

Total CT = 68,133
Total HRT = 27,347 (40.1% of CT)

Calcium + Vitamin D (CaD)
Primary Outcome: Hip Fracture
Secondary Outcomes:
Other Fractures, Colorectal Cancer

DM 48,836
PERT 16,608
ERT 10,739
CaD 36,282
53.3% of CT
WHI Clinical Trials: Percent Overlap
Total CT = 68,133 (53.3 % are in CaD)

29.4 % of HRT are in DM

DM 48,836
PERT 16,608
ERT 10,739

58.8% HRT are in CaD
44.3% CaD are in HRT Trial

17.6% PERT are in DM + CaD
59.7 %*
57.5 %*
19.5% ERT are in DM + CaD

18.4% HRT are in DM + CaD

28.1% of PERT are in DM
31.6 % of ERT are in DM
WHI HRT (N=27,347) & CaD (N=36,282): Follow-up Clinic Visits

Percent of Annual Visits Due for HRT and CaD

<table>
<thead>
<tr>
<th>AV1</th>
<th>AV2</th>
<th>AV3</th>
<th>AV4</th>
<th>AV5</th>
<th>AV6</th>
</tr>
</thead>
<tbody>
<tr>
<td>91</td>
<td>90.6</td>
<td>92</td>
<td>58.1</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>28.0</td>
<td>31</td>
<td>10.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Legend:
- Total HRT
- HystX-ERT
- Uterus-PERT
- CaD
WHI HRT & CaD: Follow-up Clinic Visits

Percent (of Due) Annual Visits Conducted in HRT & CaD

Percent

Total HRT  HystX-ERT  Uterus-PERT  CaD

AV1  AV2  AV3  AV4  AV5  AV6
### WHI HRT: Follow-up

#### Percent Stopped HRT During Interval

<table>
<thead>
<tr>
<th>AV1</th>
<th>AV2</th>
<th>AV3</th>
<th>AV4</th>
<th>AV5</th>
<th>AV6</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>9</td>
<td>7</td>
<td>6</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

*Cumulative, as of 2/01 = 33.5%*
WHI HRT: Follow-up Clinic Visits
Percent of Women with Pill Counts taking > 80% Pills

Note: % with pill counts noted above columns

<table>
<thead>
<tr>
<th>AV1</th>
<th>AV2</th>
<th>AV3</th>
<th>AV4</th>
<th>AV5</th>
<th>AV6</th>
</tr>
</thead>
<tbody>
<tr>
<td>94%</td>
<td>90%</td>
<td>92%</td>
<td>92%</td>
<td>91%</td>
<td>92%</td>
</tr>
</tbody>
</table>

- HystX-ERT
- Uterus-PERT
WHI HRT: Follow-up Clinic Visits

Percent < 50% & 50-80% Pill-taking Rate in Interval

Percent

AV1  AV2  AV3  AV4  AV5  AV5

HystX-EPT < 50%  Uterus-PERT < 50%
HystX 50-80%  Uterus 50-80%
WHI HRT: Treated Hypertension by Ethnicity and Uterine Status

Treated Hypertension by Uterine Status

- Total
- White
- Black
- Hispanic
- Asian/PI

Hysterectomy
No HystX
HRT: High Blood Pressure* by Ethnicity and Uterine Status
* (Systolic BP>140 mmHg; Diastolic BP>90 mmHg)
WHI HRT: Treated Diabetes by Ethnicity and Uterine Status

Treated Diabetes (per Questionnaire)

- Total
- White
- Black
- Hispanic
- Asian/PI

Hysterectomy
No HystX
WHI HRT: High Cholesterol requiring Pills by Ethnicity and Uterine Status

High Blood Cholesterol requiring Pills

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>White</th>
<th>Black</th>
<th>Hispanic</th>
<th>Asian/PI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hysterectomy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No HystX</strong></td>
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</tbody>
</table>
WHI HRT: History of MI or CABG/PTCA by Uterine Status and Ethnicity

Positive Response to MI or CABG/PTCA Ever

- HystX-prior MI
- No HystX-prior MI
- HystX-prior CABG/PTCA
- No HystX-prior CABG/PTCA
WHI HRT: History of Stroke by Uterine Status and Ethnicity

Positive Response to Stroke Ever

- Total
- White
- Black
- Hispanic
- Asian/PI

Percent

- Hysterectomy
- No HystX
WHI HRT: Age at First Birth (%) by Uterine Status and Ethnicity

First Birth < 20 Yrs Age or ≥ 30 Yrs of age

- Total
- White
- Black
- Hispanic
- Asian/PI

- HystX 1st Birth < 20 yrs old
- No HystX 1st Birth < 20 yrs old
- HystX-1st Birth ≥ 30 yrs old
- No HystX-1st Birth ≥ 30 yrs old
WHI HRT: No Live Births by Uterine Status and Ethnicity

No Live Births (No term pregnancy)

Percent

Total  White  Black  Hispanic  Asian/PI

Hysterectomy  No HystX
WHI HRT: Oral Contraceptive Use and Duration by Ethnicity and Uterine Status

Percent Using OC for <5, 5-<10 or ≥ 10 yrs

- HystX Used OC < 5 yrs
- HystX Used OC 5-10 yrs
- HystX Used OC ≥ 10 yrs
- No HystX Used OC < 5 yrs
- No HystX Used OC 5-10 yrs
- No HystX Used OC ≥ 10 yrs
HRT Use at Baseline and Time Since last used (%) by Ethnicity and Uterus Status

Percent Using HRT 5-<10 or ≥ 10 yrs ago

- Total
- White
- Black
- Hispanic
- Asian/PI

- HystX Used 5-<10 yrs ago
- No HystX Used 5-<10 yrs ago
- HystX Used ≥ 10 yrs ago
- No HystX Used ≥ 10 yrs ago

Graph showing the percentage of women using hormone replacement therapy (HRT) at baseline and the time since the last use, categorized by ethnicity and uterus status.