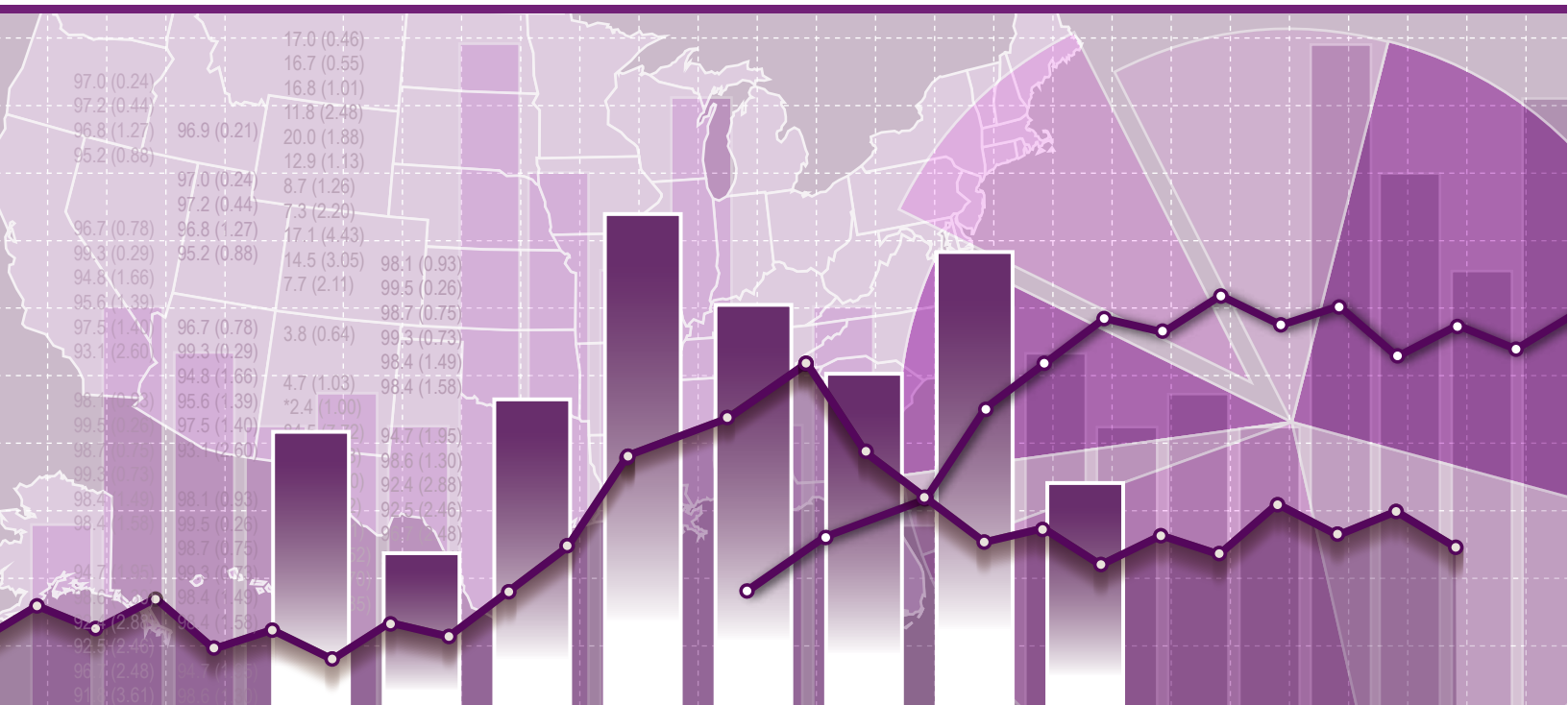


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Excess Deaths Associated With Underweight, Overweight, and Obesity: An Evaluation of Potential Bias

Analytical and Epidemiological Studies



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Center for Health Statistics

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Data from the National Health and Nutrition Examination
Survey

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Center for Health Statistics

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Excess Deaths Associated With Underweight, Overweight, and Obesity: An Evaluation of Potential Bias

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Abstract

Objectives

Previous analyses of mortality data from the National Health and Nutrition Examination Survey published in 2005 found that relative to the normal weight category of body mass index (BMI), defined as a BMI of 18.5–24.9, underweight (BMI less than 18.5) and obesity (BMI greater than or equal to 30) were associated with excess mortality, and overweight (BMI 25–29.9) was associated with reduced mortality, after adjusting for sex, smoking status, race–ethnicity group, and alcohol consumption. Possible sources of bias in those analyses include residual confounding due to imperfect adjustment for smoking and prevalent illness at baseline. This report presents an evaluation of these sources of bias.

Methods

The relative risks associated with BMI categories were calculated both before and after exclusions based on self-reported health status, physician-evaluated health status, smoking, early death, and weight stability. Additional analyses examined the effects of using BMI measured after age 70.

