BODY COMPOSITION AND AGING IN POSTMENOPAUSAL WOMEN

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Introduction

• As life expectancy continues to rise, women are expected to spend more than a third of their lifetime beyond the menopausal transition

• Results from the WHI studies have made significant contributions to our knowledge of primary and secondary disease prevention in postmenopausal women

• Still many unanswered questions about the relationship between body composition and health outcomes in postmenopausal women
Objectives

(1) to present scientific research examining the relationships between body composition and health outcomes in post-menopausal women

(2) to foster discussion and dialogue about how we can leverage existing WHI data, or potentially collect additional data, to answer questions about the role of body composition in healthy aging
Body Composition

- Body Mass Index (BMI)
- Waist circumference (WC)
- Total body fat
- Lean body mass
- Bone mineral density
WHI DXA sub-cohort

40 WHI Clinical Sites (CT & OS)

3 sites chosen for DXA sub-study

- Pittsburgh
  - n= 3590

- Tucson-Phoenix
  - n=3765

- Birmingham
  - n=3665

- Similar age distribution as WHI cohort
  - 50-59: WHI 33% vs. DXA 34%
  - 60-69: WHI 45% vs. DXA 43%
  - 70-79: WHI 22% vs DXA 23%

- Sites chosen because racially/ethnically diverse

- Longitudinal follow up
  - Baseline (n=10607), year 3 (n=8939), year 6 (n=8239), year 9 (n=4595)
Comparing race/ethnicity in total WHI cohort with DXA sub-cohort

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Total WHI cohort</th>
<th>WHI DXA sub-cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian or Pac Island</td>
<td>0.41</td>
<td>0.96</td>
</tr>
<tr>
<td>Black or AA</td>
<td>9.13</td>
<td>14.07</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>3.79</td>
<td>5.94</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>83.19</td>
<td>78.32</td>
</tr>
<tr>
<td>Other</td>
<td>1.08</td>
<td>0.43</td>
</tr>
<tr>
<td>Other</td>
<td>0.29</td>
<td></td>
</tr>
</tbody>
</table>

Percent (%)

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90

Am Ind or Alask Nat Asian or Pac Island Black or AA Hispanic/Latino Non-Hispanic White Other
Body composition and mortality

Relationship between BMI, waist circumference, total body fat, lean body mass has been examined by Jennifer Bea et al. (AJE 2015) and Zhao Chen (JAGS 2017)

- Bea et al.,
  - Evidence of “J shaped” relationship between BMI and mortality

<table>
<thead>
<tr>
<th>BMI category (kg/m²)</th>
<th>Adjusted HR</th>
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<tbody>
<tr>
<td>Underweight (&lt;18.5)</td>
<td>1.09 (0.62, 1.89)</td>
</tr>
<tr>
<td>Normal weight (18.5-24.9)</td>
<td>--</td>
</tr>
<tr>
<td>Overweight (25-29.9)</td>
<td>1.03 (0.89, 1.18)</td>
</tr>
<tr>
<td>Obese I (30-34.9)</td>
<td>1.12 (0.95, 1.32)</td>
</tr>
<tr>
<td>Obese II (35-39.9)</td>
<td>1.45 (1.16, 1.82)</td>
</tr>
<tr>
<td>Obese III (&gt;40)</td>
<td>1.84 (1.40, 2.43)</td>
</tr>
</tbody>
</table>

- No evidence of increased mortality risk with increasing body fat or lean mass
BMI and mortality

Multivariate Adjusted Hazard Ratio for All Cause Mortality Stratified by Age

Chen et al., 2017
Multivariate Adjusted Hazard Ratio for All Cause Mortality Stratified by Age

Waist circumference and mortality

Chen et al., 2017
BMI-related misclassification

• BMI is the most frequently used metric to classify individuals according to their body weight status

• One concern about the use of BMI is that it may not accurately represent an individual’s true obesity status, resulting in exposure misclassification

• The validity of BMI-defined obesity may differ across age and race/ethnicity groups
## Sensitivity and specificity of BMI

Comparing BMI defined obesity (BMI >30kg/m2) with obesity defined by percent body fat (40% BF)

