International Journal of Obesity (2008) 32, 727–729

0307-0565/08 $30.00
www.nature.com/ijo

EDITORIAL

BMI and mortality: sorting through the data to find the public health message

International Journal of Obesity (2008) **32**, 727–729; doi:10.1038/ijo.2008.35

This issue of the journal has an original article[1] and two letters[2,3] that address methodologic challenges in the estimation of the impact of body mass index (BMI) on mortality. Recently, large differences in estimates put forward by different investigators[4–7] have puzzled both the general public and obesity scientists. For example, analyses of National Health and Nutrition Examination Survey[5] did not show a positive association between overweight (BMI 25–29.9) and mortality (they in fact showed a negative association). In addition, attempts to control for confounding by exclusion of smokers did not systematically produce the hypothesized changes in the National Health and Nutrition Examination Survey estimates.[8] Given the complexities and pitfalls inherent in observational study designs, it is incumbent upon investigators to search carefully through all the methodological intricacies that could cause differences in estimates obtained from different studies. This process is healthy as it is critical to forward progress in the field and to furthering our understanding of the consequences of obesity. Nevertheless, we do not want to become so enamored with the methodological details that we fail to carefully extract the public health implications of our work.

To wade forward in this conundrum, it is important to clarify the question being addressed and terminology used. We might like to know how many excess deaths are caused by overweight and obesity, but this causal question cannot be directly addressed using an observational study. Instead, we answer other questions such as: what is the number of excess deaths per year at different levels of BMI? Or what is the association between BMI and mortality adjusted for known sources of confounding? It is relatively straightforward to answer the question of the number of deaths associated with a BMI if the sample studied represents the population to which you want to generalize. Confounding is less of a concern if your interest is knowing the association between BMI and mortality, given the naturally occurring assortment of ages, smoking, education, gender, ethnicity, minor illness, major illness and so on existing in the population. Cohorts like those from National Health and Nutrition Examination Survey provide a rich resource for this type of analysis for the United States, as the samples were carefully constructed to represent a specific national population.

Moore *et al.*[1] have attempted to estimate the association of BMI with mortality free of confounding, which is a more complex task. The investigators seem to have made the most of an unusual sample and study design to provide information on the BMI–mortality association in women. The sample they studied was well described and large ($n = 50\,186$), but it was not one with broad generalizability. It appears that mortality information was not collected during the first 10 years following BMI measurements. The investigators described their study as examining the effect of BMI measured 10 years before baseline and use the word 'baseline' to indicate the beginning of the mortality follow-up period. In fact, the study is very similar to a design in which baseline is designated as the time of the BMI measurement, and deaths occurring within the first 10 years following baseline are excluded from the analysis. The authors note that their design helps to control for confounding of the BMI–mortality association due to weight loss from preexisting illness, while at the same time recognizing that their analyses apply only to individuals who manage to survive for 10 years after their BMI was assessed. The emphasis of this paper is testing the effect of past BMI, rather than the controlling for confounding.

In contrast, Greenberg *et al.*[9,10] focus on control of confounding rather than temporal issues and use the term 'regression dilution'. The term in itself is slightly misleading, as, depending on relations with errors in other variables, random error in the exposure can artificially inflate as well as deflate or dilute a regression coefficient.[11,12] Flegal *et al.*[13] questioned whether the term was appropriately applied by Greenberg and noted that regression dilution refers to bias resulting from measurement error and actual within-individual variability. To understand the subtleties of corrections for regression dilution, I find contrasts to analyses of diet data instructive. Twenty-four-hour recalls of diet produce data with both large measurement errors and large, actual day-to-day variations,[14] whereas height and weight are precisely measured and day-to-day variations are generally trivial in adults. Measurement error in BMI calculated from objectively assessed height and weight is quite low, not even approaching the levels found in diet. Given this difference, concerns about regression dilution are often appropriate for studies of diet, but not usually of concern for BMI.

Nevertheless, it is true that over a period of years BMI can change importantly. Greenberg *et al.*[9,10] note that the use of one measurement of BMI as an assessment of long-term or adult lifetime BMI results in measurement error. The BMI at the time it is assessed may be measured very accurately, but it provides at best an imperfect estimate of lifetime BMI. In that context, it is technically correct to use the term 'regression dilution', but this focus fails to fully appreciate that repeated measures of weight over a period of years or decades capture rich information on weight history, weight change and weight trajectory. I would prefer to see analyses of repeated measures of BMI framed to focus on the public health implications of lifetime BMI, rather than to emphasize reduction of variance.

An important strength shared by the Greenberg[10] and Moore[1] studies was that BMI was calculated using measured weight and height. Both studies showed associations between obesity (BMI$\geqslant$30) and mortality, but perhaps more interesting are their analyses examining overweight. Using BMI assessed 10 years before the initiation of follow-up, Moore showed that overweight was associated with increased mortality in women after adjusting for smoking as a covariate in the analysis. Greenberg used the mean of multiple measures of weight and height over time and showed that overweight was associated with increased mortality only after excluding ever smokers and participants with preexisting illness. These exclusions reduced the number of participants in the analysis to 3916 and the number of deaths to 73. Nevertheless, results from both the Greenberg and Moore studies indicated increased risk in the overweight range of BMI and offer support for the BMI categories advocated by the World Health Organization[15]—at least for healthy nonsmokers. The risk associated with BMI in smokers and in people with chronic illness may be different for a number of reasons, including nonintentional weight loss and competing causes of death.

