



Making Sense of the Obesity Paradox

Written by Brian Hoyle

Mercedes Carnethon, PhD, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA, discussed the obesity paradox—the tendency for obese individuals, including those with chronic diseases, to survive longer than adults of normal weight as determined by body mass index (BMI).

The data supporting the obesity paradox are strong. A recent meta-analysis based on 89 studies, using normal-weight individuals as the reference, reported a relative risk of all-cause mortality of 0.93 (95% CI, 0.89 to 0.95) for overweight individuals (BMI 25 to <30 kg/m²), 1.13 (95% CI, 1.06 to 1.19) for obese individuals (BMI 30 to <35 kg/m²), and 1.25 (95% CI, 1.13 to 1.39) for extremely obese individuals (BMI ≥35 kg/m²) [Flegal KM et al. *JAMA*. 2013]. Another meta-analysis of 9 studies that addressed BMI in patients with chronic heart failure reported lower all-cause and cardiovascular mortality rates in overweight (HR, 0.84; 95% CI, 0.79 to 0.90) and obese (HR, 0.67; 95% CI, 0.62 to 0.73) individuals [Oreopoulos A. *Am Heart J*. 2008]. Another meta-analysis involving >81 000 hemodialysis patients reported a crude hazard ratio for overweight versus normal-weight patients of 0.67 (95% CI, 0.65 to 0.68). Adjustment for age, sex, diabetes, smoking, cholesterol, and chronic kidney disease produced a hazard ratio of 0.94 (95% CI, 0.92 to 0.96) [Jialin W et al. *Nephron Clin Pract*. 2012]. Yet, another meta-analysis exploring weight and acute coronary syndrome that involved >218 000 patients reported a reduced risk of death in individuals who were overweight (HR, 0.70; 95% CI, 0.64 to 0.76), obese (HR, 0.60; 95% CI, 0.53 to 0.68), and severely obese (HR, 0.70; 95% CI, 0.58 to 0.86) [Niedziela J et al. *Eur J Epidemiol*. 2014].

The list of chronic diseases linked with the obesity paradox is long and includes chronic kidney disease, chronic heart disease, heart failure, stroke, cancer, acquired immunodeficiency syndrome, rheumatoid arthritis, chronic obstructive pulmonary disease, diabetes, and hypertension.

Possible explanations for the obesity paradox include reverse causation (ie, healthier patients with the aforementioned comorbidities may be more overweight or obese) or that weight per se does not fully represent the potential adverse effects of adipose tissue. For instance, the term *metabolically obese normal weight* (MONW) was coined in 1981 to describe individuals who are not considered obese based on their height and weight (BMI <28 kg/m²) but who are hyperinsulinemic, insulin resistant, and at risk of type 2 diabetes, hypertriglyceridemia, and premature coronary heart disease [Ruderman NB et al. *Am J Clin Nutr*. 1981]. MONW is prevalent in Americans ≥50 years of age, with the prevalence exceeding 50% in those ≥65 years of age [Wildman RP et al. *Arch Intern Med*. 2008].

Those affected tend to be nonwhite, less educated, cigarette smokers, and physically inactive, with habitually inadequate sleep and a family history of metabolic diseases. MONW has been linked with increased mortality [Kramer CK et al. *Ann Intern Med*. 2013].

More than 85% of patients with type 2 diabetes are overweight or obese. The diabetes that develops in more normal-weight individuals, however, may be associated with a doubling of the risk of mortality (HR, 2.2; 95% CI, 1.4 to 3.4), including cardiovascular mortality [Carnethon MR et al. *JAMA*. 2012]. In the Look AHEAD study [NCT00017953; The Look AHEAD Research Group. *New Engl J Med*. 2013], 5145 overweight diabetics were randomized to receive intensive modifications in their lifestyle or education. The composite end point after up to 13.7 years of follow-up was fatal or nonfatal cardiovascular disease, stroke, or angina that required hospitalization. Even though the intensive lifestyle intervention focused on weight loss, improved fitness, lowered glycated hemoglobin, and reduced waist circumference, the rate of cardiovascular events was unaffected.

