The Obesity Paradox: BMI Related Health and Mortality Outcomes

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Objectives

- Mortality outcomes
- Health outcomes
- The obesity paradox
  - Are there benefits?
- Confounding variables
How does body weight affect health?

- **Obesity**
  - Impact on duration of life
  - Associated with premature disease
  - Functional decline

- **Underweight**
  - Nurses Health Study found lowest mortality for those weighing 15% below national average.
  - Confounded by smoking and disease
Obesity / Mortality

- 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
- Associated with decreased life expectancy
Adjusted Relative Risk of Death among Men and Women in the European Prospective Investigation into Cancer and Nutrition, According to BMI, Waist Circumference, and Waist-to-Hip Ratio

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
Functional decline among obese older persons.
Cause specific excess deaths associated with underweight, overweight, and obesity?

NHANES follow up combined with vital statistics data.

6,859 persons with 571,042 person years follow up
- BMI <18.5 – more non-cancer, non-CVD deaths
- BMI 25-29.9 – fewer non-cancer, non-CVD deaths
- BMI ≥30 – more CVD deaths, more cancers considered to be obesity-related

BMI-mortality association varies by cause of death.
Excess Deaths by Body Mass Index Category for Subgroups of Cardiovascular Disease and Cancer Deaths--Balanced Follow-up

<table>
<thead>
<tr>
<th>Category</th>
<th>BMI Category</th>
<th>Excess Deaths, in Thousands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary Heart Disease</td>
<td>&lt;18.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.5 to &lt;25 (reference)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25 to &lt;30</td>
<td></td>
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<tr>
<td></td>
<td>≥30</td>
<td></td>
</tr>
<tr>
<td>Other CVD</td>
<td>&lt;18.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.5 to &lt;25 (reference)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25 to &lt;30</td>
<td></td>
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<tr>
<td></td>
<td>≥30</td>
<td></td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>&lt;18.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.5 to &lt;25 (reference)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25 to &lt;30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥30</td>
<td></td>
</tr>
<tr>
<td>Cancers Considered Obesity Related</td>
<td>&lt;18.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.5 to &lt;25 (reference)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25 to &lt;30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥30</td>
<td></td>
</tr>
<tr>
<td>All Other Cancers</td>
<td>&lt;18.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.5 to &lt;25 (reference)</td>
<td></td>
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<tr>
<td></td>
<td>25 to &lt;30</td>
<td></td>
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<tr>
<td></td>
<td>≥30</td>
<td></td>
</tr>
</tbody>
</table>

Sui, X. et al. JAMA 2007; 298:2507-2516

- 2063 adults 60 yrs or older, baseline assessment 1979-2001
- Maximal treadmill exercise tolerance
- BMI, waist circumference, % body fat by skin-folds or water displacement
- Outcome – mean 12 yr follow up – all cause mortality
- Key finding – fitness was a significant mortality predictor independent of adiposity
Joint Associations of Cardiorespiratory Fitness (Fitness) and Adiposity Measures With All-Cause Mortality—Aerobics Center Longitudinal Study, 1979-2003a

<table>
<thead>
<tr>
<th>Adiposity Measure</th>
<th>No. of Deaths</th>
<th>Rateb</th>
<th>HR (95% CI)c</th>
<th>No. of Deaths</th>
<th>Rateb</th>
<th>HR (95% CI)c</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMId 18.5-24.9</td>
<td>158</td>
<td>1.2</td>
<td>1 [Reference]</td>
<td>34</td>
<td>4.9</td>
<td>3.63 (2.47-5.32)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>25.0-29.9</td>
<td>152</td>
<td>1.2</td>
<td>0.88 (0.70-1.11)</td>
<td>44</td>
<td>2.7</td>
<td>1.74 (1.23-2.46)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>30.0-34.9</td>
<td>32</td>
<td>1.6</td>
<td>1.12 (0.76-1.66)</td>
<td>18</td>
<td>2.5</td>
<td>1.68 (1.02-2.78)</td>
<td>.46</td>
</tr>
<tr>
<td>≥35.0</td>
<td>2</td>
<td>1.2</td>
<td>0.86 (0.21-3.50)</td>
<td>10</td>
<td>4.8</td>
<td>3.35 (1.74-6.44)</td>
<td>.05</td>
</tr>
<tr>
<td>Waist circumferencee</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>274</td>
<td>5.1</td>
<td>1 [Reference]</td>
<td>61</td>
<td>14.5</td>
<td>2.84 (2.15-3.75)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Abdominal obesity</td>
<td>70</td>
<td>6.2</td>
<td>1.21 (0.93-1.58)</td>
<td>45</td>
<td>13.5</td>
<td>2.65 (1.93-3.63)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Percent body fate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>151</td>
<td>9.1</td>
<td>1 [Reference]</td>
<td>29</td>
<td>26.8</td>
<td>2.94 (1.97-4.38)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Obese</td>
<td>190</td>
<td>8.7</td>
<td>0.96 (0.78-1.19)</td>
<td>72</td>
<td>21.8</td>
<td>2.39 (1.81-3.16)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.
dCross-product tests of interaction between fitness and adiposity exposures were not statistically significant: fitness-BMI ($\chi^2 = 0.05, P = .82$); fitness-waist circumference ($\chi^2 = 1.38, P = .24$); and fitness-percent body fat ($\chi^2 = 0.04, P = .84$).
dAll-cause death rates per 1000 person-years adjusted for age, sex, and examination year.
eAdjusted for age, sex, examination year, smoking status, abnormal exercise electrocardiogram responses, and presence vs absence of baseline health conditions (cardiovascular disease, hypertension, diabetes, and hypercholesterolemia).
dCalculated as weight in kilograms divided by height in meters squared.
eSee “Methods” for definitions.

- 5440 NHANES 1999-2004 participants
- NIH BMI cut points
- Cardio-metabolic abnormalities
  - Elevated BP, triglycerides, fasting glucose, C-reactive protein, and insulin resistance; low HDL cholesterol
- Findings – half of overweight and one-third of obese were “metabolically healthy”, while 23.5% of normal weight were abnormal
Age-standardized prevalence of cardiometabolic abnormalities by body size and sex (A, men; B, women)

A - male,  
B - female

Abnormal = ≥2 metabolic abnormalities


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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.
Fat mass protective in hospitalized elderly?

- 125 older patients, body composition by DEXA and BIA
- Fat mass was associated with reduced mortality and complications, while there was no relationship with lean mass or appendicular muscle mass.
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>

Lowest mortality shifts towards higher BMI for older persons

BMI and all-cause mortality at advanced age


2,995 participants (1,267 male, 1,728 female); mean age 81.4 years, followed mean 3.1 years

BMI < 18.5 was associated with increased mortality (HR 1.85, 95% CI 1.09-3.14, P=0.02), while a BMI of 25–29.9 was associated with decreased risk of mortality (HR 0.71 95% CI 0.55-0.91, P=0.007). Reference range BMI 18.5-24.9.
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.
The obesity paradox

- Are there benefits?
- Osteoporosis
- Heart failure
- Myocardial infarction
- Peripheral vascular disease
- Non-bariatric general surgery
- Suicide risk
- Older persons
Discussion: Benefits vs Risks

- Individual versus population
- Measures of adiposity
- Confounders
  - Age
  - Gender
  - Race / ethnic group
  - Disease burden
  - Smoking
  - Body composition
  - Other
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?