This is just one example of the complexity of the BMI–mortality association, which has turned out to be deceptively difficult to study. Similar to my colleagues, I labor to sort out the truth from all the findings, and currently am having difficulty getting all the 'stars to align' in the constellation of published works. Despite the current lack of total consensus among studies, for the time being, I remain comfortable with the World Health Organization BMI guidelines and the public health messages they inspire. For adults, a BMI between 18.5 and 24.9 is generally consistent with good health. This conclusion comes from decades of work on BMI and mortality, and also studies of morbidity. Work on morbidity, particularly diabetes, has shown marked increased risk with increasing BMI that extends even to the high end (BMI 22.0–24.9) of the normal range of BMI (18.5–24.9).[16] Given the associations between overweight and morbidity, it is surprising that the impact of overweight on mortality is not larger. Nevertheless, as recommendations to the public should be based on both risks of morbidity and mortality, the case for avoiding overweight remains strong.

Excess body weight is an exceptionally important preventable cause of disease and death. Recently, after many years of inattention, the scientific community turned its considerable resources to obesity. It would be most unfortunate if misunderstandings about the risks associated with obesity were to derail the current momentum.[17] We need to continue our efforts to understand the consequences of elevated BMI levels and may need to be prepared to shift our thinking in the future. It is possible that advances in medical treatments or other unidentified factors have and will continue to reduce the number of deaths from obesity-related conditions.[18] That does not change and must not confuse the need to go forward now with firm resolve to invent, develop and disseminate ways to help the world's population obtain and sustain a healthy weight.

Acknowledgements

I thank Dr Kimberly P Truesdale, Daniel R Taber and Jill E McClain for their helpful comments.

J Stevens
Departments of Nutrition and Epidemiology, University of North Carolina, School of Public Health, CB 7461, Chapel Hill, NC, USA.
E-mail: june_stevens@unc.edu

References

1 Moore SC, Mayne ST, Graubard BI, Schatzkin A, Albanes D, Schairer C *et al.* Past body mass index and risk of mortality among women. *Int J Obes (London)* 2008; **32**: 730–739 (this issue).
2 Flegal KM, Graubard BI, Williamson DF, Gail MH. Simple examples should not extrapolated to the US population. *Int J Obes (London)* 2008; **32**: 875 (this issue).
3 Greenberg J, Fontaine K, Allison DB. Simple examples should not be extrapolated to the US population (Author reply). *Int J Obes (London)* 2008; **32**: 876–877 (this issue).
4 Allison DB, Fontaine KR, Manson JE, Stevens J, VanItallie TB. Annual deaths attributable to obesity in the United States. *JAMA* 1999; **282**: 1530–1538.
5 Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. *JAMA* 2005; **293**: 1861–1867.
6 Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. *JAMA* 2004; **291**: 1238–1245.
7 Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Correction: actual causes of death in the United States, 2000. *JAMA* 2005; **293**: 293–294.
8 Flegal KM, Graubard BI, Williamson DF, Gail MH. Impact of smoking and preexisting illness on estimates of the fractions of deaths associated with underweight, overweight, and obesity in the US population. *Am J Epidemiol* 2007; **166**: 975–982.
9 Greenberg JA. Correcting biases in estimates of mortality attributable to obesity. *Obesity (Silver Spring)* 2006; **14**: 2071–2079.

10 Greenberg JA, Fontaine K, Allison DB. Putative biases in estimating mortality attributable to obesity in the US population. *Int J Obes (Lond)* 2007; **31**: 1449–1455.
11 Kristensen P. Bias from nondifferential but dependent misclassification of exposure and outcome. *Epidemiology* 1992; **3**: 210–215.
12 Rothman K, Greenland S. *Modern Epidemiology* 2nd edn. Lippincott-Raven: Philadelphia, PA, 1998, 737pp.
13 Flegal KM, Graubard BI, Williamson DF, Gail MH. Correcting bias, or biased corrections? *Obesity (Silver Spring)* 2008; **16**: 229–231.
14 Willett W. *Nutritional Epidemiology*, 2nd edn. Oxford University Press: New York, NY, 1998, 514pp.
15 WHO. *Obesity: Preventing and Managing the Global Epidemic*. World Health Organization: Geneva, 2004.
16 Field AE, Coakley EH, Must A, Spadano JL, Laird N, Dietz WH *et al*. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. *Arch Intern Med* 2001; **161**: 1581–1586.
17 Stevens J, McClain JE, Truesdale KP. Commentary: obesity claims and controversies. *Int J Epidemiol* 2006; **35**: 77–78; discussion 81–72.
18 Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM *et al*. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *JAMA* 2005; **293**: 1868–1874.