Results

No systematic or large effects of exclusions on the magnitude or direction of the relative risks were observed. Underweight was associated with elevated risk and overweight with decreased risk relative to the normal weight category, even after exclusions based on smoking, health status, early death, and weight stability. Applying these exclusionary criteria simultaneously excluded up to 85% of the original sample and 92% of the deaths.

Conclusions

These analyses of the effects of exclusions and stratification by health status do not suggest that the 2005 results were affected by large or systematic biases from residual confounding due to smoking, prevalent illness at baseline, or illness-induced weight loss.

Keywords: mortality • epidemiological methods • self-reported health • National Health and Nutrition Examination Survey

Introduction

As the prevalence of obesity has increased over time in the United States (1,2), concern over the association between body weight and excess mortality also increased. In 2005, an analysis of estimated excess deaths, relative to the normal weight category (body mass index [BMI] 18.5–24.9), that were associated with underweight (BMI less than 18.5), overweight (BMI 25.0–29.9), and obesity (BMI greater than or equal to 30) in U.S. adults in 2000 was published (3). Both underweight and obesity, particularly higher levels of obesity, were associated with increased mortality relative to the normal weight category. Obesity was estimated to be associated with 111,909 excess deaths (95% confidence interval [CI]: 53,754 to 170,064) in 2000 relative to the normal weight category, and underweight with 33,746 excess deaths (95% CI: 15,726 to 51,766). Overweight was

associated with reduced mortality (–86,094 deaths; 95% CI: –161,223 to –10,966). This report evaluates several potential sources of bias in that analysis.

Methods of Previous Paper

The published analysis (3) used all of the then-available mortality data from the National Health and Nutrition Examination Surveys (NHANES), including the first, second, and third NHANES (NHANES I, 1971–1975; NHANES II, 1976–1980; and NHANES III, 1988–1994). A statistical approach derived from the Gail model's methods for predicting breast cancer risk was used (4,5). BMI was calculated as weight divided by height squared (kg/m^2) and grouped into categories of underweight (BMI less than 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25–29.9), grade 1 obesity (BMI 30–34.9), and grades 2 and 3 obesity

(BMI greater than or equal to 35), according to categories used by the National Heart, Lung, and Blood Institute (6) and the World Health Organization (7). The normal weight category was used as the reference category. The relative risks (hazard ratios) of mortality from the combined NHANES I, II, and III data were estimated from proportional hazards survival models that used age as the time metric (8,9). Because the proportional hazards assumption was not always met, data were stratified into three age categories: 25–59, 60–69, and 70 and over. Because age was used as the time metric, a participant might be included in more than one of these groups. For example, a participant who was examined at age 59 at baseline but survived to age 70 or over would be included in age-specific analyses for all three groups.

The statistical models included the following covariates measured at baseline: sex, smoking (never, former, or current), race–ethnicity group (white, black, or other), and alcohol consumption, in grams per day (none, less than 0.07, 0.07 to less than 0.35, or greater than or equal to 0.35). The relative risks for BMI and all other covariates were applied to the joint distribution of BMI and other covariates in the population, as estimated from NHANES 1999–2002, to estimate attributable fractions. Finally, those fractions were applied to the total number of deaths in the United States in 2000 (from vital statistics data) for persons of the same ages.

All analyses included sample weights that accounted for the unequal probabilities of selection due to oversampling and nonresponse. All variance calculations incorporated the sample weights and accounted for the complex sample design. Standard errors were calculated by applying a delta method for complex sample designs. This method takes into account a) sampling variability in estimating the relative risks and the joint distribution of BMI and the other covariates, and b) additional variability due to the complex sample designs of NHANES.

Controlling for Confounding Factors by Adjustment or Exclusion

Adjusting relative risk estimates for confounding factors (e.g., age and smoking) that are associated with both obesity and mortality is important (10,11). However, when relative risks are adjusted for confounding factors, it is also necessary to use properly adjusted estimators of attributable fractions to avoid bias (12,13). The method used for this analysis accounted for confounding and allowed for effect modification across age strata. Because the goal was to make estimates for the entire U.S. adult population within each age stratum, rather than for selected subgroups, all participants were included. This approach adjusted for confounding by calculating the hazard ratios for BMI categories and the confounding factors, and applying these hazard ratios to the then-current distribution of BMI and the confounding factors in the U.S. population.

For studies estimating the relative risks of mortality associated with different levels of BMI, it is sometimes recommended that rather than using statistical adjustments for or stratification by confounding factors, participants with certain characteristics simply be excluded from the analytic sample (14,15). This is believed to avoid possible biases due to illness-induced weight loss or residual confounding by smoking or prevalent illness at baseline.

