

Reviewer's report

Title: Estimating health-adjusted life expectancy conditional on risk factors: results for smoking and obesity

Version: 1 **Date:** 10 July 2006

Reviewer: Kenneth G. Manton

Reviewer's report:

1) Assessment of work is question new?

The question is not new in the U.S. Indeed there has been a major controversy at the U.S. CDC (Center for Disease Control) and in the national scientific and popular press about estimates of the health effects of obesity versus smoking as a risk factor for excess mortality. The controversy was generated because a number of analyses produced by CDC in 1999, 2000, and 2001 had suggested the obesity was overtaking smoking as the number one risk factor with regard to excess mortality.

In a series of peer-reviewed articles by Flegal and other analysts at CDC using NHANES and other more recent data showed that due to the use of inappropriate statistical methods and old data in the prior CDC studies that the excess mortality due to obesity had been greatly over estimated with smoking remaining the number one risk factor for excess mortality but with obesity being only the seventh ranked risk factor (e.g., Flegal et al., 2004, 2005; Fox et al., 2004). A large part of the reduction of the estimated effect of obesity was due to recent data showing that, in part improved treatment of diabetes and hypertension had reduced stroke and other more immediate causes of death using recent data from NHANES. Furthermore the data indicated that the effects of obesity attenuated with age not being strongly related to mortality or health service use above age 70 to 75. These results seem at variance with the estimates for obesity made in the reviewed paper at age 65. Also of importance in the analyses was the observation that smoking and obesity were correlated, i.e., weight gains of 10 to 15 pounds in smokers were frequently observed; as were weight gains in persons using current medications to control blood glucose levels. New medications may eliminate those gains. I did not see any place in the current model where such interactions were represented or discussed.

2) The methods seem in general satisfactory, but, as indicated in 1, some assumptions appears unrealistic. One assumption that is problematic is that the risk cohorts are defined to be homogenous discrete groups (see definition above equation 1). The risk categories are not, in fact, homogenous meaning that, over age, the heaviest smokers and the most obese trend to die early reducing the mean level of smoking, and possibly obesity, with age. This would lower the risk at later ages as the risk factor average value is reduced by selection on a heterogeneous population. Obesity has a more complex age trajectory than smoking in that body composition (lean vs. fat body mass) changes with age related endocrine and metabolic changes implying that BMI is not a measure whose health implications are stable over age due to changes in metabolism.

A second assumption is that no transitions occur between risk factor classes over time (where risk factor classes are homogenous). I would question the validity of this assumption. A concern with the three categories selected for BMI is that the U.S. studies found that the relation of risk to BMI was non-linear (e.g., quadratic) with a large flat interior region centering on a BMI of 25-29 which had the lowest risk level "consistent with estimates of health optimal BMI levels made by Fogel and Costa of about 27.2. Significant risk elevations were restricted to the morbidly obese " a relatively small proportion of the population.

3) I am not familiar with the datasets employed but apparently the disability weights are derived from "œa large panel of experts"□, i.e., based on subjective probability assessments. Disability is likely multi-dimensional and not easily scalable on a single 0.0 to 1.0 scale. Disability weights could be constructed from objective measures of function.

4) The data appears to correspond to standards for reporting and data disposition.

5) The discussion and conclusion appear to correspond to the numerical results reported. Not much discussion is provided at the end of the paper about the implications of the results about compression.

6) The title and abstract appear to reflect the topic of the analyses.

7) In general the writing is acceptable. There are a few sentences that need revision.

In terms of the overall impression, I think the results of Flegal et al on obesity versus smoking in the U.S. needs to be discussed given that the U.S. evidence on obesity effects appear contradictory. Also the implication of the assumptions about obesity and smoking categories on results need to be better discussed. These are compulsory changes.

In terms of recommendation, I feel that a decision would be difficult to reach without a response to the above question.

In terms of the interest level of the article, I found the article to be of importance in its field " but with questions about its conclusions.

References

Flegal, K. M., B. I. Graubard, and D. F. Williamson. 2004. "Methods of calculating deaths attributable to obesity," *American Journal of Epidemiology* 160(4): 331-338.

Flegal, K. M., Graubard, B. I., Williamson, D. F., & Gail, M. H. (2005) Excess deaths associated with underweight, overweight, and obesity. *Journal of the American Medical Association*, 293, 1861-1867.

Fox, C. S., Coady, S., Sorlie, P. D., Levy, D., Meigs, J. B., D'Agostino, R. B., Wilson, P. W. F., & Savage, P. J. (2004). Trends in cardiovascular complications of diabetes. *Journal of the American Medical Association*, 292, 2495-2499.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.