Obesity and mortality: summary of best evidence with explanations for the obesity paradox

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Abstract

The link between obesity and increased risk of mortality is well established. However, those who are obese have greater survival when they have chronic diseases such as rheumatoid arthritis or cardiac failure; this is known as the “obesity paradox”. The obesity paradox is most probably attributable to obese individuals being more susceptible to milder forms of disease than normal-weight individuals, although other mechanisms may also operate. The benefits of weight loss in the general population are also unclear, as some study participants also lose weight through disease. Further work is required to help guide weight recommendations in both healthy individuals and those with chronic diseases.

Keywords: Cardiovascular disease, death, mortality, obesity, obesity paradox

The patterns of association between adiposity and increased risk of death in the general population are now well established and exemplified by two recent powerful studies. A meta-analysis of 57 studies involving 894,576 participants, the Prospective Studies Collaboration [1], recently showed that all-cause mortality is lowest at body mass index (BMI) 22.5–25 kg/m², after adjustment is made for age, sex, and smoking status, and excluding deaths in the first 5 years of follow-up. For each 5 kg/m² increase above BMI 25 kg/m², there was a 39% greater mortality from ischemic heart disease, 39% from stroke, 116% from diabetes, 59% from renal disease, and 82% from liver disease. These results were broadly similar to results from the European Prospective Investigation into Cancer and Nutrition [2], which followed 359,387 participants for approximately 10 years and adjusted for key potential confounders of educational attainment, smoking, alcohol, physical activity, and height. They found the lowest risk of death to be at BMI 25.3 kg/m², with a 28% increase in mortality at BMI 30–34.9 kg/m² and 106% at BMI >35 kg/m², compared with BMI 23.5–25 kg/m².

The obesity paradox

The link between obesity and mortality in the general population is well established; however, there is conflicting evidence in disease states, with obesity seemingly having a protective effect against mortality; this is known as the “obesity paradox”. For example, in a meta-analysis of studies with a total of 28,209 patients with cardiac failure [3], patients with a BMI in the overweight and obese categories had 16% and 27%, respectively, lower all-cause mortality during 2.7 years of follow-up than patients in the normal weight (BMI 18.5–24.9 kg/m²) category. A similar pattern was observed for patients with coronary artery disease [4]: in the follow-up of 250,152 such patients, even after adjustment for confounding factors, the
The evidence for the effect of weight-loss treatments on mortality is surprisingly poor, given the importance of this topic and the current recommendations for weight loss [10]; this is because of the considerable difficulties associated with study design. Most obesity treatments only produce modest weight loss – in the region of 5 kg – and thus large sample sizes and long-term follow-up would be required. To be able to attribute any differences in mortality to weight loss would require a pure obesity treatment; obesity drugs may have effects on mortality that are independent of weight loss [11]. Simply looking at weight change in large cohort studies has produced results that are in disagreement with current recommendations: they show that weight loss is associated with increased mortality [12,13]. However, these non interventional studies dealing with small amounts of weight change are heavily confounded by the effects of non intentional weight loss in disease states.

Obesity treatment and mortality

Studies involving bariatric surgery have the benefit of large weight loss that would far exceed any disease-related non intentional weight loss (>20 kg); however, large randomized trials are not financially viable, and the resulting studies have the bias of those in the cohort who elected to have surgery, versus those that chose not to. Nevertheless, two large studies have been published showing a beneficial effect on mortality of weight loss from bariatric surgery. The Swedish Obese Subjects study, a prospective cohort study of 2010 patients having a variety of bariatric surgery operations compared with 2017 patients having non surgical obesity management, showed a 29% reduction in mortality in the operated group over 10.9 years of follow-up [14]. A similar retrospective cohort study matched, for weight, 9949 patients having gastric bypass with a control group from among driving license applicants, and showed a 40% reduction in mortality among the operated group over 7 years, with 49% fewer cardiovascular deaths and 60% fewer cancer deaths [15]; however, weight was self-reported by driving license applicants, and the death data were from death certification, so the accuracy of the data used could not be guaranteed.
Key points

- In the general population, risk of death increases with a body mass index $>25 \text{ kg/m}^2$.
- In studies of patients with disease such as heart failure and rheumatoid arthritis, increasing body mass appeared to be associated with decreased mortality – the “obesity paradox”.
- The obesity paradox may be explained by overweight and obese individuals getting symptomatic, but less severe, forms of disease at an earlier age than normal-weight individuals, biasing their survival.
- The effects of intentional weight loss on risk of death are not clear, as studies have been confounded by non intentional disease-related weight loss.
- Large-scale weight loss with bariatric surgery does appear to have a beneficial effect on mortality, with a reduction in mortality of between 27 and 40% compared with similarly obese individuals choosing not to have surgery.

Summary

The best available evidence supports an adverse effect of obesity on mortality. However, there is little evidence available, other than in bariatric surgery, that reducing weight with obesity treatments decreases mortality rates. Until there is an improvement in data about the long-term benefits or otherwise of weight loss in those already obese, efforts should continue to focus on the prevention of obesity, and on the weight maintenance of those already overweight and obese.

*see glossary for definition of this term.*

REFERENCES