Obesity
- the obesity paradox in old age

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I have no relevant conflicts of interest to declare
Synopsis

• What is the obesity paradox?
• Why is it a paradox?
• The conflicting evidence
• Is there a simple catch?
• If it’s true, what’s the explanation?
What is the obesity paradox?

• About 2/3 of the adult populations of US/UK are overweight or obese by usual criteria
• It is regarded as major public health challenge
• But in presence of chronic disease, overweight patients and those with mild (+possibly moderate) obesity may have a better survival
• And, in the older population in various settings, traditional obesity related risk factors of cardiovascular death (BMI, serum cholesterol, BP etc) are associated with lower risk of death.
What is the obesity paradox?

• This phenomenon is also called "reverse epidemiology"
• Also seen in a variety of chronic diseases states such as end-stage renal disease requiring dialysis, chronic heart failure, rheumatoid arthritis, and AIDS.
Why a paradox?

• Obesity in adults generally predicts grief
• Obesity in older adults also is associated with poor function
Multipurpose Household Survey - 352,020 subjects, aged 20–89 y

- self-reported height, weight, ≥2 co-morbidities, self-rated health

- Obesity is associated with comorbidity and self-rated health
- For obese subjects these states at any age category were similar to (or worse than) those found for older normal weight subjects of the next older age category.
Why a paradox?

- Obesity in adults generally predicts grief
- Obesity in older adults also is associated with poor function
- Weight gain is associated with deteriorating physiology
Effects of Body Composition and Adipose Tissue Distribution on Respiratory Function in Elderly Men and Women: The Health, Aging, and Body Composition Study

Andrea P. Rossi,¹ Nora L. Watson,² Anne B. Newman,² Tamara B. Harris,³ Stephen B. Kritchevsky,⁴ Douglas C. Bauer,⁵,⁶ Suzanne Satterfield,⁷ Bret H. Goodpaster,⁸ and Mauro Zamboni¹
• 957 men, 1024 women, mean age 73, healthy
• Body composition by DXA, FEV1/FVC
• 5 year follow up
• Baseline: FEV1 and FVC positively associated with height and muscle mass, negatively with fat mass
• 5 year changes:

Weight gain associated with greater decline in respiratory function
Could there be an error in measurement or interpretation?
Problems with BMI and Obesity

- The contribution of fat and muscle in any specific BMI will vary, according to genetics, health status etc.
- Subcutaneous and visceral adiposity have differential effects
- Weight loss may suggest muscle loss rather than fat loss
Problems with BMI and Obesity

• The contribution of fat and muscle in any specific BMI will vary, according to genetics, health status etc.
• Subcutaneous and visceral adiposity have differential effects
• Weight loss may suggest muscle loss rather than fat loss

And in some studies, when fat mass and/or fat free mass are used instead of BMI, then the paradox is absent or diminished
Sarcopenia (Rosenberg 1989)

Young, active

Old, sedentary
Muscle function correlates with clinical outcomes better than muscle mass

- Hospitalisation
- Falls
- Fractures
- Loss of mobility
- Mortality
Muscle function correlates with clinical outcomes better than muscle mass

- Hospitalisation
- Falls
- Fractures
- Loss of mobility
- Mortality

There are several explanatory factors but one of these is the presence or absence of obesity, with its impact on muscle function.
Prevalence of sarcopenia and sarcopenic obesity increases with age (USA) (Baumgarter et al, Ann NY Acad Sci, 2000)

Sarcopenia becomes more prevalent than obesity in >80s
Weight and ADL functioning
(Snih et al, Am J Epidemiology 2010)

- 6166 people in Central/South America
- X-sectional study
- Adjusted for age, gender, smoking, city, education (all associated with ADL)

Indicates that underweight? Sarcopenia is part of explanation
Is there something else confounding the association?
The possibility of reverse causality

• In a random sample, some people are losing weight because they are ill
• They will become over represented in the lower BMI groups
• This reduces the survival rate of these groups

But the paradox persists in some studies when those reporting recent weight loss are excluded and early deaths are eliminated from the analysis.
Inadequate case mix adjustment

