The prevalence of obesity in Western countries has escalated to alarming proportions in recent years. In 2009, the prevalence of obesity reached 36% among US adults, and is estimated to reach 50% by 2030 if current rates do not subside.\(^1,2\) This epidemic is not limited to Western countries. Countries such as China, with large populations undergoing rapid transitions to an urbanized and Western diet and lifestyle, are particularly susceptible to the public health burden of obesity, given their high absolute number at risk, despite lower overall prevalence of obesity.\(^3\)

Overweight and obesity are major risk factors for type 2 diabetes and cardiovascular disease, likely through the metabolic consequences of excess adipose accumulation (insulin resistance, dyslipidaemia, inflammation). Additionally, hormone-secreting adipose tissue may also increase risk of some cancers. Asians tend to be particularly susceptible to many of these consequences, as they tend to develop type 2 diabetes, hypertension and other metabolic diseases at lower body mass index (BMI) levels than Caucasians. This is likely due to differences in body composition.\(^4\)

For this reason, lower BMI cut-off points for classifying overweight and obesity have been proposed for Asian populations. In China, for example, BMI cut-off points of 24 and 28 are widely used to define overweight and obesity, respectively.\(^5\)

Despite overwhelming evidence associating excess body weight with several chronic disease end points, its relationship with mortality has been widely debated. In particular, there is controversy surrounding the shape of association curve between BMI and mortality. Various J-shaped, U-shaped and linear relationships have been identified in epidemiological literature, with some suggesting overweight BMI status is associated with increased mortality, and others showing no or even slightly decreased mortality, compared with normal weight individuals.\(^6\) The estimated number of deaths attributable to overweight and
obesity have also varied widely, 7,8 further fuelling the debate and public confusion.

Discrepancies in study findings for the association between BMI and mortality highlight many methodological challenges in analysing this relationship. Reverse causation is one potential source of inconsistency, and is a type of bias that occurs when a low BMI is the result of underlying illness rather than the cause of the illness. This may be a direct consequence of the disease process itself (e.g. cancer, chronic obstructive pulmonary disease) or the result of conscious weight loss attempts motivated by a serious diagnosis. Residual confounding by smoking is another major concern, as smokers tend to weigh less than non-smokers, but have significantly higher mortality rates. 9 Statistical adjustment for smoking status may not sufficiently capture the many sources of variation in smoking, such as duration of smoking and intensity of inhalation. Therefore, populations of individuals with a low BMI may consist of healthy active people, smokers and people with diagnosed or underlying chronic disease. Third, several biological intermediates (e.g. diabetes, hypertension, dyslipidaemia) have been included in some statistical models of obesity and mortality, which may substantially underestimate the effects. Finally, effect modification by age may be another source of disparity between study findings. Although the relative risk (RR) of BMI on mortality may appear lower in older vs younger populations, the absolute increase in death rates is much greater in the elderly given their overall higher mortality risk.

In this issue of International Journal of Epidemiology, Chen et al. 10 present findings from a rigorous analysis of a large Chinese cohort that supports the existence of several of these methodological concerns. The investigators recruited 224,064 nationally representative men 40–79 years of age from across China in 1990–1991. There were 40,700 deaths observed after 15 years of follow-up. After including only the 142,214 men without history of disease at baseline and at least 5 years of follow-up, and adjusting for smoking status (current, ex- or never regular smoker), the authors still observed an overall U-shaped association between BMI and mortality. Nonetheless, the lowest all-cause mortality was observed among men with a BMI 22.5–25 kg/m2, similar to the optimal BMI range for total mortality observed in Western populations. 11,12

Similar to findings from previous cohort studies, 11,12 exclusion of current and ex-smokers flattened the left side of the curve, presenting a more linear association between BMI and total mortality. In the subgroup of participants with baseline BMI 15–23.5 kg/m2, the inverse association between BMI and mortality was more pronounced among those with prior disease at baseline [RR = 0.66 [95% confidence interval (CI) 0.61–0.72] vs RR = 0.86 [95% CI:0.82, 0.91]]. These observations support residual confounding by smoking and reverse causation as major sources of bias for the association between BMI and total mortality.

Analysis of cause-specific mortality is another major strength of this paper by Chen et al. When stratified by baseline BMI, among those with BMI 15–23.5 kg/m2, BMI was inversely associated with a significant increased risk of mortality from respiratory diseases, lung cancer and stomach cancer. For those with baseline BMI 23.5–35 kg/m2, higher BMI was associated with a significantly higher risk of mortality from stroke, coronary heart disease, hypertensive heart disease and diabetic, hepatic or renal causes. These findings also support major concerns for residual confounding by cigarette smoking and underlying preclinical diseases among participants in lower BMI ranges.

The careful analysis by Chen et al. goes beyond previous studies by dissecting different causes of deaths at both lower and higher spectrums of the BMI distribution. After carefully addressing several sources of bias, the optimal BMI for mortality was observed at the normal weight range instead of the overweight range that was found in some previous studies. 8,13 A significant increase in mortality at lower BMIs is likely due to a combination of residual confounding by smoking, reverse causation bias as a result of pre-existing chronic diseases and true health effects of undernutrition, which is still common in rural Chinese populations.

This study provides strong evidence for the association between higher BMI and increased risk of mortality due to cardiovascular disease, particularly stroke, in the Chinese population. It is interesting to note that the increased risk of stroke mortality associated with overweight and obesity is much higher in China than in the USA. By addressing the aforementioned major methodological issues, this study also suggests that previous estimates for the excess mortality attributable to BMI in China may have simultaneously underestimated the impact of BMI at higher ranges and overestimated the impact at lower ranges.

The BMI distribution will continue to shift further to the right as a result of the rapid nutrition transition in China, exacerbating the impact of overweight and obesity on total and cardiovascular mortality, and consequently, worsening the deleterious curve between BMI and mortality. Therefore, a top public health challenge in China and globally in coming years and decades is to curb this trend and minimize the health and economic impacts of the rising tide of the obesity epidemic.

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References

1 Centers for Disease Control and Prevention (CDC). Vital signs: state-specific obesity prevalence among


