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

Average Follow-up:
- DM: 8.5 years
- HRT: 8.4 years

Overlap: 11.8%
• **Background for HRT 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, decr. 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
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

Average Follow-up 8.4 years

PERT 16,608

ERT 10,739
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>
</tr>
<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>
</tr>
</tbody>
</table>
WHI HRT: Baseline Age Distribution
Mean ± SD: HystX-ERT = 63.6 ± 7.3; Uterus-PERT = 63.3 ± 7.1

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

ERT = 31%; PERT = 33%  ERT = 45%; PERT = 45%  ERT = 24%; PERT = 22%
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%)
WHI HRT: Mean (± SD) Baseline Age Distribution
White: 63.9±7.1  Black: 61.3±7.0  Hispanic: 59.7±6.4  Asian/PI: 63.2±7.5

Total HRT Goal: 50-59=30% 60-69=45% 70-79=25%
WHI HRT: Differences among Minority Groups

Total Percent with Hysterectomy by Ethnic Group

HystX - ERT

No HystX - PERT

- Total
- Whites
- Blacks
- Hispanic
- Asian/PI
WHI HRT: Age by Uterine Status and Ethnicity

- White, N=22,027
- Black, N = 2741
- Hispanic, N = 1543
- Asian/PI, N = 527

Mean Age by Ethnic Group and Uterine Status:

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

- HystX - ERT
- No HystX - PERT
WHI HRT: Body Mass Index (kg/m^2) by Uterine Status

Mean BMI by Ethnic Group and Uterine Status:

- Total: 30.1 kg/m^2
- White: 28.5 kg/m^2
- Black: 29.7 kg/m^2
- Hispanic: 32.2 kg/m^2
- Asian/PI: 30.5 kg/m^2

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

- < H.S. Diploma Equiv.: 9.9% ERT; 6.8% PERT
- Gr 0-8: 2.6% HysterX-ERT, 2.6% Uterus-PERT, 2.6% HRT Total
- Gr 9-11: 5.4% HysterX-ERT, 5.4% Uterus-PERT, 5.4% HRT Total
- HS/GED: 20.8% HysterX-ERT, 20.8% Uterus-PERT, 20.8% HRT Total
- Some College: 40.7% HysterX-ERT, 40.7% Uterus-PERT, 40.7% HRT Total
- ≥ College Degree: 30.6% HysterX-ERT, 30.6% Uterus-PERT, 30.6% HRT Total

- Some College: 67.4% ERT; 73.8% PERT

Note: ERT = Estrogen Receptor Therapy; PERT = Progesterone Receptor Therapy; HRT = Hormone Replacement Therapy.
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

% 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%

<table>
<thead>
<tr>
<th>Activity Level</th>
<th>HystX-ERT</th>
<th>Uterus-PERT</th>
<th>HRT Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Activity</td>
<td>19.6</td>
<td>15.3</td>
<td>15.3</td>
</tr>
<tr>
<td>Some</td>
<td>44.1</td>
<td>21.0</td>
<td>21.0</td>
</tr>
<tr>
<td>2 - &lt;4/wk Moderate</td>
<td>15.3</td>
<td>21.0</td>
<td>21.0</td>
</tr>
<tr>
<td>= &gt;4/wk</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
WHI HRT: Alcohol Intake and Smoking

**Alcohol Intake**
- None/Past
- <1 drinks/wk
- 1 to < 7/wk
- 7+ drinks/wk

**Smoking Status**
- Never Smoked
- Past Smoker
- Current Smoker

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

< $20K ERT (28.2%); PERT (20.5%)  > $50K ERT (22.9%) PERT (30.9%)
WHI CaD: End-Points, Relationship to CT

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

Calcium + Vitamin D (CaD)
Primary End-Point: Hip Fracture
Secondary End-Points:
Other Fractures, Colorectal Cancer

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

at 1st (or 2nd) Annual Visit

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
- 31.6 % of ERT are in DM
- 17.6% PERT are in DM + CaD
- 44.3% CaD are in HRT Trial
- 58.8% HRT are in CaD
- 59.7 %*
- 57.5 %*

DM 48,836
PERT 16,608
ERT 10,739
CaD 36,282

18.4% HRT are in DM + CaD
WHI HRT (N=27,347) & CaD (N=36,282):
Follow-up Clinic Visits