In clinical populations, the distribution of other risk factors may be weighted towards those without the risk factor of obesity eg smoking,
Obesity in Older People With and Without Conditions Associated With Weight Loss: Follow-up of 955,000 Primary Care Patients

Kirsty Bowman, João Delgado, William E. Henley, Jane A. Masoli, Katarina Kos, Carol Brayne, Praveen Thokala, Louise Lafortune, George A. Kuchel, Alessandro Ble, and David Melzer; as part of the Ageing Well Programme of the NIHR School for Public Health Research, England
Large study exploring potential confounders

- Overall, obesity 1 (BMI 30-35) associated with lower death rates
- Among the younger 65-69, obesity more common in long term survivors
Cross-sectional estimates of the percentage of subjects by conventional body mass index category and number of years to death, for the 65–69 age group.
Large study exploring potential confounders

• Overall, obesity 1 (BMI 30-35) associated with lower death rates
• Among the younger 65-69, obesity more common in long term survivors
• Overall, the BMI fell during follow up
• After excluding confounders (smoking, dementia, multimorbidity, recent cancer, heart failure), AND shorter follow up (< years)
  ➢ nadir is BMI 23-27 for younger, rising with age
Spline point estimates for continuous body mass index by age group for the “healthier agers.”

Nadir moves to the right with age

Large study exploring potential confounders

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- Among the younger 65-69, obesity more common in long term survivors
- Overall, the BMI fell during follow up
- After excluding confounders (smoking, dementia, multimorbidity, recent cancer, heart failure), AND shorter follow up (< years)
  - nadir is BMI 23-27 for younger, rising with age
  - DM and Heart disease: associated with increased weight at least to age 84
Is the paradox selective?

There is evidence that suggests that the adverse effects are not applicable to all groups, eg. Survival is better for overweight/obese individuals -

- after acute stroke
- acute medical hospitalisation of older people
- cardiological interventions
Survival at 1 year after PCI for IHD
Bundhun PK et al. Systematic Review and Meta-Analysis of Randomized Controlled Trials and Observational Studies Medicine (Baltimore). 2015 Nov;94

- 22 studies from 2000 to 2015
- 242,377 patients:
  - 73,143 normal weight
  - 103,608 overweight
  - 65,626 obese.
- Obese>Overweight>normal - younger, higher cardiovascular risk factors and more medications
FIGURE 3. The 12 months follow-up for mortality risk among overweight and obese patients as compared to normal weight patients after percutaneous coronary intervention.
Similar results for in hospital mortality and survival after one year.

**FIGURE 3.** The 12 months follow-up for mortality risk among overweight and obese patients as compared to normal weight patients after percutaneous coronary intervention.
Summary - body composition and disability

- Adiposity seems to confer disability risk
- So does sarcopenia
- And sarcopenia predominates in the older old
- And sarcopenia is more dangerous in the short term
- ______________________

- Whilst the underlying sarcopenia may explain the negative effect of low BMI, it does not explain the apparent benefit of higher BMIs
- What additional explanation might exist?
Cardiorespiratory fitness
-the "fit fat" controversy

• 15 studies, age >60, included measures of BMI, body composition, cardiorespiratory fitness and physical activity (PA)
• 14 reported the obesity/mortality paradox, despite adjustment for fitness and PA
• 2 studies stratified fitness but paradox persisted
Individual studies (adapted by Yerrakalva et al)

Overweight nearly always better survival than thin/normal (generally unadjusted)

Obese variable
Stratification by CR fitness
adapted from Woo J et al. Age (Omaha), 2013

Obese high fitness survival
similar to
Normal weight low fitness
• The paradoxical better survival with higher BMI was strongest in those with co-morbidities (2 studies)
  ➢ in context of stresses eg acute/chronic illness, additional mass (?fat and/or muscle) is protective
• There really is such a thing as “healthy obesity”
“Healthy obesity”

• This is absence of the expected cardiometabolic risk factors:
  ➢ higher BP, TGs, glucose, inflammatory markers and
  ➢ lower HDL-C, insulin resistance
• Hypothesis is that cardiorespiratory fitness intervenes
• Supported by exercise RCTs showing impact on same factors
• Plus, direct effects of adipose tissue
Possible benefits of adipose tissue

• Causes increased production of TNF alpha receptors, thus mitigating adverse effect of circulating TNF alpha
• improved hemodynamic stability in the obese
• lipoprotein protection against endotoxins
• lipophilic toxin sequestration by the adipose tissue.
What seems to be the best guess?

