Overweight and Obesity in Older Persons: Impact Upon Health and Mortality Outcomes

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Objectives

- Health outcomes
- Mortality outcomes
- The obesity paradox
- What do the findings mean?
Obesity-Related Outcomes

- Premature disease
- Functional decline
- Duration of life
  - Early studies that did not show relationship were confounded by smoking.
  - Obesity does not generally confer health benefit
  - J-shaped mortality curve in relation to BMI
  - Associated with all cause mortality
  - Stronger predictor at younger ages
  - Decreased life expectancy
Obesity related co-morbidities

- Cardiovascular disease / hypertension
- Sleep apnea / obesity hypoventilation
- Diabetes
- Dyslipidemia
- Metabolic syndrome
- Hirsutism, menstrual disorders, preeclampsia, endometrial disorders
- Cholecystitis / cholelithiasis
- Malignancy
  - colon
  - prostate
  - endometrium
  - cervical
  - ovarian
  - breast
- Osteoarthritis – destructive joint disease
- Gout
The obesity paradox in the elderly: potential mechanisms and clinical implications.

- In the elderly, obesity is paradoxically associated with a lower, not higher, mortality risk.
Association of all-cause mortality with BMI categories

- Systematic review and meta-analysis
  - Prospective studies that applied standard BMI categories to general populations of adults.
  - 97 studies with 2.88 million persons and 270K deaths
- Referent to desirable BMI, class 2 and 3 obesity had significantly greater all-cause mortality while class 1 obesity was not associated with higher mortality and overweight was associated with significantly lower mortality.
### Summary Hazard Ratios of All-Cause Mortality (95% CI)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>BMI 25-&lt;30</th>
<th>BMI ≥30</th>
<th>BMI 30-&lt;35</th>
<th>BMI ≥35</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>0.92 (0.90-0.97)</td>
<td>1.21 (1.12-1.31)</td>
<td>0.97 (0.90-1.04)</td>
<td>1.34 (1.21-1.47)</td>
</tr>
<tr>
<td>Measured BMI</td>
<td>0.92 (0.88-0.96)</td>
<td>1.11 (1.03-1.20)</td>
<td>1.00 (0.92-1.09)</td>
<td>1.32 (1.20-1.46)</td>
</tr>
<tr>
<td>Self-report BMI</td>
<td>0.95 (0.90-1.01)</td>
<td>1.33 (1.21-1.47)</td>
<td>0.94 (0.84-1.05)</td>
<td>1.35 (1.16-1.57)</td>
</tr>
<tr>
<td>Age ≥65</td>
<td>0.90 (0.86-0.95)</td>
<td>1.05 (0.92-1.21)</td>
<td>0.88 (0.69-1.12)</td>
<td>1.28 (0.93-1.76)</td>
</tr>
<tr>
<td>Measured BMI</td>
<td>0.90 (0.84-0.96)</td>
<td>1.02 (0.81-1.29)</td>
<td>0.90 (0.70-1.16)</td>
<td>1.12 (0.89-1.43)</td>
</tr>
<tr>
<td>Self-report BMI</td>
<td>0.91 (0.84-0.98)</td>
<td>1.08 (0.93-1.25)</td>
<td>0.82 (0.46-1.47)</td>
<td>1.40 (0.64-3.07)</td>
</tr>
</tbody>
</table>

Controversy


How to interpret these findings for health professionals and the public?
Lowest mortality shifts towards higher BMI for older persons

Sarcopenic Obesity
Overweight only protective in patients with high muscle mass

- AGES-Reykjavik cohort, 637 participants with diabetes aged 66-96 years old.
- Median follow up 6.66 years.
- Thigh muscle by CT scan.
- Highest mortality in those with low muscle mass in either normal or overweight.
- Normal weight participants had elevated mortality risk compared to overweight. This paradox was partly mediated by muscle size.
Risk of mortality in relation to BMI and body composition

- Women’s Health Initiative, n=10,525, underwent DEXA, followed 13.6 years
- Overall BMI ≥35 was associated increased mortality (HR 1.45, 95% CI 1.16-1.82), while TBF and LBM were not.
- For women 50-59 years >TBF increased mortality (2.44, 1.38-4.34) and >LBM decreased mortality (0.41, 0.23-0.74).
- These findings were reversed for women aged 70-79 years.
BMI and All-Cause Mortality among Older Adults

