Jacques Rossouw, MD
Chief, WHI Branch
Program for Prevention and Population Sciences
Division of Cardiovascular Sciences

October 31, 2012
Mission

To address etiology and prevention of morbidity and mortality in older women

- WHI Clinical Trial and Observational Study Cohort
- Set of grants and contracts
WHI was:

- **Hormone Therapy Trial:**
  - 1<sup>st</sup> Coronary Heart Disease,
  - 2<sup>nd</sup> Fractures
  - Adverse effect for Breast Cancer?

- **Calcium/Vitamin D Trial:**
  - 1<sup>st</sup> Fractures & Colorectal Cancer

- **Dietary Modification Trial:**
  - 1<sup>st</sup> Breast & Colorectal Cancers
  - 2<sup>nd</sup> Coronary Heart Disease

- **Observational Study**

161,808 women total
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Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results From the Women's Health Initiative Randomized Controlled Trial


Google Scholar: 6428 Citations as of August, 2012
Other highly cited articles

- 2004 Estrogen* - 3007
- 2006 CaD fractures* - 938
- 2006 Diet and CVD* - 571
- 2007 Air pollution and CVD - 567
- 2006 CaD and colorectal cancer* - 541
- 2006 Diet and breast cancer* - 490
- 2006 Estrogen and breast cancer* - 418
- 2003 E+P and gynecologic cancers* - 336
- 2003 Breast cancer and NSAIDS - 255

* Trial data
U.S. Hormone Therapy Trends by Route of Administration

![Graph showing patient visits in thousands by year and route of administration.]

- Oral ET: 62% decrease
- Oral EPT: 76% decrease
- Vaginal: 32% increase
- Transdermal: 
- Intramuscular: 58% decrease

Tsai et al, 2010
The Decrease in Breast-Cancer Incidence in 2003 in the United States

Peter M. Ravdin, Ph.D., M.D., Kathleen A. Cronin, Ph.D., Nadia Howlader, M.S., Christine D. Berg, M.D., Rowan T. Chlebowski, M.D., Ph.D., Eric J. Feuer, Ph.D., Brenda K. Edwards, Ph.D., and Donald A. Berry, Ph.D.

WHI now is:

1 Observational Study

- **93,515 TOTAL**
  - **22,301**
    - *Self-report followed by documentation and central adjudication + CMS + NDI
  - **8,000**
    - **Self-report + CMS + NDI**
    - (except cancer fully documented)
  - **Medical Records Cohort (AA, Hispanic, HT women)**
  - **Long Life Study (age ≥63)**
Data Collection in Both CT and OS

- Extensive set of baseline variables
- Bloods at baseline and follow-up
- Updates of exposures and outcomes (self report, adjudicated, CMS)
- Cardiovascular, cancer, fracture, other outcomes

Allows for analyses of wide range of exposures (including trial exposures) and outcomes
Numbers Enrolled at Beginning of Each Study Period

<table>
<thead>
<tr>
<th>Age Range</th>
<th>50-79</th>
<th>57-91</th>
<th>62-95+</th>
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<tbody>
<tr>
<td>% of Eligibles Enrolled</td>
<td>77%</td>
<td>87%</td>
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</table>

1993-2005:
- White: 133,537
- Native American: 6,512
- Asian/Pacific Islander: 14,627
- Hispanic: 7,702
- Other: 2,963

2005-2010:
- White: 94,735
- Native American: 7,702
- Asian/Pacific Islander: 2,963
- Hispanic: 6,128
- Other: 2,469

2010-2015:
- White: 81,620
- Native American: 6,128
- Asian/Pacific Islander: 2,469
- Hispanic: 6,128
- Other: 2,469
Study factors leading to increased risk of CVD in older women of diverse race and ethnicity

- CHD, stroke, HF, AF, PAD, AS and VTE, and
- Conversely what factors determine absence of CVD as part of successful aging
New Mission
2010-2015

• Increase dissemination and mentoring
  • Leverage large numbers to facilitate ancillary studies, consortium studies, publications
  • Make data and biologic resources widely available
  • Mentor new investigators
New Mission
2010-2015