For example, cigarette smoking is associated both with lower body weight (16,17) and increased mortality (18). If smoking were not completely adjusted for, this could overestimate the relative risk associated with underweight, and underestimate the relative risk associated with overweight and obesity with respect to normal weight. One approach to this problem is to statistically adjust for smoking status (19,20). An alternative approach is to exclude all current and former smokers and calculate relative risks only for the remaining never smokers (14). It has been stated that, “the best way to assess the impact of overweight on risk of mortality is simply to exclude current and past smokers” (14). This is, in effect, a method of adjusting for confounding by calculating relative risks for only the unexposed level of the confounder.

The actual exclusions used to control for the effects of smoking, prevalent illness, and illness-induced weight loss vary considerably from study to study but can be grouped into four main types. First, current and former smokers may be excluded (21–25). Second, deaths occurring within the first few years after the baseline examination may be excluded to eliminate those with prevalent illness at baseline from the analysis. These “early death” exclusions may eliminate the first 5 years (26), 4 years (24), or 2 years (21) of deaths. A third type of exclusion is to exclude from analysis those with various self-reported health conditions at baseline. Common exclusions include those with self-reported cancer or cardiovascular disease at baseline (26); those with self-reported history of cancer, heart disease, stroke, respiratory disease, or any current illness (22); or those with self-reported heart disease, cancer, stroke, or poor health (25). A fourth type of exclusion involves weight stability. Exclusions of this type remove from the analytic sample those with a self-reported weight change of 4.5 kg or more over the first 5 years of the study (26), those with a self-reported weight loss of 4.5 kg or more in the year before baseline (22), those with a self-reported weight loss of 4.5 kg or more in the 2 years before baseline (25), and those with a self-reported weight gain or loss of 4 kg or more in the first 4 years after baseline (24). These exclusions are intended to eliminate from the analysis people who may have experienced recent weight loss due to illness, although people who report weight gain after baseline are sometimes also excluded (24).

Evaluation of Potential Bias

To assess the possibility that systematic biases related to smoking or prevalent illness at baseline had affected the estimates, relative risks within subgroups based on exclusionary criteria, alone and in combination, were examined. The previous analyses by Flegal et al. (3) found that underweight was associated with a relative risk greater than 1, overweight with a relative risk less than 1, and obesity with a relative risk greater than 1. If these results had been biased by illness-induced weight loss, prevalent disease at baseline, or residual confounding due to incomplete control for cigarette smoking, analyses excluding participants with these factors would be expected to show a relative risk associated with underweight close to or under 1, a relative risk associated with overweight greater than 1, and a relative risk associated with obesity higher than previously observed.

Flegal et al. (3) reported the relative risks from analyses limited to never smokers, and described the results from a) analyses that excluded the first 3 or 5 years of deaths, and b) analyses (for NHANES I only) that were limited to persons whose measured weight had not changed by more than 2 kg over an approximately 10-year period. These exclusions were done separately and not in combination. None of the exclusions described in the published article resulted in any large or systematic differences in estimates of relative risk compared with the full-sample estimates without exclusions.

This report presents detailed results of the effects of exclusions on relative risk estimates. The effects of exclusions based on health status are presented, as well as the effects of simultaneous exclusions of several different factors. Also discussed are some limitations of the exclusionary approach when attempting to estimate the absolute number of excess deaths associated with body weight in the total U.S. population.

Methods

Data Sources

The NHANES program of the National Center for Health Statistics (NCHS) includes a series of cross-sectional, nationally representative health examination surveys beginning in 1960. In each survey, a nationally representative sample of the U.S. civilian noninstitutionalized population was selected using a complex, stratified, multistage probability cluster sampling design. Previous national surveys include the first National Health Examination Survey (NHES I, 1960–1962) and the first, second, and third National Health and Nutrition Examination Surveys (NHANES I, 1971–1975; NHANES II, 1976–1980; and NHANES III, 1988–1994) (27–30). Beginning in 1999, NHANES became a continuous survey. The procedures followed to select the samples and conduct the interviews and examinations were similar across surveys, each of which includes an interview

in the household and a physical examination in a mobile examination center.

At the time of the previous analysis (3), data on subsequent mortality among survey participants were available for three of these surveys: NHANES I, NHANES II, and NHANES III. The NHANES I Epidemiologic Follow-up Study (NHEFS) consisted of several waves of follow-up (31,32). Participants were recontacted, and medical records and death certificates were obtained. In the NHANES II Mortality Study, vital status for NHANES II participants was assessed by searching the National Death Index and the Social Security Administration Death Master File for deaths occurring in the United States (33). Causes of death were obtained from the NCHS Multiple Cause of Death file or from death certificates. Similar procedures were followed for the NHANES III Mortality Study. Mortality data were available through 1992 for both NHANES I and NHANES II, and through 2000 for NHANES III.