- Geisinger Rural Aging Study (GRAS)
- N=4565, age 74.0±4.7 with BMI 29.5±5.3 at baseline and followed for mean 10.9±3.8 years.
- Model 1 – adjusting for age and sex
- Model 2 – above plus smoking status and alcohol use
- Model 3 – all of above plus blood glucose, diabetic medication, triglyceride, HDL cholesterol, LDL cholesterol, cholesterol medication, diastolic blood pressure, hypertension medication, and disease burden
<table>
<thead>
<tr>
<th>BMI</th>
<th>Events</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>12/14</td>
<td>3.30</td>
<td>2.72</td>
<td>3.35</td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>920/1866</td>
<td>0.83 (0.74-0.93)</td>
<td>0.84 (0.75-0.94)</td>
<td>0.80 (0.71-0.90)</td>
</tr>
<tr>
<td>25-29.9</td>
<td>578/1202</td>
<td>0.90 (0.80-1.02)</td>
<td>0.91 (0.80-1.03)</td>
<td>0.78 (0.69-0.89)</td>
</tr>
<tr>
<td>30-34.9</td>
<td>252/480</td>
<td>1.11 (0.95-1.30)</td>
<td>1.13 (0.96-1.32)</td>
<td>0.96 (0.81-1.12)</td>
</tr>
<tr>
<td>35-39.9</td>
<td>97/171</td>
<td>1.46 (1.17-1.82)</td>
<td>1.55 (1.24-1.93)</td>
<td>1.17 (0.93-1.47)</td>
</tr>
<tr>
<td>≥40</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

All-cause mortality in relation to BMI (reference BMI 18.5-24.9)
BMI and All-Cause Mortality among Older Adults

- U-shaped relationship between BMI as continuous variable and all-cause mortality.
- Adjusting for age, sex, smoking, alcohol, lab values, medications, and comorbidity.
  - Those with BMI<18.5 had significantly greater risk of all-cause mortality.
  - Those with overweight BMI or class I obesity had significantly lower risk of all-cause mortality.
  - Findings were consistent using propensity score weights and among never-smokers with 2 and 5-year lag analyses and those with no identified chronic disease.
Relative to BMI 23, the lowest mortality risk was between BMI 28 and 30* (restricted cubic spline).

*HR denotes hazard ratio and 95% CI denotes 95% confidence interval. All estimates are adjusted for age, sex, smoking status, alcohol drinker, LDL cholesterol (mg/dL), hypercholesterolemia drug, and disease burden (0, 1, 2, or ≥ 3 diseases).
Metabolic Health Status and the Obesity Paradox in Older Adults


Geisinger Rural Aging Study (GRAS)
N=4551, age 74.0±4.7 categorized by BMI and the presence/absence of metabolic health using Adult Treatment Panel III criteria.

Metabolically unhealthy was ≥ 2 risk factors.
Covariates - age, sex, smoking, alcohol, metabolic labs, medications, and disease burden.
Sensitivity Analyses

- Fully adjusted model with never-smokers with no disease burden.
- Defined metabolically unhealthy to include all individuals meeting any diabetes criterion.
- Defined metabolically healthy to include only those with no metabolic risk criteria.
- Analysis of never-smokers excluding individuals that died during first 5 years of follow up.
- Analysis excluding those who became metabolically unhealthy during follow up.
- Medication use exclusions – cholesterol lowering, diabetes, and blood pressure medications.
Results

- 2294 deaths over mean 10.9 years of follow up.
- Metabolically healthy overweight or obesity was not associated with a significantly greater mortality risk.
- Findings unchanged by exclusions tested in sensitivity analyses and by propensity scoring.
- Association between BMI and mortality was more pronounced for blood glucose >100 mg/dL and for a diabetes diagnosis.
Proportion of metabolically unhealthy increased at higher levels of obesity

Metabolic Health Status by BMI Class

Desirable | Overweight | Obese Class I | Obese Class II/III

Metabolically healthy | Metabolically unhealthy

65% | 10%
All Participants

Figure 2A. All Participants (n = 4,551)