• CMS data
  • Validation against WHI outcomes
  • Exploring trial effects/observational associations using CMS data
  • Health care utilization studies

• Launch a new generation of large, simple, low-risk prevention trials focused on health of older women
Major Initiatives
2010-2015

- Complete in person visit for Long Life Study of 8,000 older women (coupled with ancillary study of objective measures of physical activity)

- Expanding genomics and other -omics data, e.g.
  - BAA focused on systems biology related to CVD/aging
  - Encourage
    - follow up genotyping of current GWAS, exome sequencing
    - studies of telomere length, expression, metabolomics
Reorganization
2010-2015

• 40 field centers reorganized to 4 Regional Centers and CCC
• Increased centralization of operations
• Funding of Regional Centers to mentor new investigators
Some Initial Results: Dissemination and Mentoring 2010-2015

- Total ancillary studies = 191 (July, 2012)
  - Before 2010 52% led by new investigators
  - After 2010 70% led by new investigators

- Publications = 698 (July, 2012)
  - Before 2010 30% led by new investigators
  - Since 2010 49% led by new investigators
Number of Ancillary Studies by Year of Award and WHI Affiliation of PI (July 2012)

- New Investigators to WHI
- WHI Investigators


Number of Studies

After Reorganization
WHI Publications by Year and WHI Affiliation of Lead Author (July 2012)

- **New Investigators to WHI**
- **WHI Investigators**

**After Reorganization**
**APPROVED MANUSCRIPT PROPOSALS 2010-2012**

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<tr>
<th>Category</th>
<th>Count</th>
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<td>Own analysis</td>
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<tr>
<td>CCC</td>
<td>105</td>
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<td>RC</td>
<td>73</td>
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<td>SHARe AC</td>
<td>18</td>
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<td><strong>Total</strong></td>
<td><strong>460</strong></td>
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Initial Results: Analysis of Data
Initial Results: Dissemination

- Publications based on consortia = 46
- Publications from BAAs = 37 (proposals = 99)
- Authorized data requests
  - BioLINCC = 66 since 2006 (8 known publications)
  - dbGAP = 69 since 2010
### Initial Results:

**CVD vs Non-CVD Related**

#### APPROVED MANUSCRIPT PROPOSALS

<table>
<thead>
<tr>
<th>Year</th>
<th>CVD Related</th>
<th>Non-CVD Related</th>
<th>Total</th>
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<tr>
<td>2010-2012</td>
<td>138 (30%)</td>
<td>322</td>
<td>460</td>
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<tr>
<td>2004-2009</td>
<td>160 (36%)</td>
<td>266</td>
<td>426</td>
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### APPROVED ANCILLARY STUDIES

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<thead>
<tr>
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<th>2010-2012</th>
<th>2004-2009</th>
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<tbody>
<tr>
<td>CVD Related</td>
<td>24 (33%)</td>
<td>41 (34%)</td>
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<tr>
<td>Non-CVD Related</td>
<td>49</td>
<td>81</td>
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<td><strong>Total</strong></td>
<td><strong>73</strong></td>
<td><strong>122</strong></td>
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Current Cost per Publication During CT and Follow Up Periods (October, 2012)

Active CT (+OS)  Follow Up
Current Cost per Publication During Follow Up (Detail)

Before Reorganization

After Reorganization
## WHI Citation Indices

Source: Google Scholar

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<thead>
<tr>
<th>Citation indices</th>
<th>All</th>
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### Yearly Citations Trend

![Graph showing yearly citation trend from 2001 to 2012](image)
Conclusions

- WHI cohort study
  - Productive
  - Cost-effective
  - High impact
- Mentoring and dissemination efforts are showing results
- Need more focus on CVD in older women
- Anticipated future payoffs
  - CMS – 21 approved manuscript proposals, 1 in press
  - Large simple prevention trials – 2 under development
  - Systems biology
Creative Transformation of Observational Studies

• refocused scientific questions

• centralized and integrated governance

• digitally-enabled exposure and outcome measures

• embedded clinical and policy trials.

M. Lauer, JAMA 2012