The 1982–1984 follow-up in NHEFS included a measurement of weight as part of a home examination. Thus, for NHANES I only, measured weights are available at two different time points. This report primarily examines the relative risks for mortality in NHANES I from baseline (1971–1975), with follow-up through 1992. Several analyses also estimate the relative risks for NHANES I from baseline (1971–1975) though the 1982–1984 follow-up, and the relative risk from the 1982–1984 follow-up through 1992. For analyses of data from the 1982–1984 follow-up through 1992, BMI was calculated from weight measured in the 1982–1984 follow-up and height measured at baseline.

Health Status Reports

In each of the NHANES surveys, respondents were asked to evaluate their own health as excellent, very good, good, fair, or poor. These responses were grouped into two categories (excellent or very good health, and good, fair, or poor health) and results were stratified by these two levels of health status.

In NHANES III only, the examining physician at baseline was also asked to rate the respondent's overall health condition using the same five categories of excellent, very good, good, fair, or poor. Many large epidemiologic cohort studies do not include a baseline evaluation by a physician. Physician-evaluated health condition was grouped into two categories: a) excellent or very good health and b) good, fair, or poor health.

In NHANES III, physician-evaluated health status was compared with self-reported health status. Additionally, both physician-evaluated health status and self-reported health status were compared against reported history of cancer (other than skin cancer), congestive heart failure, stroke, heart attack, diabetes, and emphysema.

In NHANES III, respondents were asked to report their current weight at baseline and their weight 10 years ago.

For some analyses of NHANES III data, respondents who reported any net weight loss greater than 2.5 kg over the 10 years before baseline, based on the two self-reported measurements, were excluded.

In NHANES II, participants were asked if they had had unexplained weight loss in the previous 6 months. This question should identify respondents with recent weight loss due to illness. Some analyses for NHANES II were limited to those participants who did not report any unexplained weight loss.

Various combinations of these exclusions were examined. To have sufficient deaths for analyses in younger age groups, the sample was divided into two age groups: under 70 and 70 and over. A person who was examined at an age under 70 at baseline but survived to age 70 or over would be included in age-specific analyses for both groups, because age was used as the time metric.

Table A. Adjusted relative risk (95% confidence interval) of mortality, by age group, survey, and body mass index category: National Health and Nutrition Examination Survey I, II, and III, 1971–1994

Survey and body mass index category	25–59 years	60–69 years	70 years and over
NHANES I			
1971–1975 to 1982–1984			
Under 18.5	2.09 (0.98–4.45)	2.71 (1.52–4.83)	2.96 (1.90–4.61)
¹ 18.5–24.9	1	1	1
25.0–29.9	0.95 (0.63–1.42)	0.99 (0.70–1.40)	0.79 (0.67–0.94)
30.0–34.9	1.41 (0.86–2.32)	1.51 (0.95–2.39)	1.11 (0.84–1.47)
35.0 and over	2.28 (1.18–4.40)	1.67 (0.86–3.24)	1.62 (1.05–2.50)
NHANES I			
1982–1984 to 1992 ²			
Under 18.5	1.85 (0.73–4.72)	1.97 (0.82–4.76)	1.78 (1.26–2.53)
¹ 18.5–24.9	1	1	1
25.0–29.9	0.76 (0.45–1.28)	0.74 (0.51–1.07)	0.89 (0.73–1.08)
30.0–34.9	1.36 (0.80–2.30)	1.11 (0.73–1.71)	1.03 (0.83–1.28)
35.0 and over	0.96 (0.47–1.98)	0.70 (0.29–1.68)	1.33 (0.84–2.10)
NHANES II			
1976–1980 to 1992			
Under 18.5	0.85 (0.36–1.99)	1.47 (0.74–2.93)	1.50 (1.06–2.11)
¹ 18.5–24.9	1	1	1
25.0–29.9	0.71 (0.45–1.13)	0.80 (0.63–1.02)	0.86 (0.75–0.99)
30.0–34.9	0.71 (0.41–1.22)	0.95 (0.65–1.40)	1.11 (0.86–1.42)
35.0 and over	1.18 (0.75–1.87)	1.29 (0.85–1.97)	0.98 (0.75–1.29)
NHANES III			
1988–1994 to 2000			
Under 18.5	1.35 (0.41–4.38)	3.18 (1.78–5.68)	1.67 (1.21–2.30)
¹ 18.5–24.9	1	1	1
25.0–29.9	0.86 (0.55–1.34)	1.01 (0.68–1.48)	0.89 (0.74–1.06)
30.0–34.9	1.26 (0.67–2.37)	0.94 (0.56–1.57)	0.91 (0.74–1.11)
35.0 and over	1.64 (0.90–2.97)	1.66 (0.83–3.32)	0.98 (0.66–1.46)

¹Reference category.

²Body mass index was calculated using height measured in 1971–1975 and weight measured in 1982–1984.

NOTES: NHANES is National Health and Nutrition Examination Survey. Relative risks are adjusted for sex, smoking status, race–ethnicity group, and alcohol consumption. Body mass index is calculated as weight in kilograms (kg) divided by height in meters squared (m²).

