Is Obesity a Disease?

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What do we know?

- Obesity predisposes to a wide range of illnesses.
- BMI levels >40 kg/m² are associated with premature mortality.
- Weight regulation has very strong biological underpinnings. No one chooses to be obese.
- Weight loss improves many aspects of health.

Relationship Between BMI and Risk of Type 2 Diabetes Mellitus

[Graph showing the relationship between BMI and risk of Type 2 Diabetes Mellitus.]

BMI
Percentage
20
25
30
35
40

Relationship between BMI and crude percentage of women reporting medical problems, surgical procedures, symptoms, and health care utilization.


Hypertension

Relationship Between BMI and Cardiovascular Disease Mortality

Relative Risk of Death

Body Mass index

Lean
Overweight
Obese


Behavioral Weight Loss: The Look AHEAD (Action for Health in Diabetes) Trial

• 5,145 subjects with T2 DM recruited from 16 intervention centers across the US.
• Hypothesis: weight loss would reduce cardiovascular events.
Effect of Weight Loss on Glycemic Control in Type 2 Diabetes (Look AHEAD)

New data, new directions:

- Mortality data
- The obesity paradox
- Metabolically healthy obesity
- Normal weight obesity
- Weight loss: Look Ahead vs bariatric surgery
- What do we do with all this?
Hazard Ratio (risk) of Mortality and Obesity

Mortality is lowest with BMI 25-30 kg/m²

Mortality is not significantly different with BMI 30-35 kg/m²

Excess mortality from obesity is likely due to those with BMI >35 kg/m²

Flegal, JAMA Jan 2, 2013, 309: 71-82

Secular Trends in Risk Factors

NHANES surveys 1960-2000

JAMA. 2005;293:1868-1874

Secular Trends in Drug Treatment

NHANES surveys 1960-2000

JAMA. 2005;293:1868-1874
#1 Somebody that I used to know
Gotye and Kimbra

#1 Physical by Olivia Newton John

Is old data on mortality still true?

BMI/Mortality in Older People

American Cancer Society, >300,000 People all cause Mortality age 30-80


Sarcopenic Obesity in the Elderly

4,200 men age 60-79 followed for 11 years. 1,300 deaths
Interim Summary

- Older BMI/Mortality data may no longer be representative
  - Secular changes in mortality/risk factors
  - Changes in prevalence of obesity
- BMI/Mortality relationship is likely different in older people
  - Sarcopenia may be important
- Why do we attribute causality to obesity but not low weight?

**The “Obesity Paradox”: Risk is Lower**

The graph shows overall mortality and cardiac death rates across body mass index (BMI) categories.

The table lists cardiovascular diseases and conditions where the presence of the obesity paradox has been reported:

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic heart failure</td>
<td>[54]</td>
</tr>
<tr>
<td>Acute heart failure</td>
<td>[54]</td>
</tr>
<tr>
<td>Heart failure with preserved ejection fraction</td>
<td>[54, 55]</td>
</tr>
<tr>
<td>Coronary artery disease with cardiovascular risk profile</td>
<td>[90]</td>
</tr>
<tr>
<td>Acute coronary syndromes</td>
<td>[103, 104]</td>
</tr>
<tr>
<td>Unstable angina/NSTEMI</td>
<td>[105]</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>[106, 107]</td>
</tr>
<tr>
<td>Acute cerebral stroke or transient ischemic attack</td>
<td>[108]</td>
</tr>
<tr>
<td>Diabetes + cardiovascular risk profile</td>
<td>[109]</td>
</tr>
<tr>
<td>Cardiovascular rehabilitation</td>
<td>[110]</td>
</tr>
<tr>
<td>Acute MI</td>
<td>[111]</td>
</tr>
<tr>
<td>Percutaneous coronary intervention (PCI)</td>
<td>[112, 113]</td>
</tr>
<tr>
<td>Acute percutaneous coronary intervention (PCI)</td>
<td>[114]</td>
</tr>
<tr>
<td>Transcatheter aortic valve replacement (TAVR)</td>
<td>[115]</td>
</tr>
<tr>
<td>Carotid endarterectomy</td>
<td>[116]</td>
</tr>
<tr>
<td>Bypass surgery</td>
<td>[117, 118]</td>
</tr>
<tr>
<td>Vascular surgery</td>
<td>[119, 120]</td>
</tr>
<tr>
<td>Vascular surgery</td>
<td>[121, 122]</td>
</tr>
<tr>
<td>Heart transplantation</td>
<td>[123]</td>
</tr>
</tbody>
</table>


