pating ICUs adopted the use of a standard care plan including temperature management soon after the seminal articles,[1,2] making the excellent survival rates depicted in this graph representative of the "temperature-management era." Second, the relevant comparison group for baseline survival from the Hypothermia after Cardiac Arrest Study Group trial[1] is the control group, which received no regimented care with respect to temperature management. Although control patients were highly selected from a group with a high likelihood of survival, hospital mortality was 50% (69 of 138 patients), substantially higher than the hospital mortality of 44% (411 of 939 patients) in the TTM trial involving less selected patients. Third, if the ANZICS APD includes patients admitted to the ICU, it may not capture deaths that occur in the emergency department or during pre-ICU procedures. Despite this limitation, we do appreciate a modest decline in hospital deaths over the decade from more than 60% to its current level.

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Since publication of their editorial, the authors report no further potential conflict of interest.

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BMI and Mortality among Adults with Incident Type 2 Diabetes

TO THE EDITOR: Tobias et al. (Jan. 16 issue)[1] found no evidence of lower mortality among obese patients with incident type 2 diabetes, as compared with their normal-weight counterparts. An "obesity paradox" (i.e., an association between obesity and reduced mortality) had been reported, in particular in patient populations with a short survival time, whereas obesity by its nature is a risk factor for increased long-term mortality. Our earlier results show that short follow-up and the advanced age of populations with chronic diseases are major limitations of such studies: over short periods, a high body-mass index (BMI) was not associated with increased mortality among patients with end-stage renal disease, but it was also not associated with increased mortality in the general population of equal age.[2] Moreover, different underlying causes of the disease and coexisting illnesses impede a valid comparison between patients with a high BMI and those with a low BMI. Because of these limitations, it is not possible to translate such observations into causal interpretations — for example, to advise a high body weight in these patients. The findings by Tobias et al. are a timely reminder of the many biases that need to be taken into account before a causal interpretation of population data is possible.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Although Carnethon et al.[1] found a better prognosis in obese patients with type 2 diabetes as compared with patients of "normal" weight, Tobias and colleagues did not find an obesity paradox. They explained that prior analyses were limited by short follow-up, a small number of deaths, and a lack of data on smoking or undiagnosed diseases.

We are concerned, however, that neither study mentioned above accounted for fitness, especially because obese but fit persons with type 2 diabetes have a considerably better prognosis

than lean and unfit persons.[2] We found that fitness alters the relationship between adiposity and prognosis in pre–type 2 diabetes, coronary heart disease, and heart failure.[3,4] Despite the fact that physical activity was approximately 25% lower in overweight or mildly obese participants (BMI [the weight in kilograms divided by the square of the height in meters], 27.5 to 34.9) and approximately 50% lower in moderately obese participants (BMI, ≥35) than in normal-weight participants (BMI, 18.5 to 24.9) in the study by Tobias et al., we were surprised that they did not correct for physical activity in their multivariate analyses. We wonder whether one can adequately adjust for such huge differences, similar to their expressed concerns about smoking. We suspect that an obesity paradox would be present in those with type 2 diabetes and low physical activity or fitness.

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Dr. Lavie reports receiving consulting fees and speaking fees from Coca-Cola and writing a book on the obesity paradox with potential royalties. Dr. Church reports receiving consulting fees, speaking fees, and unrestricted research grants from Coca-Cola and consulting fees and speaking fees from Technogym, Jenny Craig, ACAP Health, and Catapult Health. Dr. Blair reports receiving consulting fees, speaking fees, and unrestricted research grants from Technogym; consulting fees, speaking fees, and unrestricted research grants from Coca-Cola; consulting fees and speaking fees from Santech; and unrestricted research grants from BodyMedia. No other potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Tobias and colleagues reported a linear relationship between BMI and mortality in type 2 diabetes, in contrast to the J-shaped relationship observed in other studies, including our own large, general population–based study.[1] We performed analyses that excluded smokers, adjusting for cardiovascular risk factors and excluding deaths within 5 years (to account for coexisting conditions), with no attenuation of results, and we had the advantage of physician-reported weight and diabetes diagnosis.

The conflicting results may partially reflect the timing of the studies; our data were mainly from 2000 and after, whereas Tobias et al. have analyzed data from the 1970s. Not only have there been substantial increases in body mass since then, there have also been improvements in the management of diabetes and the life expectancy of patients with the disease, which may have been disproportionate across the range of BMI categories. We would suggest that to resolve differences, further studies with the use of contemporary data in the general population are needed. Lifestyle-intervention studies would be even better but, given decreasing mortality in diabetes, difficult to power.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: The analysis of BMI and mortality by Tobias et al. contradicts recent studies on the obesity paradox proposing that weighing more than "normal" may provide a mortality advantage in type 2 diabetes. All these studies share weaknesses. The notion of an obesity paradox arises from the biologically implausible concept that humans throughout their life cycle have a

constant, optimal weight range that is not altered by age, sex, ethnic group, or state of health. Consistent reports indicate that with aging[1] and a growing list of chronic diseases characterized by compromised nutrition, sarcopenia, weakness, impaired physical function, and frailty,[2,3] the nadir of the mortality:weight curve is in the "overweight" or "class I obese" range. Additional lean or fat reserves, not adequately measured by weight or BMI, may be adaptive, providing resilience, and therefore the elderly overweight and class I obese (by younger normative standards) patients benefit more from lifestyle programs focused on quality nutrition, physical activity, fitness, and maintenance of function[4] than from achievement of "normal" weight, which may mask sarcopenia.

