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

Gordon L Jensen, MD, PhD
Senior Associate Dean for Research
Professor of Medicine and Nutrition

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.

- Oreopoulos A, Clin Geriatr Med. 2009; Nov;25(4):643-59.
- In the elderly, obesity is paradoxically associated with a lower, not higher, mortality risk.

Association of all-cause mortality with BMI categories

- Flegal KM, at al. JAMA 2013;309:71-82.
- 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)

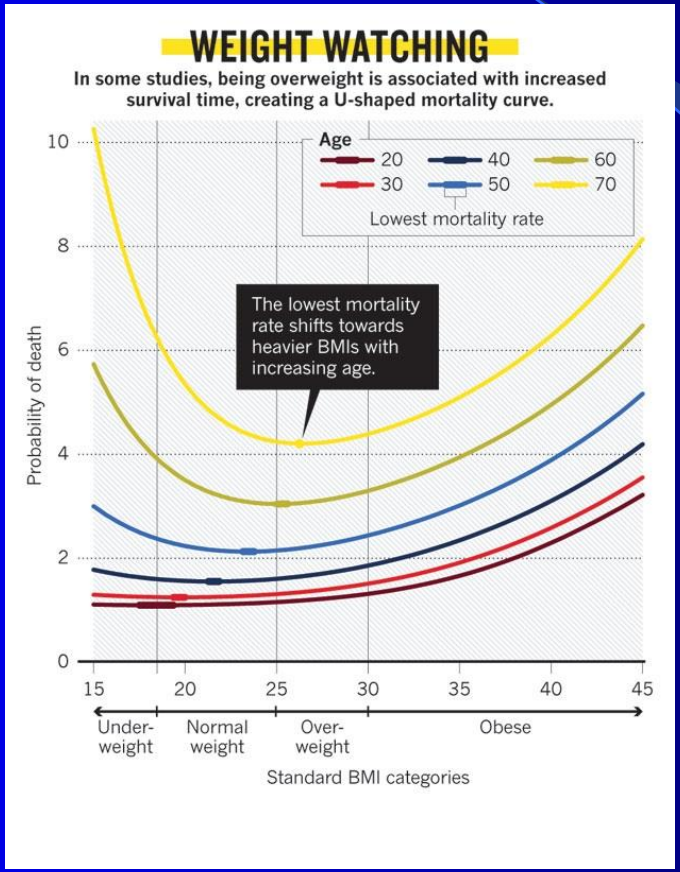
Age Group	BMI 25-<30	BMI ≥30	BMI 30-<35	BMI ≥35
All ages	0.92 (0.90-0.97)	1.21 (1.12-1.31)	0.97 (0.90-1.04)	1.34 (1.21-1.47)
Measured BMI	0.92 (0.88-0.96)	1.11 (1.03-1.20)	1.00 (0.92-1.09)	1.32 (1.20-1.46)
Self-report BMI	0.95 (0.90-1.01)	1.33 (1.21-1.47)	0.94 (0.84-1.05)	1.35 (1.16-1.57)
Age ≥65	0.90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

Flegal KM, at al. JAMA 2013;309:71-82.