Percent of Annual Visits Due for HRT and CaD

AV1  AV2  AV3  AV4  AV5  AV6
□ Total HRT  ■ HystX-ERT  □ Uterus-PERT  ■ CaD
WHI HRT & CaD: Follow-up Clinic Visits
Percent (of Due) Annual Visits Conducted in HRT & CaD

<table>
<thead>
<tr>
<th>Year</th>
<th>Total HRT</th>
<th>HystX-ERT</th>
<th>Uterus-PERT</th>
<th>CaD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AV1</td>
<td>97</td>
<td>97</td>
<td>98</td>
<td>94</td>
</tr>
<tr>
<td>AV2</td>
<td>95</td>
<td>95</td>
<td>94</td>
<td>97</td>
</tr>
<tr>
<td>AV3</td>
<td>94</td>
<td>94</td>
<td>97</td>
<td>92</td>
</tr>
<tr>
<td>AV4</td>
<td>92</td>
<td>92</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>AV5</td>
<td>92</td>
<td>94</td>
<td>94</td>
<td>94</td>
</tr>
<tr>
<td>AV6</td>
<td>91</td>
<td>94</td>
<td>94</td>
<td>94</td>
</tr>
</tbody>
</table>
WHI HRT: Follow-up

Percent Stopped HRT During Interval

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></th>
<th>AV1</th>
<th>AV2</th>
<th>AV3</th>
<th>AV4</th>
<th>AV5</th>
<th>AV6</th>
</tr>
</thead>
<tbody>
<tr>
<td>HystX-ERT</td>
<td>94%</td>
<td>90%</td>
<td>92%</td>
<td>92%</td>
<td>91%</td>
<td>92%</td>
</tr>
<tr>
<td>Uterus-PERT</td>
<td>94%</td>
<td>90%</td>
<td>92%</td>
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<td>91%</td>
<td>92%</td>
</tr>
</tbody>
</table>
WHI HRT: Follow-up Clinic Visits

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

![Bar chart showing pill-taking rate in different intervals.](chart_image)
WHI HRT: Treated Hypertension by Ethnicity and Uterine Status

CHART

- Percent

- 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

![Bar chart showing the percentage of treated diabetes by ethnicity and uterine status. The chart compares 'Hysterectomy' (white bars) and 'No HystX' (black bars) across Total, White, Black, Hispanic, and Asian/PI populations. The data indicates higher percentages of treated diabetes in Black and Hispanic populations.]
WHI HRT: High Cholesterol requiring Pills by Ethnicity and Uterine Status

Percent

Total  White  Black  Hispanic  Asian/PI

Hysterectomy  No HystX

Graph showing the percentage of women within different ethnic groups and uterine status categories who are on high cholesterol medication requiring pills.
WHI HRT: History of MI or CABG/PTCA by Uterine Status and Ethnicity

![Bar chart showing the percentage of women with a history of MI or CABG/PTCA by uterine status and ethnicity. The chart compares HystX-prior MI, No HystX-prior MI, HystX-prior CABG/PTCA, and No HystX-prior CABG/PTCA across total, white, black, Hispanic, and Asian/PI groups.](chart.png)
WHI HRT: History of **Stroke**
by Uterine Status and Ethnicity

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

**Legend:**
- **Hysterectomy**
- **No HystX**

Percent: 0 to 3
WHI HRT: Age at First Birth (%) by Uterine Status and Ethnicity

- Total
  - No HystX No term pregnancy
  - No HystX 1st Birth < 20 yrs old
  - No HystX-1st Birth > 30 yrs old
- White
  - HystX 1st Birth < 20 yrs old
  - HystX-1st Birth > 30 yrs old
- Black
  - HystX 1st Birth < 20 yrs old
  - HystX-1st Birth > 30 yrs old
- Hispanic
  - HystX 1st Birth < 20 yrs old
  - HystX-1st Birth > 30 yrs old
- Asian/PI
  - HystX 1st Birth < 20 yrs old
  - HystX-1st Birth > 30 yrs old
WHI HRT: No Live Births by Uterine Status and Ethnicity

- 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

Percent

Total
White
Black
Hispanic
Asian/PI

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

Percent

Total  White  Black  Hispanic  Asian/PI

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

- 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