The plausibility of the obesity paradox can be assessed based on several factors. One is nutrition. Obesity, which results from overnutrition, has been linked with longer-term mortality. Wasting, which is due to undernutrition, is associated with short-term mortality. It may be that those with chronic disease do not live long enough to suffer from the adversities of overnutrition

Peer-Reviewed
Highlights From

ObesityWeek

November 2–7, 2014
Boston, MA



[Kalantar-Zadeh K et al. *Curr Opin Clin Nutr Metab Care*. 2007]. In this scenario, a leaner body may reflect more advanced disease or increased comorbidities, whereas a heavier body type has greater metabolic wherewithal to withstand illnesses.

A second plausibility factor is age-related loss of muscle mass and strength. Sarcopenia is associated with declining function and higher rate of mortality, and it can be accelerated by factors such as physical inactivity, poor diet, and kidney disease. In older people, increased fat and declining muscle and bone can reduce overall weight. In these people, BMI may be an inappropriate measure because it cannot discriminate the distribution of fat and bone, or body composition (ie, body fat vs muscle mass). Increased abdominal fat is associated with sarcopenia; whether the fat is subcutaneous or visceral is important in determining the risk of mortality.

A third factor is the level of physical activity. Obese individuals who are physically active have a lower risk of mortality than lean individuals who are physically inactive. Fitness, regardless of weight, is associated with lower mortality [Barry VW et al. *Prog Cardiovasc Dis*. 2014].

A fourth factor is smoking. Smokers tend to have a lower BMI, which has been linked with increased mortality, compared to normal-weight individuals [Tobias TK et al. *New Engl J Med*. 2014].

Given the emphasis on BMI in examining the obesity paradox, it is germane to consider that risk factors other than BMI that are difficult to measure, such as genetics and lifestyle, may be operative. If these other factors are associated with higher mortality, then BMI could appear to be inversely related with mortality (ie, a lower BMI would be linked with increased risk of mortality) [Lajous M et al. *Epidemiology*. 2014].

To summarize, the obesity paradox is biologically plausible. In nonobese individuals, factors like diabetes may present a high risk due to underlying factors that cannot be measured. Smoking and physical inactivity may be confounders. On the other hand, the obesity paradox may not be real. Rather, it could reflect a selection bias in studies, with other factors like genetics and lifestyle being the true basis in diabetes and other chronic diseases.

Studies suggesting that obesity is nonproblematic receive prominent coverage in the popular media. With obesity rates rising, there could be a tendency to wish for a normalization of obesity, rather than confront a reality that the present course is undesirable and that a societal change is required. Clearly, more studies are needed.



