



HHS Public Access

Author manuscript

Obesity (Silver Spring). Author manuscript; available in PMC 2014 March 01.

Published in final edited form as:

Obesity (Silver Spring). 2013 September ; 21(9): 1744–1745. doi:10.1002/oby.20588.

Perspective: Overweight, mortality and survival

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Keywords

BMI; overweight; mortality; epidemiologic methods; survival; obesity paradox

A large number of general population studies that compare all-cause mortality across established body mass index (BMI; weight(kg)/height(m) squared) categories have found slightly lower all-cause mortality among those with BMI 25-<30 (overweight) than among those with a BMI of 18.5-<25 (normal weight).(1) The association of BMI with mortality appears to vary by age and other factors. In the general population, at younger ages there is often a curvilinear relation between BMI and mortality, with the lowest mortality sometimes found at BMI values toward the upper end of the normal weight category. This can lead to similar or slightly lower mortality in the overweight category (BMI 25-<30) than in the full range of the normal weight category (BMI 18.5-<25). In the elderly, low BMI is often associated with higher mortality, while higher BMI levels appear either to have no association with higher mortality or even to provide some survival advantage.(2)

In individuals with chronic disease states such as heart failure, chronic kidney disease or chronic obstructive pulmonary diseases, the BMI-mortality association is either reverse J shape or inverse with higher BMI categories associated with greater survival.(3) This phenomenon is sometimes known as the “obesity paradox” or “reverse epidemiology,” a term also used for similar alterations in risk-factor-survival patterns for other cardiovascular risks as hypercholesterolemia. Although the observation of improved survival in heavier patients was not new, the specific term “obesity paradox” seems to have first been used by Gruberg et al. in 2002(4), who found that among patients with coronary artery disease who underwent percutaneous coronary intervention, very lean patients and those with BMI within the normal range were at the highest risk for in-hospital complications, cardiac death

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Competing interests: The authors have no competing interests.

Required disclaimer: The findings and conclusions in this report are those of the authors and not necessarily the official views of the Centers for Disease Control and Prevention

and one-year mortality. Modestly improved survival among overweight patients relative to normal weight patients has repeatedly been observed in diverse situations, for example in a review of findings in the surgical population(5), in a meta-analysis of acutely ill patients (6) and in a study of driver mortality in vehicle crashes.(7)

All-cause mortality reflects the net effect of incidence and survival across all causes of death. Although overweight is a risk factor for certain medical conditions, including coronary heart disease, diabetes and some types of cancer, the relative risk for mortality from these conditions among the overweight is not necessarily as high as the relative risk for incidence. In addition, some medical conditions leading to mortality may have little or no association with higher weight, and some conditions leading to mortality, such as lung cancer or hip fracture, appear to be inversely related to BMI.(8) (9) The association of overweight with modestly increased survival across many conditions could result in a net decrease in the risk of all-cause mortality associated with overweight.

Hypothetical scenarios have been put forward to explain these oft-repeated epidemiologic findings in the general population of similar or lower mortality among the overweight relative to normal weight as being due to bias from smoking or pre-existing illness. It is sometimes argued that the increased mortality risk at low BMI levels among smokers is evidence of residual confounding by unmeasured aspects of smoking, but the same phenomenon of increased mortality risk at low BMI levels is seen among never smokers (10, 11) making residual confounding an unlikely explanation. Former smoking has little or no association with BMI levels (10, 11) and is thus an even less likely source of residual confounding. Similarly little evidence exists to show that illness-related weight loss is a source of bias or to identify the possible direction or magnitude of any bias.(12) Deletion of the first few years of mortality, a maneuver suggested to at least partially adjust for possible illness-related weight losses, has generally been shown to have little or no effect on the results. (13) Researchers sometimes delete the majority of deaths (70 to 90 percent) in a sample to address these putative biases. The deletion of such a large proportion of the sample may itself increase bias, although in many studies such deletions have been found to have little or no effect on the results (1)

A more parsimonious explanation for the mortality advantage seen among overweight people is that overweight people have modest survival advantages in a wide variety of adverse situations that are not outweighed by the increased risk of some medical conditions. The repeated observations of curvilinear relations at younger ages and null to inverse relations at older ages are consistent with the evolving body of research suggesting that for patients with a variety of conditions, survival may be slightly better for the heavier patients. Many of these studies are clinical studies or analyses of registry data and thus based on patients whose medical history and severity of illness are well characterized, making bias from undiagnosed illness less likely.

The underlying reasons for the increased survival among overweight and even obese patients have not been well elucidated. Potential suggestions include both physiologic and behavioral factors. Some research suggests that overweight and obese patients may receive better medical treatment (14), but other studies suggest they may receive less appropriate

treatment (15); this might vary by medical condition or other factors. Lean people who develop conditions such as hypertension or diabetes mellitus may have more severe forms of the disease than obese people. As a result, mortality risk estimates derived from lean people with these conditions may overestimate the mortality risk among heavier people with those conditions. Suggested physiological mechanisms have included endocrine effects of adipose tissue, cardioprotective effects of leptin and adiponectin, and increased lean body mass and fat mass in heavier patients.

The all-cause mortality advantage seen in mildly overweight people in observational studies in the general population is small but consistent. The extensive literature on the modest survival benefits of overweight in a variety of adverse situations, including chronic and acute illness and medical procedures, supports and reinforces the findings of the general population studies.

Acknowledgments

Funding Source: KKZ is supported by grants from the National Institute of Diabetes, Digestive and Kidney Disease of the National Institute of Health (R01-DK078106), and a philanthropic grant from Mr. Harold Simmons.

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