Questions Arising Since The HRT/WHI Newsletter (September, 2002)

How does the older age of participants in the WHI affect our interpretation of the results?

- Average age in the WHI was 63 years (healthy postmenopausal women; HRT not used for acute symptoms).
- 5,522 subjects were in the lower, 50-59 year age subgroup.
- The original WHI article (JAMA 2002;288: 21-333) included a preliminary sub-analysis stating:
  - No noteworthy interactions with age, race/ethnicity, body mass index, prior hormone use, smoking status, blood pressure, diabetes, aspirin use, or statin use were found for the effect of estrogen plus progestin on CHD, stroke, or VTE.
  - No interactions between estrogen plus progestin and age, race/ethnicity, family history, parity, age at first birth, body mass index, or Gail-model risk score were observed for invasive breast cancer.
  - [Link](http://jama.ama-assn.org/issues/v288n3/ffull/joc21036.html)

How does the 5 year WHI - Global Index (overall risk/benefit of evaluated clinical outcomes) vary with age?

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Estr+Prog 5 Year Index</th>
<th>Placebo 5 Year Index</th>
<th>NNH (Number needed to treat for one net harm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>4.78</td>
<td>4.16</td>
<td>161 (NS)</td>
</tr>
<tr>
<td>60-69</td>
<td>8.94</td>
<td>7.69</td>
<td>80</td>
</tr>
<tr>
<td>70-79</td>
<td>15.8</td>
<td>14.4</td>
<td>71 (NS)</td>
</tr>
<tr>
<td>ALL</td>
<td>8.82</td>
<td>7.69</td>
<td>88</td>
</tr>
</tbody>
</table>

NS=not statistically significant; study not powered to evaluate risks for subgroups.

Unpublished WHI Data; accessed from NIH: 15Nov02.
[http://www4.od.nih.gov/orwh/htslides/stefanici2.ppt](http://www4.od.nih.gov/orwh/htslides/stefanici2.ppt)

- For all age groups, risk (cardiovascular & breast cancer) exceeded benefit (colorectal cancer & fracture); however, since baseline risk is lower for younger women, the number needed to harm (NNH) would be correspondingly higher. This trend was seen in the WHI; confidence intervals lack statistical power for the sub-analysis. The Odds Ratio consistently suggested 5.2 year risks outweighed benefits for all age groups. (Quality of Life issues not evaluated.)

Is the risk of combination HRT small?

- It all depends! The risk of breast cancer expressed as **8 extra cases per 10,000 women per year** seems small to most people. However the risk of any adverse event (breast cancer, coronary heart disease, stroke, blood clots) **over 5.2 years** was **± 1.5%** or **one extra adverse event for every 66 women**. This number is not so small, and shows how perceived risk can vary depending on duration of therapy, and addition of multiple risks. The individual risk would vary depending on a patient’s age and baseline risk factors. Individual assessment must weigh potential benefits with potential risks.

Isn’t the WHI just one of many studies? Are there more studies coming?

- The WHI is a landmark study. Previous evidence that HRT had very positive effects on heart disease were based on observational trials such as the Nurses Health Study. There are few Level-1 (randomized, double blind placebo controlled) HRT outcome trials.
- The other major Level-1 trial that was in progress (WISDOM) has been halted due to the analysis of the WHI results. (BMJ:2002;325:987) It had hoped to evaluate combination HRT outcomes in >20,000 women over 10 years.
- The only large scale randomized controlled trials currently in progress are estrogen-only studies.
- Further sub-analysis and follow-up studies are planned for the WHI – combination HRT arm trial.
- There is a need for good outcome studies related to the many questions yet unanswered (e.g. regarding alternate hormonal regimens; HRT use in symptomatic menopausal women; early versus late initiation of HRT)
- For an interesting summary of questions remaining & consensus versus lack of consensus, see recent report in JAMA: [http://jama.ama-assn.org/issues/v288n19/ffull/jmn1120-2.html](http://jama.ama-assn.org/issues/v288n19/ffull/jmn1120-2.html)

Where can I get a patient information sheet that summarizes HRT & the WHI for my patients?

- Copies for non-profit educational use may be made as noted at bottom of page.