<table>
<thead>
<tr>
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<th>Non-Hispanic White</th>
<th>Non-Hispanic Black</th>
<th>Hispanic</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>50-59 60-69 70-79</td>
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</tr>
<tr>
<td><strong>Sensitivity (%)</strong></td>
<td>56.8 (52.9, 60.7)</td>
<td>49.5 (45.1, 53.8)</td>
<td>42.1 (36.2, 48.1)</td>
</tr>
<tr>
<td></td>
<td>73.7 (65.5, 82.8)</td>
<td>59.7 (55.1, 64.3)</td>
<td>52.4 (45.9, 58.9)</td>
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<tr>
<td></td>
<td>85.6 (75.6, 95.5)</td>
<td>69.1 (63.5, 74.8)</td>
<td>62.5 (55.0, 70.0)</td>
</tr>
<tr>
<td><strong>Specificity (%)</strong></td>
<td>96.8 (95.6, 98.0)</td>
<td>97.5 (96.7, 98.4)</td>
<td>98.2 (97.5, 98.9)</td>
</tr>
<tr>
<td></td>
<td>94.2 (91.9, 96.6)</td>
<td>96.4 (95.0, 97.8)</td>
<td>97.3 (96.2, 98.4)</td>
</tr>
<tr>
<td></td>
<td>88.5 (81.3, 95.7)</td>
<td>94.6 (92.5, 96.7)</td>
<td>96.0 (94.1, 97.8)</td>
</tr>
</tbody>
</table>

(Banack et al., in press)
Quantitative bias analysis

- Used sensitivity and specificity to ‘correct’ misclassified obesity (BMI) using probabilistic bias analysis
- Estimated the obesity-mortality relationship (hazard ratio (95% CI))

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<tbody>
<tr>
<td></td>
<td>Conventional estimate (95% CI)</td>
<td>Bias-adjusted Estimate (95% SI)</td>
<td>Conventional estimate (95% CI)</td>
<td>Bias-Adjusted Estimate (95% SI)</td>
<td>Conventional estimate (95% CI)</td>
<td>Bias-Adjusted Estimate (95% SI)</td>
</tr>
<tr>
<td>50-59</td>
<td>1.34 (1.22, 1.46)</td>
<td>1.82 (1.63, 2.01)</td>
<td>1.22 (1.05, 1.40)</td>
<td>1.67 (1.26, 2.23)</td>
<td>1.82 (1.31, 2.52)</td>
<td>3.00 (1.98, 4.34)</td>
</tr>
<tr>
<td>60-69</td>
<td>1.22 (1.11, 1.32)</td>
<td>1.63 (1.50, 1.76)</td>
<td>1.05 (0.91, 1.22)</td>
<td>1.94 (1.39, 2.81)</td>
<td>1.67 (1.26, 2.20)</td>
<td>2.01 (1.37, 2.76)</td>
</tr>
<tr>
<td>70-79</td>
<td>1.13 (1.07, 1.21)</td>
<td>1.24 (1.15, 1.33)</td>
<td>1.15 (0.87, 1.52)</td>
<td>1.54 (1.01, 2.22)</td>
<td>0.97 (0.66, 1.41)</td>
<td>1.47 (0.95, 2.08)</td>
</tr>
</tbody>
</table>

(Banack et al., in press)
Many unanswered questions….

• Is it time to re-evaluate BMI cutpoints in postmenopausal women? Or time to move away from cutpoints altogether?

• Should cutpoints be based on the relationship between:
  • BMI and adiposity
  • BMI and health outcomes (i.e., for risk prediction)

• Would considering waist circumference measures within BMI categories add valuable information for risk prediction?
Using DXA scans to estimate abdominal fat

Andrew Odegaard (UC Irvine) is working on a project using results from the WHI DXA scans to estimate visceral abdominal fat (R01, Co-I: Bea & Chen, Arizona)
Hologic Apex Software
Looking ahead

• How can we better use this resource?
  • Cross sectional analyses vs. longitudinal
  • SIG collaborations

• Should we collect additional body composition data from the participants?
  • Building on current resources
  • Return visit to WHI centers? Body composition scan at non-WHI clinic?
  • Exploring options other than DXA (e.g., low dose CT, MRI)

• Pooled cohort analyses (e.g., MrOs. Health ABC)
  • MrOS (n=5994) scans baseline, year 5, 7,14
  • Health ABC (n=3075) scans annually years 1-6, year 8, 10
We have a unique and underutilized resource that has tremendous potential to advance science. **We need to do more with it!**
Thank you!!

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