The study by Xu and colleagues describes their findings from the Framingham Heart Study on the association between history of body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) over 24 years and mortality risk. A primary exposure of interest in the analysis was the maximum BMI, estimated as the highest BMI measured for each person over 24 years when BMI was directly and repeatedly measured. The 24-year window preceded the start of follow-up for mortality. This approach may help lower bias from reverse causality, when underlying disease influences both body weight and mortality risk, and allow for clearer inferences on the longer-term effect of BMI on mortality risk. Each individual was classified into the standard overweight and obese BMI categories based on their maximum BMI, with normal BMI (18.5-24.9) as the reference group. The analytical sample included 6197 adult men and women from the original cohort and the offspring cohort. An increased risk in mortality was observed with increasing maximum BMI category, and maximum BMI carried higher risk among never smokers compared with ever smokers. Among never smokers in the maximum BMI categories, the mortality hazard ratios point estimates were 1.31 (95% CI, 1.13-1.51) for overweight, 1.57 (95% CI, 1.34-1.85) for obese I, and 2.38 (95% CI, 1.95-2.90) for obese II (BMI >35). While these results for maximum BMI among never smokers on the surface appear to be strong and follow a dose-response pattern, many other important analyses were conducted that must be carefully considered. The story of BMI history and mortality is far from straightforward. These primary highlighted findings may be misleading without proper context and consideration of generalizability.

The original Framingham cohort was initiated in 1948 (baseline age, 26-62 years), before the modern obesity epidemic started (approximately 1980). The offspring cohort, while closer in time to the present, is still quite old, with initiation in 1971 (baseline age, 20-59 years). Both cohorts grew into their adult body frames and achieved their maximum BMIs either before the obesity epidemic or, in the case of a subset of the offspring cohort, early in the epidemic. In the analysis stratified by cohort, the mortality risk of overweight and obesity was substantially lower for the offspring than for the original cohort. In the offspring cohort, maximum BMI in the overweight and normal weight categories carried no significant increased mortality risk for either the analyses of all individuals or the analyses of never smokers. Thus, in the offspring cohort, there was no increased risk for overweight or mild obesity, consistent with a comprehensive meta-analysis that included 97 studies, 2.88 million individuals, and 270,000 deaths, as well as analyses using representative samples of US adults. It is possible that the mortality risk of elevated BMI has been dampened by the obesity epidemic itself, that is, by our new obesogenic environment preying on our collective genetic predisposition toward fat accumulation and storage. To be overweight or mildly obese today, relative to 4 or more decades ago, appears to be the new normal. Indeed, much recent research has focused on describing phenotypes of metabolically healthy obese and metabolically unhealthy normal-weight individuals.

Within their window of 24 years of BMI being repeatedly measured, the authors further classified individuals on both maximum BMI and baseline BMI. The bottom line from these analyses was that the lowest mortality risk was observed among individuals who remained in the normal
weight or overweight categories over time. There was no difference in mortality risk for those who remained overweight and those who remained normal weight (hazard ratio, 1.04; 95% CI, 0.94-1.14). Persistent obesity over time was associated with higher mortality risk, as was weight loss. At least from these models, the bottom line is weight gain prevention, as the authors importantly included in their discussion of the study implications. However, there is much information missing from these analyses that would help with interpretation, including dynamics of weight change (eg, from minimum rather than maximum BMI), weight loss intentionality, and, importantly, stratification on original vs offspring cohorts. It is still quite possible that reverse causality by underlying illness may have contributed to the weight loss results. Nonetheless, the key finding of those with stable overweight having similar risk as stable normal weight is an important observation in support of lifestyle and environment changes to prevent chronic diseases and mortality among overweight and obese individuals. Indeed, multiple large-scale randomized clinical trials of diabetes prevention have clearly shown that decreases in disease incidence are possible through improved diet and physical activity among overweight and obese individuals, whether weight loss is achieved or not.4-7

REFERENCES