Heart Fail Rev DOI 10.1007/s10741-014-587-4

587 articles on Obesity Paradox
Obesity Paradox in ESRD

Prog in Cariovasc Dis 56:415-425-2014

BMI CHF Mortality

Meta-analysis of 30 studies including >39,000 patients
With heart failure

Eur Heart J, 2013; 34:1404–1413

Mortality in ICU

Dutch National Intensive Care Evaluation Registry
n=154,300 ICU patients

Crit Care Med 2013; 41:1878–1883
Mortality with Diabetes

J Gen Intern Med 29(1):25–33

74,710 adults followed as part of the National Health Interview Survey, 1997-2002 followed for 9 years

Mortality with Diabetes


BMI Mortality Relationships

Metabolically Healthy Obesity (MHO)

- Not all obese people are at risk for metabolic diseases
- No widely accepted definition of MHO, often simply those without abnormal metabolic markers
- May also relate to those who are obese but physically fit
- If they are not at risk for health problems how can their 'obesity' be a disease?

Phillips CM. Rev Endocr Metab Disord. 2013:

The Metabolically Healthy Obese

- Meta-analysis of eight studies (n=61,386; 3988 events) all cause mortality or CVD events. If you look at studies with > than 10 yr follow up:

<table>
<thead>
<tr>
<th>Group</th>
<th>RR</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolically healthy normal weight</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Metabolically Healthy Obese</td>
<td>1.24</td>
<td>1.02 - 1.55</td>
</tr>
<tr>
<td>Metabolically unhealthy normal weight</td>
<td>3.14</td>
<td>2.36 - 3.93</td>
</tr>
<tr>
<td>Metabolically unhealthy obese</td>
<td>2.65</td>
<td>2.18 - 3.12</td>
</tr>
</tbody>
</table>

- Their conclusion is MHO doesn’t really exist


Metabolically Healthy Obesity

- all cause mortality or CVD events. If you look at studies with > than 10 yr follow up.

Ann Intern Med. 2013;159:758-769
Interim Summary 2

• Obesity appears to be ‘protective’ in patients with other serious medical conditions
• Some obese people are pretty healthy
• Some normal weight people are metabolically unhealthy
• May relate to sarcopenia, fitness or other physiological processes.

Look AHEAD Trial

Subjects were able to exercise and were compliant with healthcare. Perhaps 8% weight loss does not add that much in people like this?

Behavioral Weight Loss: The Look AHEAD (Action for Health in Diabetes) Trial


• Problem was that the study was powered for an event rate of 3.125%/year and at the 3 year mark the event rate was 0.7%/year
• This was due to
  – “healthier” than those in epidemiologic cohorts.
  – GXT excluded people with low exercise tolerance
Swedish Obese Subjects Trial  
Bariatric Surgery vs Usual Care

• Nonrandomized prospective controlled study
• 2010 pts had surgery compared to 2037 contemporaneously matched controls
• Median follow up 14.7 years
• 30% weight loss in gastric bypass group
• Significantly reduced mortality from cancer, CAD

Interim Summary 3

• 5% weight loss prevents diabetes
• 8% weight loss in those with diabetes improves metabolic markers
• 8% weight loss in people with diabetes does not reduce mortality compared to usual care
• 30% weight loss in those with severe obesity appears to reduce mortality

The development of weight related illnesses
Obesity as a “Modifiable Risk Factor”

- We have learned that there is not “one best” LDL-C level, the goal is tailored to risk
- We have learned that too aggressive treatment of glucose or blood pressure may be bad for people with diabetes
- We do not yet know what the appropriate goals are for obese patients, but they likely will vary by individual

Summary

- people with a BMI >30 kg/m² have increased risk of morbidity or mortality
- Obesity is a modifiable risk factor because for many people it is one of several factors that contribute to the development of a range of other conditions
- We need to better understand what ‘obesity’ is to better target treatment appropriately