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: We agree with de Mutsert et al. that studies with short follow-up or of older patient populations may be especially prone to reverse-causation bias, owing in part to the influence of underlying illnesses.

Lavie et al. raise the potential of confounding by fitness in our analysis; however, adjustment for physical activity with the use of our validated measure did not appreciably alter the results. Physical activity was actually included in our multivariable models, as described in the Statistical Analysis section. We inadvertently omitted physical activity from the list of covariates in multivariable models in the tables and figures. In further analyses (Table 1), we found that the

Table 1. Hazard Ratios for All-Cause Mortality among Participants with Incident Type 2 Diabetes, According to BMI Shortly before Diagnosis of Type 2 Diabetes, Smoking Status, and Physical Activity Level.*

Variable	No. of Deaths/ Person-Yr	Hazard Ratio According to BMI Category (95% CI)						P Value for Linear Trend
		18.5–22.4	22.5–24.9	25.0–27.4	27.5–29.9	30.0–34.9	≥35.0	
Total participants								
Low physical activity level	1612/87,394	1.13 (0.83–1.54)	1.00	1.12 (0.92–1.38)	1.11 (0.77–1.60)	1.07 (0.87–1.30)	1.26 (1.02–1.55)	<0.001
High physical activity level	1158/71,478	1.44 (1.05–1.96)	1.00	1.13 (0.92–1.39)	1.17 (0.93–1.46)	1.55 (1.27–1.91)	1.34 (1.04–1.73)	0.009
Those who never smoked								
Low physical activity level	598/13,272	1.55 (0.90–2.66)	1.00	1.36 (0.93–1.99)	1.46 (1.01–2.13)	1.28 (0.90–1.84)	1.60 (1.11–2.32)	0.03
High physical activity level	441/31,330	1.02 (0.30–3.51)	1.00	1.17 (0.83–1.65)	1.18 (0.48–2.92)	1.84 (0.87–3.88)	1.64 (0.90–3.00)	<0.001

* Shown are the results for the combined Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS) cohorts. The results for the two cohorts were combined with the use of a fixed-effect meta-analysis. In the NHS cohort, P=0.19 for interaction in total participants and P=0.08 for interaction in those who never smoked. In the HPFS cohort, P=0.30 for interaction in total participants and P=0.37 for interaction in those who never smoked. Data were adjusted for age, race, marital status, menopausal status (for the NHS cohort only), presence or absence of a family history of diabetes, smoking status, alcohol intake, and Alternate Healthy Eating Index score. The low physical activity level was defined as less than nine metabolic-equivalent tasks per week, and the high physical activity level as nine or more metabolic-equivalent tasks per week. CI denotes confidence interval.

association between BMI and mortality was similar in persons with a high level of physical activity and those with a low level (P=0.19 for interaction in women and P=0.37 for interaction in men). In a previous study, we found that BMI and physical activity were independently associated with the risk of death.[1] In the Aerobics Center Longitudinal Study, a high BMI was the most important modifiable risk factor for low cardiorespiratory fitness, and obesity was found to offset the benefits of physical activity on fitness.[2] Furthermore, weight loss through lifestyle interventions was highly effective in improving physical fitness.[3]

In response to Logue et al.: although our Nurses' Health Study and Health Professionals Follow-up Study cohorts were enrolled in 1976 and 1986, respectively, our analyses included incident diabetes cases through January 1, 2010. Thus, our cohorts reflected contemporary populations of patients with diabetes. Because body weight is substantially influenced by disease severity and methods of treatment, it is important to use BMI before or at the time of a diabetes diagnosis. As shown in our data and those of others, weight loss is common in patients with diabetes, even shortly before the diagnosis. Therefore, use of the postdiagnosis weight increases the potential for reverse-causation biases.

Dixon and Kral note that overweight and obesity might be protective against premature death in older populations by providing metabolic reserves, although this hypothesis has yet to be tested. However, among older participants (≥65 years of age) at diabetes diagnosis, we found no survival advantage associated with overweight or obesity. BMI is a less valid measure of excess body fat in elderly populations than in younger populations, owing to differential loss of muscle mass related to sarcopenia and increased frailty. Future studies involving elderly populations should pay particular attention to these methodologic issues, especially weight loss due to chronic diseases, and should also include measures of body-fat distribution such as waist circumference.

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Acute Osteomyelitis in Children

TO THE EDITOR: In their article on acute osteomyelitis in children, Peltola and Pääkkönen (Jan. 23 issue)[1] proposed measurement of serum C-reactive protein (CRP) levels and erythrocyte sedimentation rate, blood culture, and plain radiography for the primary evaluation of a child with presumed acute osteomyelitis. The first step in their algorithm that initiates action (further evaluation) is elevation of CRP levels or the erythrocyte sedimentation rate, whereas normal CRP levels and erythrocyte sedimentation rates indicate observation and later reevaluation or, if clinically indicated, the same evaluation as for an elevation of either value. Given that an elevated erythrocyte sedimentation rate is not specific for osteomyelitis,[2,3] and that a normal rate persists long after the development of osteomyelitis (long after CRP levels become elevated),[4] there is, in our opinion, no evidence for measuring the erythrocyte sedimentation rate in patients with acute disease. The relatively low cost of measuring the erythrocyte sedimentation rate may argue in its favor, but every test is expensive if it does not improve diagnostic specificity or sensitivity, particularly when ordered frequently. Furthermore, a false posi-