SOURCES: NCHS, NHANES, 1971–1994, and NHANES I Epidemiologic Follow-up Study, 1982–1992.

Results

Separate relative risks for the two parts of NHANES I and relative risks for NHANES II and III are shown in [Table A](#). To examine whether the higher relative risks in NHANES I might be due to the longer follow-up in NHANES I, the relative risks from the first phase of NHANES I through the 1982–1984 follow-up were compared with the relative risks from NHANES II and III. Thus, the follow-up period was similar for all surveys (10 years for NHANES I, 14 years for NHANES II, and 9 years for NHANES III). The NHANES I relative risks over the first 10 years of follow-up were higher in almost every BMI–age subgroup compared with the relative risks from the other surveys. Thus, even after controlling for length of follow-up, NHANES I tended to have higher relative risks than the other surveys.

As also displayed in [Table A](#), in NHANES I, the relative risks through 1992 associated with weights measured in the 1982–1984 follow-up were lower in almost all subgroups than the relative risks from 1971–1975 through the 1982–1984 follow-up, suggesting a possible decrease in relative risks over time, although the differences were small.

To assess the longer-term effects of a given weight, excluding possible effects of major weight gains or losses, the NHANES I analyses were repeated for a subgroup of participants whose weight had not changed by more than 2 kg between baseline (1971–1975) and 1982–1984, looking at mortality from the 1982–1984 follow-up through 1992. In these analyses, the relative risks for this subgroup in NHANES I ([Table B](#)) did not differ systematically from those for the whole NHANES I sample over the same time period from the 1982–1984 follow-up through 1992 ([Table A](#)), and differences were slight. Overweight (BMI 25–29.9) that had persisted for at least 10 years was still associated with no excess risk, and underweight was still associated with an increased relative risk.

Table B. Adjusted relative risk (95% confidence interval) of mortality for respondents with weight change of 2 kg or less between 1971–1975 and 1982–1984, by age group and body mass index category: National Health and Nutrition Examination Survey, 1971–1975, and National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study, 1982–1984 and 1992

Body mass index category	25–59 years	60–69 years	70 years and over
Under 18.5	2.41 (0.95–6.13)	1.23 (0.31–4.85)	2.16 (0.89–5.28)
¹ 18.5–24.9	1	1	1
25.0–29.9	0.52 (0.18–1.50)	1.00 (0.42–2.37)	1.00 (0.73–1.37)
30.0–34.9	0.59 (0.14–2.57)	0.91 (0.34–2.44)	1.23 (0.72–2.08)
35.0 and over	0.73 (0.14–3.98)	0.60 (0.10–3.68)	2.36 (0.73–7.56)

¹Reference category.

NOTES: Relative risks are adjusted for sex, smoking status, race–ethnicity group, and alcohol consumption. Body mass index is calculated as weight in kilograms (kg) divided by height in meters squared (m²).

SOURCES: NCHS, National Health and Nutrition Examination Survey, 1971–1975, and National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study, 1982–1984 and 1992.

Table C. Adjusted relative risk (95% confidence interval) of mortality before and after excluding deaths occurring in the first 3 or 5 years after baseline, by age group and body mass index category: National Health and Nutrition Examination Survey, 1971–1994

Body mass index category	25–59 years	60–69 years	70 years and over
Including all deaths			
Under 18.5	1.38 (0.82–2.32)	2.30 (1.70–3.13)	1.69 (1.38–2.07)
¹ 18.5–24.9	1	1	1
25.0–29.9	0.83 (0.65–1.06)	0.95 (0.80–1.13)	0.91 (0.83–1.01)
30.0–34.9	1.20 (0.84–1.72)	1.13 (0.89–1.42)	1.03 (0.91–1.17)
35.0 and over	1.83 (1.27–2.62)	1.63 (1.16–2.30)	1.17 (0.94–1.47)
Excluding deaths			
In the first 3 years after baseline:			
Under 18.5	1.29 (0.77–2.18)	1.94 (1.33–2.82)	1.56 (1.29–1.89)
¹ 18.5–24.9	1	1	1
25.0–29.9	0.86 (0.65–1.13)	0.95 (0.78–1.17)	0.92 (0.83–1.02)
30.0–34.9	1.12 (0.77–1.64)	1.26 (0.97–1.63)	1.07 (0.94–1.22)
35.0 and over	1.88 (1.27–2.79)	1.94 (1.32–2.87)	1.21 (0.97–1.51)
In the first 5 years after baseline:			
Under 18.5	1.48 (0.86–2.55)	1.76 (1.14–2.72)	1.54 (1.21–1.98)
¹ 18.5–24.9	1	1	1
25.0–29.9	0.85 (0.61–1.17)	0.90 (0.73–1.11)	0.95 (0.85–1.07)
30.0–34.9	1.25 (0.82–1.92)	1.25 (0.94–1.67)	1.11 (0.95–1.29)
35.0 and over	2.18 (1.36–3.48)	2.02 (1.38–2.97)	1.15 (0.91–1.46)

¹Reference category.