- BMI is about more than obesity
- Obese people are a heterogeneous group— the distribution matters, especially muscle
- Sarcopenia explains some of the low BMI disadvantage
- Case mix adjustment suggests that for healthier people, there is no paradox
- For obese/overweight, fitness mitigates negative impact
- In clinical populations, higher BMI may provide resilience
Suggestions for future research
(also drawing on Yerrakalva 2015, Bahat and Inhan, 2016, Ahmadi 2015)

• Prospective studies
• Measures of BMI *plus* body composition
• Visceral, abdominal and total adiposity
• Stratification by healthy, comorbid, frail and end of life
• Objective measures of physical activity and fitness
The public health and clinical message

• Weight loss sometimes indicates occult disease, and this explains some of the low BMI = low survival observation
• Muscle matters for metabolic reserve
• Weight loss without exercise may be counterproductive – causing sarcopenic (milder) obesity
• Increasing physical activity, including through prescribed exercise programmes trumps weight loss for “overweight” and obese older adults
Thank you
Sarcopenic obesity

= sarcopenia + obesity in older adults

• currently lacks a consensus (operational) definition

• obesity + reduced strength $\rightarrow$ increased risk
  - poor physical function and falls
  - low BMD and fractures.

• obesity + reduced muscle mass $\rightarrow$ probable risk
  - cardiovascular disease, type II diabetes and mortality
Sarcopenia is >3 times more predictive than obesity

### ADL disability and Body Composition

**Table 4. Odds ratios (95% CI) for three or more physical disabilities, balance and gait abnormalities, and falls in the past year by sarcopenia body fat classification: New Mexico Elder Health Survey (n = 883)**

<table>
<thead>
<tr>
<th></th>
<th>Three or more Disabilities</th>
<th>One or more abnormalities of Balance</th>
<th>Gait</th>
<th>Falls in Past Year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
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<tr>
<td>Normal Muscle</td>
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<tr>
<td>Nonobese</td>
<td>1.00</td>
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<tr>
<td>Obese</td>
<td>1.34 (0.48–4.12)</td>
<td>1.90 (0.54–8.83)</td>
<td>1.24 (0.63–2.51)</td>
<td>1.41 (0.80–2.52)</td>
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<tr>
<td>Sarcopenic</td>
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<tr>
<td>Nonobese</td>
<td>3.78 (1.36–11.67)</td>
<td>5.16 (1.46–24.33)</td>
<td>1.08 (0.46–2.49)</td>
<td>2.12 (1.08–4.18)</td>
</tr>
<tr>
<td>Obese</td>
<td>8.72 (2.52–32.80)</td>
<td>3.96 (0.64–24.43)</td>
<td>4.41 (1.53–13.04)</td>
<td>3.34 (1.37–8.26)</td>
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<tr>
<td><strong>Women</strong></td>
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<tr>
<td>Normal Muscle</td>
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<tr>
<td>Nonobese</td>
<td>2.15 (1.11–4.30)</td>
<td>0.84 (0.29–2.54)</td>
<td>1.34 (0.65–2.71)</td>
<td>1.45 (0.80–2.64)</td>
</tr>
<tr>
<td>Obese</td>
<td>2.96 (1.35–6.60)</td>
<td>0.98 (0.30–3.19)</td>
<td>0.95 (0.40–2.19)</td>
<td>1.66 (0.80–3.42)</td>
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</tr>
<tr>
<td>Obese</td>
<td>11.98 (3.07–61.56)</td>
<td>1.21 (0.15–6.67)</td>
<td>5.45 (1.44–22.58)</td>
<td>2.12 (0.86–5.05)</td>
</tr>
</tbody>
</table>

Note: Data suggests that sarcopenia is a better predictor of ADL disability than obesity, with odds ratios more than 3 times higher for sarcopenic individuals compared to nonobese and obese groups.