2014 CONFERENCE REPORTS

- 37th Annual San Antonio Breast Cancer Symposium
December 9-13 • San Antonio, Texas, USA
- 50th American Society of Clinical Oncology 2014 Annual Meeting Science & Society
May 30-June 3 • Chicago, Illinois, USA
- American Academy of Neurology
April 28-May 3 • Philadelphia, Pennsylvania, USA
- American Academy of Ophthalmology 2014
May 18-21 • Chicago, Illinois, USA
- American Academy of Orthopaedic Surgeons
March 11-15 • New Orleans, Louisiana, USA
- American Academy of Otolaryngology-Head and Neck Surgery Foundation Annual Meeting & OTO EXPO
September 21-24 • Orlando, Florida, USA
- American Association for the Study of Liver Disease
November 4-7 • Boston, Massachusetts, USA
- American Association of Diabetes Educators
August 6-9 • Orlando, Florida, USA
- American College of Cardiology 63rd Annual Scientific Session & Expo*
March 29-31 • Washington, DC, USA
- American College of Chest Doctors
October 25-30 • Austin, Texas, USA
- American College of Emergency Physicians (ACEP14)
October 27-30 • Chicago, Illinois, USA
- American College of Rheumatology 78th Annual Scientific Meeting
November 13-18 • Boston, Massachusetts, USA
- American Congress of Obstetricians and Gynecologists 2014 Annual Clinical Meeting
April 26-30 • Chicago, Illinois, USA
- American Diabetes Association 74th Scientific Sessions*
June 13-17 • San Francisco, California, USA
- American Heart Association Scientific Sessions 2014*
November 15-19 • Chicago, Illinois, USA
- American Orthopaedic Society for Sports Medicine*
July 10-13 • Seattle, Washington, USA
- American Psychiatric Association 2014 Annual Meeting
May 3-7 • New York, New York, USA
- American Psychiatric Nurses Association
October 22-25 • Indianapolis, Indiana, USA
- American Society for Microbiology—54th Interscience Conference on Antimicrobial Agents and Chemotherapy*
September 5-19 • Washington, DC, USA
- American Society for Radiation Oncology
September 14-17 • San Francisco, California, USA
- American Society for Surgery of the Hand
September 18-20 • Boston, Massachusetts, USA
- The American Society of Hematology
December 6-9 • San Francisco, California, USA
- American Society of Nutrition Scientific Sessions & Annual Meeting at Experimental Biology 2014*
April 26-30 • San Diego, California, USA
- American Society of Plastic Surgeons Plastic Surgery The Meeting 2014
October 10-14 • Chicago, Illinois, USA
- American Stroke Association 2014 International Stroke Conference*
February 11-14 • San Diego, California, USA
- American Thoracic Society 2014 Annual Meeting*
May 16-21 • San Diego, California, USA
- American Veterinary Medical Association
July 25-29 • Denver, Colorado, USA
- Cardio Alex 2014
June 10-13 • Alexandria, Egypt
- Care for Acute Cardiovascular Conditions
October 18-20 • Geneva, Switzerland
- Caribbean Cardiac Society 29th Caribbean Cardiology Conference 2014
July 23-July 26 • Atlantis, Paradise Island, The Bahamas
- Cardiostim EHRA Europace 2014*
June 23-26 • Nice, France
- The Endocrine Society—ICE/ENDO 2014
June 21-24 • Chicago, Illinois, USA
- ESMO World Congress on Gastrointestinal Cancer
June 25-28 • Barcelona, Spain
- European Association for the Study of Diabetes 49th Annual Meeting*
September 15-19 • Vienna, Austria
- European Committee for Treatment and Research in Multiple Sclerosis
September 10-13 • Boston, Massachusetts, USA
- European League Against Rheumatism 2014 Annual Congress
June 11-14 • Paris, France
- European Lung Cancer Conference
March 26-29 • Geneva, Switzerland
- European Society of Cardiology ESC Congress 2014*
August 30-September 4 • Barcelona, Spain
- European Society of Cardiology EuroEcho 2014
December 3-6 • Vienna, Austria
- European Society of Hypertension 2014 Annual Scientific Meeting*
June 13-16 • Athens, Greece
- European Society of Medical Oncology
September 26-30 • Madrid, Spain
- European Society Traumatology, Knee Surgery, and Arthroscopy
May 14-17 • Amsterdam, The Netherlands
- Heart Failure 34th Annual Scientific Sessions
May 17-20 • Athens, Greece
- Heart Rhythm Society 34th Annual Scientific Sessions*
May 7-10 • San Francisco, CA, USA
- International Federation of Foot and Ankle Surgery/American Orthopaedic Foot & Ankle Society*
September 19-23 • Chicago, Illinois, USA
- Kidney Week
November 5-10 • Atlanta, Georgia, USA
- Movement Disorder Society
June 9-12 Stockholm, Sweden
- North American Spine Society
November 12-15 • San Francisco, California, USA
- Obesity Week
November 2-7 • Boston, Massachusetts, USA
- Orthopaedic Trauma Association
October 15-18 • Tampa, Florida, USA
- Radiological Society of North America
November 30-December 5 • Chicago, Illinois, USA
- The Society for Cardiovascular Angiography & Interventions (SCAI)
May 28-31 • Las Vegas, NV, USA
- Transcatheter Cardiovascular Therapeutics 2014 Interventional Conference
September 13-17 • Washington, DC, USA

*Proudly produced in official collaboration with the host society 1143145