Controversy

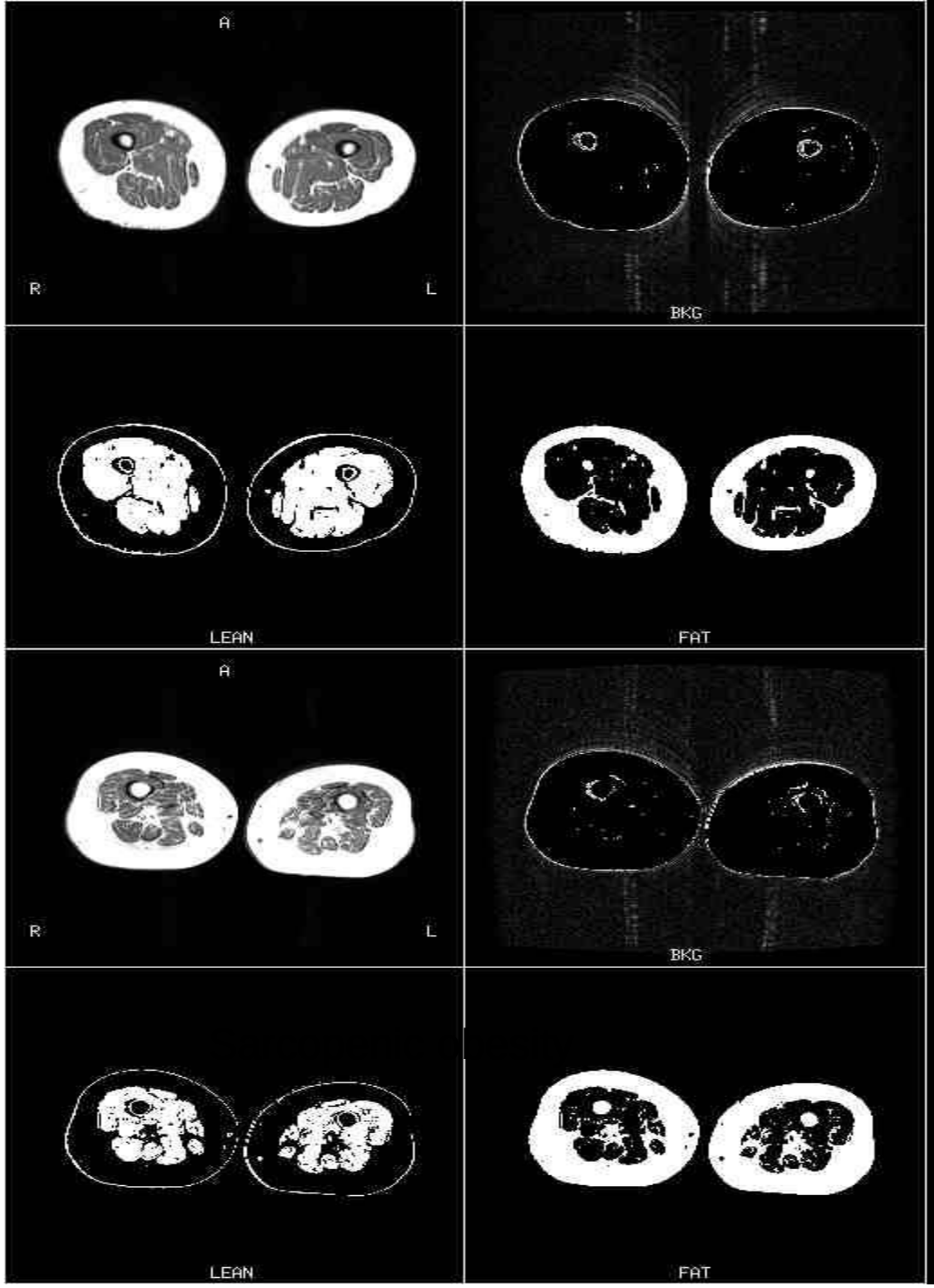
- The Big Fat Truth – Hughes V. Nature 2013; 497: 428-30.
- How to interpret these findings for health professionals and the public?

Lowest mortality shifts towards higher BMI for older persons



Source: Childers, D.K. & Allison, D.B. Int. J. obesity 34, 1231–1238 (2010).

Sarcopenic Obesity



Overweight only protective in patients with high muscle mass

- Murphy RA, et al. Diabetes Care 2014; 37:3213-9.
- 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

- Bea, JW, et al, Am J Epidemiol 2015;182: 585-96.
- 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

- Cheng FW, et al. Obesity 2016, Aug 29, Epub ahead of print.
- 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