NOTE: Body mass index is calculated as weight in kilograms (kg) divided by height in meters squared (m²).

SOURCE: NCHS, National Health and Nutrition Examination Survey, 1971–1994.

To examine whether the increased relative risks at lower BMI levels might be related to possible weight loss associated with illness and increased mortality, which could have decreased the relative risks associated with overweight and obesity, the analyses excluding the first 3 or 5 years of deaths were repeated; little change in the relative risk estimates was seen (Table C).

Health Status Analyses

Self-reported health

The association between self-reported health status and mortality was investigated using similar proportional hazards models and controlling for sex, BMI category, smoking, race–ethnicity group, and alcohol consumption. The self-reported health variable with five levels was a significant predictor of mortality in each survey and in the combined data set, as shown in Table D. Relative to the category of excellent or very good health, a self-report of good, fair, or poor health was also a significant predictor of mortality, as shown in Table E. These results suggest that self-reported health is a reasonable indicator of overall health.

For the combined sample, two categories of self-reported health status (excellent or very good, and good, fair, or poor) were stratified. Additionally, analyses for never smokers, stratified by health status, were repeated. After excluding the first 3 years of deaths, these analyses were repeated for never smokers stratified by health status. Thus, six sets of relative risks were calculated for each age group: excellent or very good health; good, fair, or poor health; never smokers with excellent or very good health; never smokers with good, fair, or poor health; never smokers with excellent or very good health, excluding the first 3 years of deaths; and never smokers with good, fair, or poor health, excluding the first 3 years of deaths.

The estimates of relative risk from these analyses are shown in Table F for the categories of underweight (BMI less than 18.5), overweight (BMI 25–29.9), grade 1 obesity (BMI 30–34.9), and grades 2 and 3 obesity (BMI greater than or equal to 35). In the combined analyses, stratification by health status, limiting the sample to never smokers, and excluding the first 3 years of deaths did not change the direction of the relative risk estimates for underweight or overweight. In all cases, the relative risk for underweight

was greater than 1 and the relative risk for overweight was under 1.

For underweight, the relative risks did not tend to be closer to 1 after these exclusions. For example, for those aged 70 and over who never smoked and were in excellent or very good health at baseline, after exclusion of the first 3 years of deaths, the relative risk for underweight was 2.20 compared with 1.69 for the full sample.

For overweight, the relative risk for those aged 70 and over was 0.91 in the full sample. Depending on the exact exclusions or stratifications, the relative risk for overweight ranged from 0.89 to 0.99. For those under age 70, the relative risks for overweight varied from 0.40 to 0.91. For never smokers aged 25–69 in excellent or very good health at baseline, after excluding the first 3 years of deaths, the relative risk for overweight was 0.45.

These exclusions sometimes changed the direction of the relative risks for obesity categories from above 1 to below 1. For grade 1 obesity, the relative risks for those aged 70 and over ranged from 1.00 (for those in good, fair, or poor health at baseline) to 1.18 (for never smokers in good, fair, or poor health at baseline after excluding the first 3 years of deaths). For grade 1 obesity for younger never smokers, regardless of baseline health status and regardless of excluding the first 3 years of deaths, the relative risks were always below 1.

Physician-evaluated health status

The association between physician-evaluated health status and mortality in NHANES III was also investigated. The physician-evaluated health variable was a significant predictor of mortality in NHANES III (Table G). Relative to the excellent or very good category, a physician evaluation of health as good, fair, or poor was associated with increased mortality in NHANES III (Table H). When self-reported health status and physician-reported health status were both included in the models, both were

Table D. Adjusted relative risk (95% confidence interval) of mortality associated with self-reported health status, by age group and survey: National Health and Nutrition Examination Survey, 1971–1994