<table>
<thead>
<tr>
<th>Event/n</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>447/832</td>
<td>1.0 (Reference)</td>
</tr>
<tr>
<td>920/1,866</td>
<td>0.80 (0.71-0.90)</td>
</tr>
<tr>
<td>578/1,202</td>
<td>0.80 (0.71-0.91)</td>
</tr>
<tr>
<td>349/651</td>
<td>1.06 (0.92-1.23)</td>
</tr>
<tr>
<td>139/293</td>
<td>1.0 (Reference)</td>
</tr>
<tr>
<td>187/401</td>
<td>0.90 (0.73-1.13)</td>
</tr>
<tr>
<td>50/164</td>
<td>0.58 (0.42-0.80)</td>
</tr>
<tr>
<td>19/63</td>
<td>0.78 (0.48-1.27)</td>
</tr>
<tr>
<td>308/539</td>
<td>1.24 (1.01-1.52)</td>
</tr>
<tr>
<td>733/1,465</td>
<td>0.96 (0.80-1.16)</td>
</tr>
<tr>
<td>528/1,038</td>
<td>1.04 (0.86-1.26)</td>
</tr>
<tr>
<td>330/588</td>
<td>1.34 (1.10-1.64)</td>
</tr>
</tbody>
</table>

- BMI 18.5-24.9
- BMI 25.0-29.9
- BMI 30.0-34.9
- BMI ≥35.0
Never Smoker with No Identified Chronic Disease Burden

Figure 2B. Never-Smoker with No Identified Chronic Disease Burden (n=1,046)

<table>
<thead>
<tr>
<th>Event/n</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18/83</td>
<td>1.0 (Reference)</td>
</tr>
<tr>
<td>21/107</td>
<td>1.11 (0.59-2.09)</td>
</tr>
<tr>
<td>5/30</td>
<td>0.91 (0.34-2.44)</td>
</tr>
<tr>
<td>3/18</td>
<td>0.96 (0.28-3.27)</td>
</tr>
<tr>
<td>38/117</td>
<td>1.69 (0.96-2.97)</td>
</tr>
<tr>
<td>80/342</td>
<td>1.20 (0.72-2.01)</td>
</tr>
<tr>
<td>60/222</td>
<td>1.40 (0.83-2.39)</td>
</tr>
<tr>
<td>39/127</td>
<td>1.88 (1.07-3.31)</td>
</tr>
</tbody>
</table>

- ■ BMI 18.5-24.9
- ♦ BMI 25.0-29.9
- ● BMI 30.0-34.9
- ▲ BMI ≥35.0
Figure 2C. Never-Smoker, 5-Year Lag Analysis (n=2,367)

<table>
<thead>
<tr>
<th>Event/n</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>51/168</td>
<td>1.0 (Reference)</td>
</tr>
<tr>
<td>72/220</td>
<td>1.01 (0.71-1.45)</td>
</tr>
<tr>
<td>13/82</td>
<td>0.46 (0.25-0.84)</td>
</tr>
<tr>
<td>10/40</td>
<td>1.00 (0.51-1.98)</td>
</tr>
<tr>
<td>106/264</td>
<td>1.29 (0.93-1.81)</td>
</tr>
<tr>
<td>275/744</td>
<td>1.17 (0.86-1.58)</td>
</tr>
<tr>
<td>192/521</td>
<td>1.28 (0.94-1.75)</td>
</tr>
<tr>
<td>152/328</td>
<td>1.85 (1.34-2.55)</td>
</tr>
</tbody>
</table>

- BMI 18.5-24.9
- BMI 25.0-29.9
- BMI 30.0-34.9
- BMI ≥35.0
Metabolic Health Status and the Obesity Paradox in Older Adults

- Metabolically healthy overweight or obesity was not associated with a significantly greater mortality risk than metabolically healthy desirable BMI.
- The “obesity paradox” in previous studies may be partially explained by the inclusion of metabolically healthy overweight and obese persons who do not have an elevated mortality risk.
- Based on rigorous sensitivity analyses, our prospective cohort study showed that methodological issues could not fully explain the “obesity paradox”.
Conclusion: Benefits vs Risks

- Obesity does not generally confer mortality or health benefits.
- Current use of NIH BMI guidelines warrants reevaluation for older persons.
  - Disease burden is likely a key issue.
  - Body composition is likely a key factor. Elevated BMI may have no protective effect in the presence of reduced muscle mass (sarcopenic obesity).
- How do we best interpret these findings for health professionals and the public?