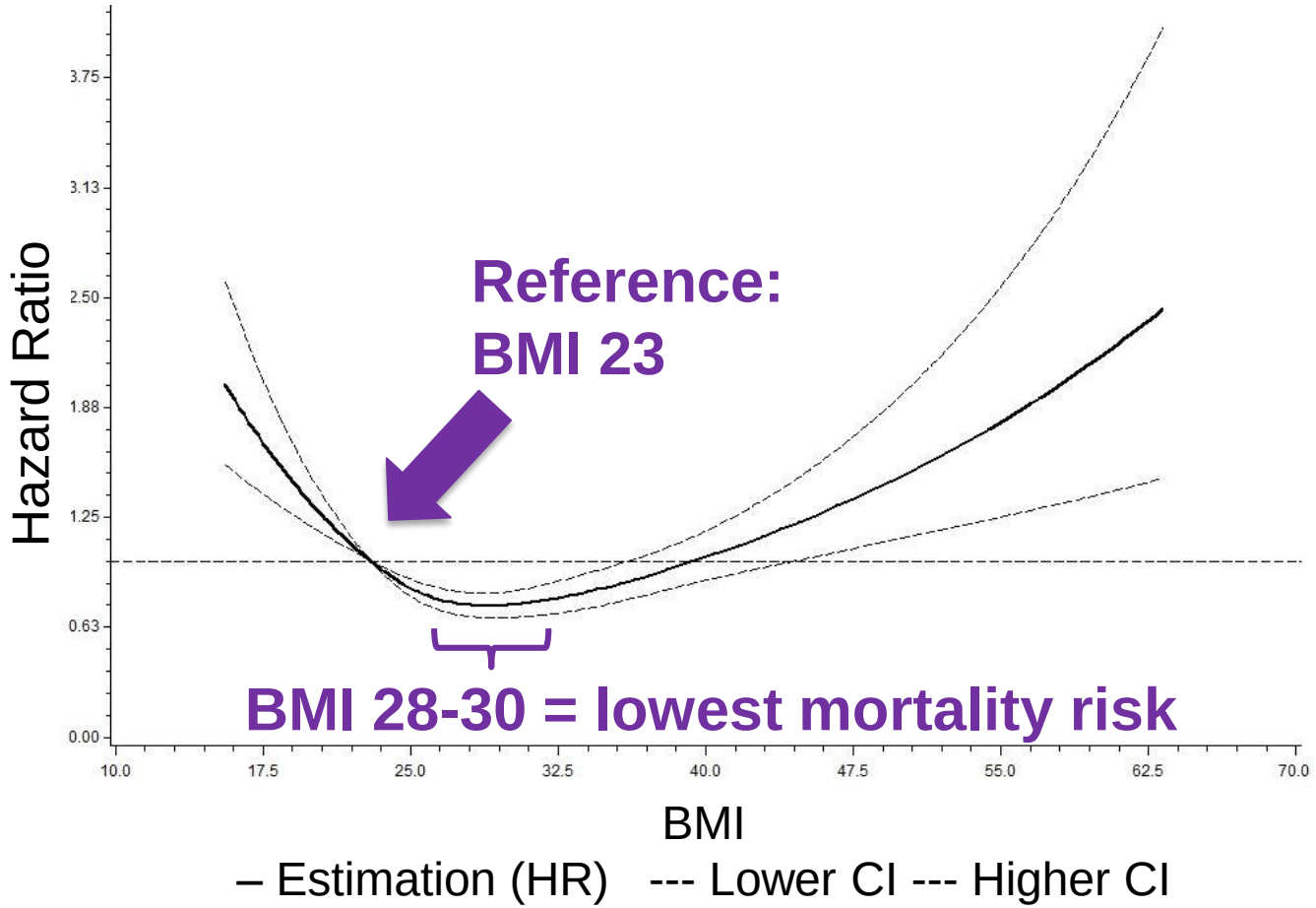
All-cause mortality in relation to BMI
(reference BMI 18.5-24.9)

	BMI <18.5	**BMI 25-29.9**	**BMI 30-34.9**	**BMI 35-39.9**	**BMI ≥40**
Events	12/14	920/1866	578/1202	252/480	97/171
Model 1	3.30 (1.86-5.86)	0.83 (0.74-0.93)	0.90 (0.80-1.02)	1.11 (0.95-1.30)	1.46 (1.17-1.82)
Model 2	2.72 (1.53-4.84)	0.84 (0.75-0.94)	0.91 (0.80-1.03)	1.13 (0.96-1.32)	1.55 (1.24-1.93)
Model 3	3.35 (1.88-5.96)	0.80 (0.71-0.90)	0.78 (0.69-0.89)	0.96 (0.81-1.12)	1.17 (0.93-1.47)

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

- Chen FW, et al. J Nutr Gerontol Geriatr 2016;35:1-16.
- 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.