Survey and health status	25–59 years	60–69 years	70 years and over
NHANES I			
Excellent ¹	1	1	1
Very good	1.44 (0.94–2.23)	1.03 (0.65–1.62)	1.04 (0.76–1.42)
Good	1.46 (0.90–2.38)	1.44 (0.94–2.21)	1.24 (0.93–1.66)
Fair	2.52 (1.60–3.98)	1.70 (1.13–2.54)	1.61 (1.21–2.15)
Poor	3.77 (2.06–6.87)	2.94 (1.71–5.07)	1.56 (1.09–2.24)
NHANES II			
Excellent ¹	1	1	1
Very good	2.69 (1.43–5.06)	1.10 (0.64–1.87)	1.08 (0.87–1.34)
Good	2.53 (1.36–4.71)	1.44 (0.92–2.24)	1.39 (1.13–1.72)
Fair	3.18 (1.59–6.38)	2.34 (1.40–3.91)	1.76 (1.44–2.16)
Poor	5.72 (2.77–11.8)	3.79 (2.30–6.24)	2.38 (1.94–2.91)
NHANES III			
Excellent ¹	1	1	1
Very good	1.01 (0.51–2.01)	0.91 (0.47–1.76)	1.07 (0.86–1.35)
Good	1.60 (0.90–2.85)	1.61 (0.84–3.09)	1.30 (1.09–1.55)
Fair	4.16 (2.01–8.61)	3.14 (1.60–6.18)	1.70 (1.37–2.12)
Poor	4.25 (1.95–9.26)	6.17 (2.80–13.6)	2.58 (1.90–3.51)
NHANES I, II, and III combined			
Excellent ¹	1	1	1
Very good	1.44 (1.00–2.07)	0.99 (0.72–1.36)	1.07 (0.93–1.25)
Good	1.75 (1.25–2.46)	1.47 (1.10–1.98)	1.31 (1.16–1.49)
Fair	3.49 (2.28–5.32)	2.34 (1.72–3.19)	1.69 (1.46–1.95)
Poor	4.23 (2.75–6.51)	4.00 (2.82–5.67)	2.29 (1.90–2.77)

¹Reference category.

NOTES: NHANES is National Health and Nutrition Examination Survey. Relative risks are adjusted for body mass index category, sex, smoking status, race–ethnicity group, and alcohol consumption.

SOURCE: NCHS, NHANES, 1971–1994.

Table E. Adjusted relative risk (95% confidence interval) of mortality for self-reported good, fair, or poor health relative to self-reported excellent or very good health, by age group and survey: National Health and Nutrition Examination Survey, 1971–1994

Survey and health status	25–59 years	60–69 years	70 years and over
NHANES I			
Excellent or very good ¹	1	1	1
Good, fair, or poor	1.52 (1.13–2.05)	1.62 (1.23–2.13)	1.36 (1.15–1.60)
NHANES II			
Excellent or very good ¹	1	1	1
Good, fair, or poor	1.61 (1.11–2.34)	1.87 (1.48–2.38)	1.58 (1.37–1.82)
NHANES III			
Excellent or very good ¹	1	1	1
Good, fair, or poor	2.27 (1.50–3.42)	2.53 (1.56–4.12)	1.48 (1.28–1.70)
NHANES I, II, and III combined			
Excellent or very good ¹	1	1	1
Good, fair, or poor	1.85 (1.47–2.34)	1.98 (1.61–2.42)	1.47 (1.34–1.61)

¹Reference category.

NOTES: NHANES is National Health and Nutrition Examination Survey. Relative risks are adjusted for body mass index category, sex, smoking status, race–ethnicity group, and alcohol consumption.

SOURCE: NCHS, NHANES, 1971–1994.

Table F. Adjusted relative risk (95% confidence interval) of mortality, by age group, body mass index category, and selected exclusionary criteria: National Health and Nutrition Examination Survey, 1971–1994

Subgroup	Body mass index under 18.5		Body mass index 25–29.9		Body mass index 30–34.9		Body mass index 35 and over	
	Under 70 years	70 years and over	Under 70 years	70 years and over	Under 70 years	70 years and over	Under 70 years	70 years and over
All	1.88 (1.43–2.45)	1.69 (1.38–2.07)	0.90 (0.78–1.03)	0.91 (0.83–1.01)	1.16 (0.92–1.44)	1.03 (0.91–1.17)	1.75 (1.35–2.26)	1.17 (0.94–1.47)
Excellent or very good health	1.33 (0.50–3.56)	1.73 (1.10–2.70)	0.91 (0.69–1.20)	0.90 (0.75–1.09)	1.01 (0.65–1.58)	1.02 (0.82–1.28)	1.79 (1.05–3.04)	1.11 (0.67–1.84)
Good, fair, or poor health	1.74 (1.25–2.41)	1.65 (1.29–2.11)	0.85 (0.72–1.00)	0.91 (0.80–1.02)	1.05 (0.80–1.36)	1.00 (0.84–1.19)	1.36 (0.99–1.86)	1.04 (0.81–1.33)
Excellent or very good health, never smoked	3.36 (0.75–15.1)	2.00 (1.22–3.28)	0.40 (0.21–0.76)	0.97 (0.76–1.24)	0.53 (0.26–1.11)	1.14 (0.84–1.53)	1.67 (0.74–3.78)	0.63 (0.32–1.28)
Good, fair, or poor health, never smoked	1.45 (0.67–3.14)	1.23 (0.82–1.85)	0.77 (0.50–1.20)	0.89 (0.76–1.04)	0.92 (0.60–1.39)	1.15 (0.94–1.41)	1.21 (0.77–1.91)	0.98 (0.72–1.33)
Excellent or very good health, never smoked, first 3 years of deaths excluded	–	2.20 (1.22–3.94)	0.45 (0.22–0.90)	0.99 (0.76–1.29)	0.50 (0.21–1.16)	1.11 (0.83–1.49)	1.87 (0.78–4.44)	0.75 (0.38–1.50)
Good, fair, or poor health, never smoked, first 3 years of deaths excluded	1.47 (0.60–3.59)	1.21 (0.80–1.83)	0.76 (0.45–1.28)	0.89 (0.75–1.06)	0.89 (0.56–1.42)	1.18 (0.94–1.49)	1.37 (0.84–2.24)	0.90 (0.65–1.22)

– Quantity zero.