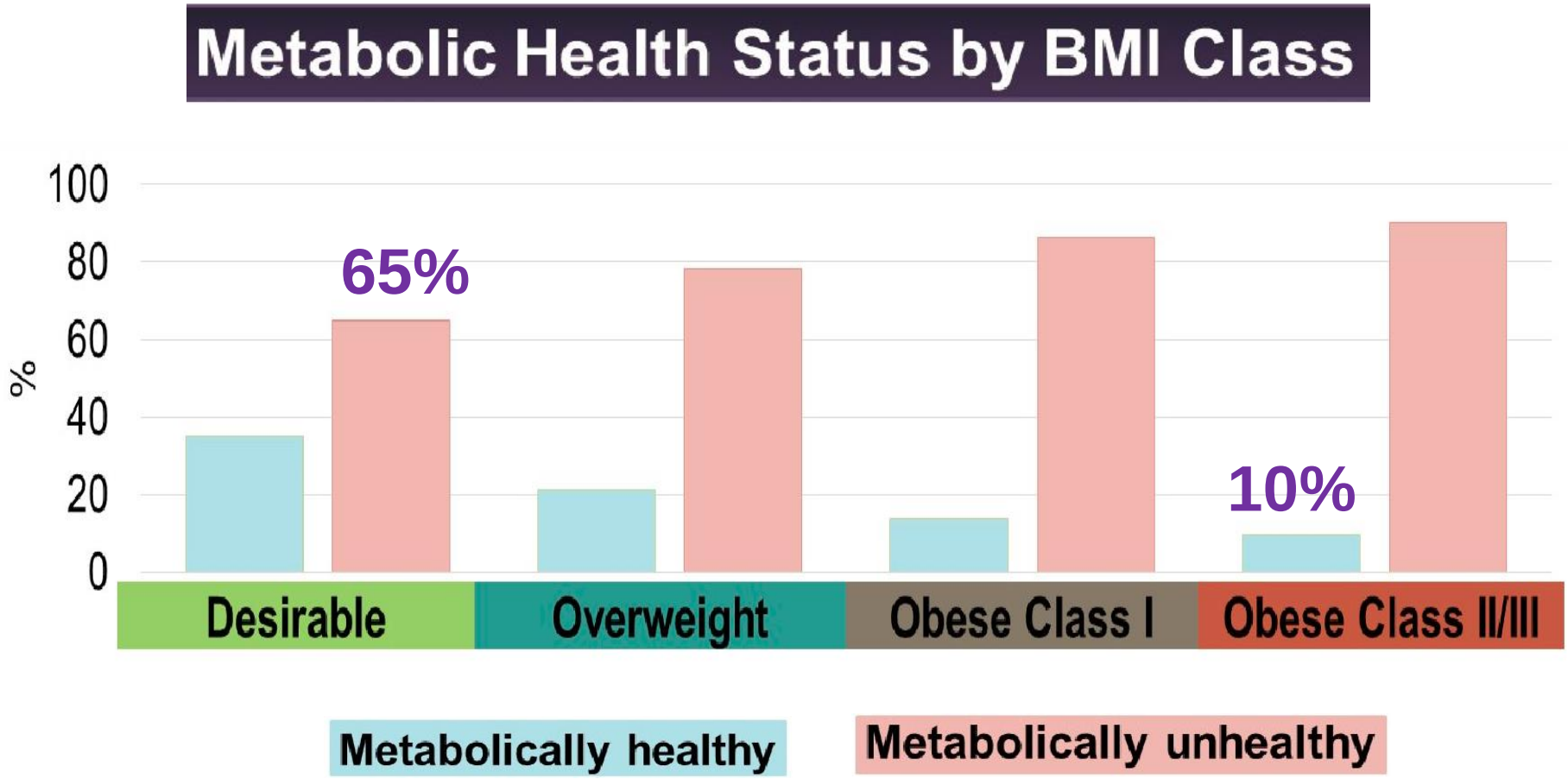
Sensitivity Analyses

- 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

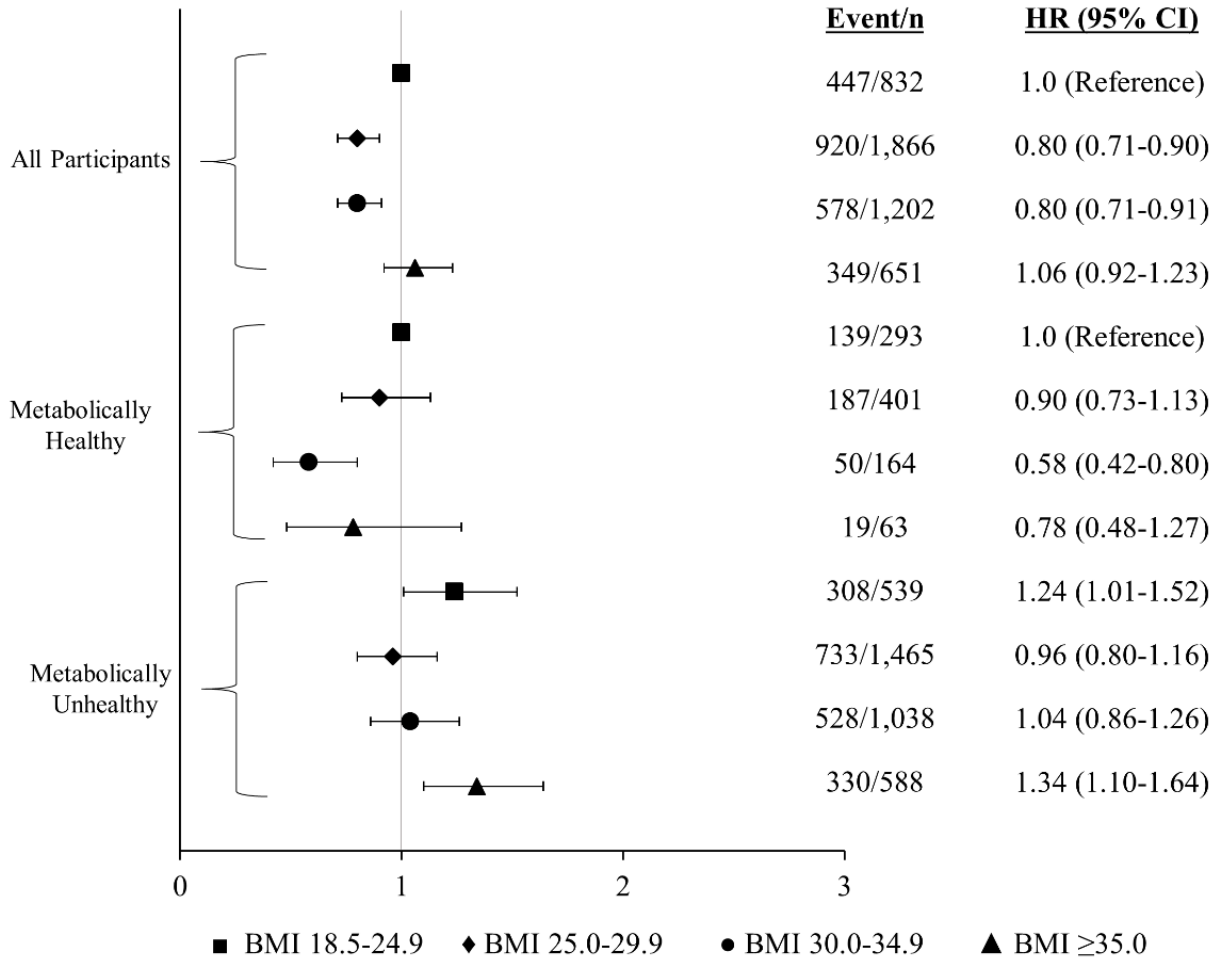
- 2294 deaths over mean 10.9 years of follow up.
- Metabolically healthy overweight or obesity was not associated with a significantly greater mortality risk.
- Findings unchanged by exclusions tested in sensitivity analyses and by propensity scoring.
- Association between BMI and mortality was more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

Proportion of metabolically unhealthy increased at higher levels of obesity



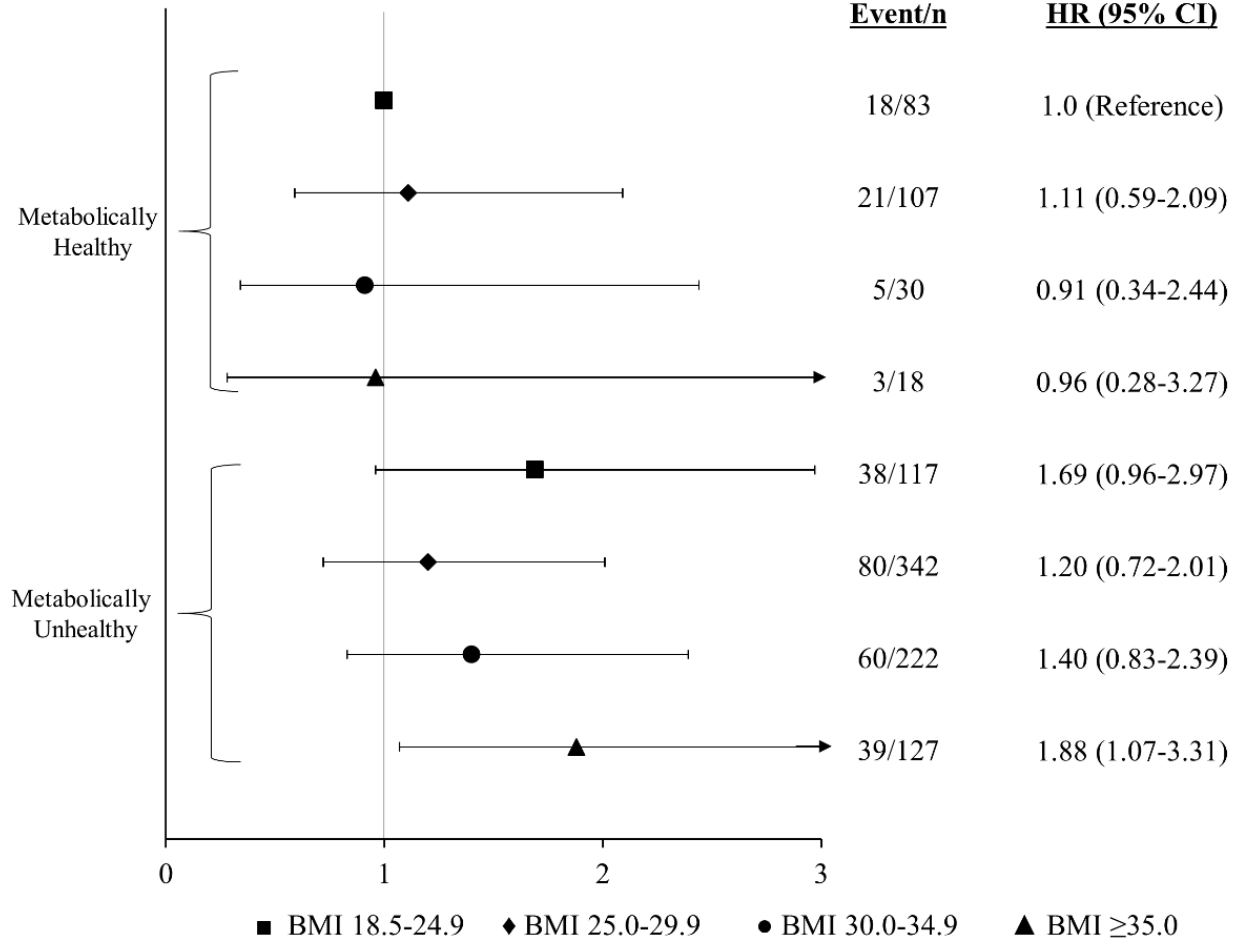
All Participants

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



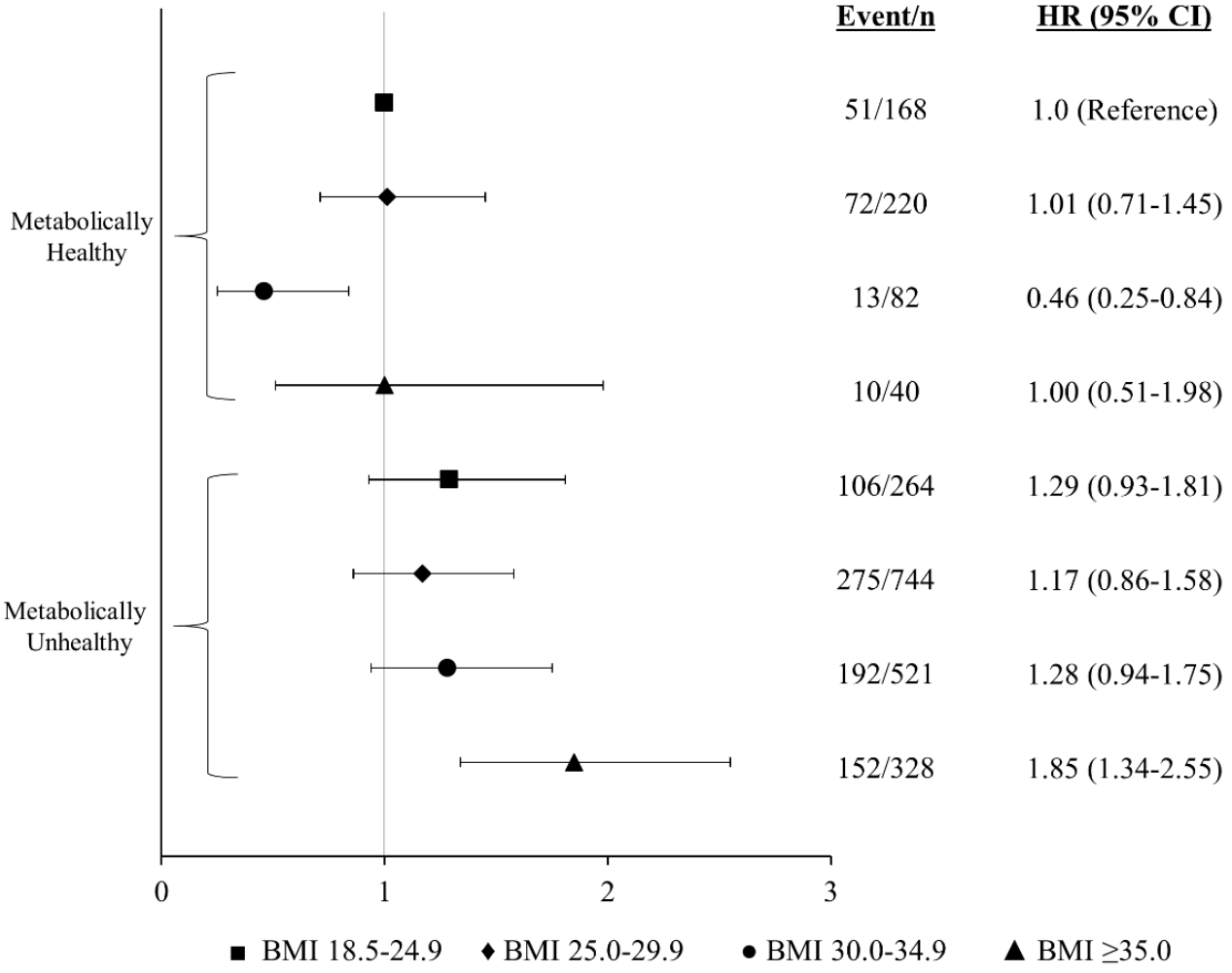
Never Smoker with No Identified Chronic Disease Burden

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



Never Smoker 5-year Lag Analysis

Figure 2C. Never-Smoker, 5-Year Lag Analysis (n=2,367)



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?