NOTES: Relative risks are adjusted for sex, smoking status, race–ethnicity group, and alcohol consumption. Body mass index is calculated as weight in kilograms (kg) divided by height in meters squared (m²). Reference category is body mass index 18.5–24.9.

SOURCE: NCHS, National Health and Nutrition Examination Survey, 1971–1994.

Table G. Adjusted relative risk (95% confidence interval) of mortality associated with five categories of physician-evaluated health status, by age group and model: National Health and Nutrition Examination Survey, 1988–1994

Model and health status	25–59 years	60–69 years	70 years and over
Model 1 (sex, smoking, body mass index, alcohol consumption, and race–ethnicity group)			
Excellent ¹	1	1	1
Very good	0.89 (0.51–1.54)	1.36 (0.74–2.52)	1.18 (0.92–1.51)
Good	1.42 (0.92–2.21)	1.63 (0.89–2.99)	1.62 (1.30–2.02)
Fair	6.39 (3.53–11.6)	3.74 (1.98–7.08)	2.57 (2.02–3.26)
Poor	4.96 (1.60–15.4)	11.7 (3.98–34.2)	3.93 (3.15–4.92)
Model 2 (Model 1 plus self-reported health status)			
Excellent ¹	1	1	1
Very good	0.85 (0.49–1.46)	1.37 (0.75–2.50)	1.17 (0.91–1.49)
Good	1.28 (0.85–1.91)	1.38 (0.78–2.42)	1.54 (1.22–1.95)
Fair	4.56 (2.53–8.21)	2.56 (1.38–4.76)	2.30 (1.80–2.94)
Poor	3.84 (1.34–11.0)	6.08 (2.12–17.5)	3.32 (2.65–4.18)

¹Reference category.

SOURCE: NCHS, National Health and Nutrition Examination Survey, 1988–1994.

significant predictors of mortality. Of respondents who reported their health status as excellent or very good, 71.6% were also considered by the physician to have excellent or very good health. Of respondents who reported their health status as good, fair, or poor, 49.1% were also considered by the physician to have good, fair, or poor health. Of respondents who reported their health as excellent or very good, 90.5% reported no history of any of the following conditions: cancer (other than skin cancer), congestive heart failure, stroke, heart attack, emphysema, or diabetes. Of

those who reported their health as good, fair, or poor, 73.5% also reported none of those conditions. The corresponding values for physician-evaluated health were 89.0% of those judged to be in excellent or very good health and 67.1% of those judged to be in good, fair, or poor health.

For NHANES III, in which data were available on physician-evaluated health status, the analyses stratified by physician-evaluated health status at baseline were repeated, with results shown in [Table J](#). These analyses use data from only

Table H. Adjusted relative risk (95% confidence interval) of mortality for two categories of physician-evaluated health status, by age group and model: National Health and Nutrition Examination Survey, 1988–1994

Model and health status	25–59 years	60–69 years	70 years and over
Model 1 (sex, smoking, body mass index, race–ethnicity group, and alcohol consumption)			
Excellent or very good health ¹	1	1	1
Good, fair, or poor health	2.13 (1.47–3.09)	1.88 (1.14–3.11)	1.81 (1.60–2.06)
Model 2 (Model 1 plus self-reported health status)			
Excellent or very good health ¹	1	1	1
Good, fair, or poor health	1.93 (1.37–2.72)	1.62 (0.99–2.66)	1.72 (1.50–1.97)

¹Reference category.

SOURCE: NCHS, National Health and Nutrition Examination Survey, 1988–1994.

Table J. Adjusted relative risk (95% confidence interval) of mortality before and after stratifying by physician-evaluated health status and selected exclusionary criteria, by age group and body mass index category: National Health and Nutrition Examination Survey, 1988–1994

Subgroup	Body mass index under 18.5		Body mass index 25–29.9		Body mass index 30–34.9		Body mass index 35 and over	
	Under 70 years	70 years and over	Under 70 years	70 years and over	Under 70 years	70 years and over	Under 70 years	70 years and over
All	2.18 (1.19–4.00)	1.67 (1.21–2.30)	0.92 (0.68–1.24)	0.89 (0.74–1.06)	1.10 (0.70–1.73)	0.91 (0.74–1.11)	1.65 (1.02–2.68)	0.98 (0.66–1.46)
Excellent or very good health	0.89 (0.16–5.00)	1.61 (0.91–2.87)	1.04 (0.60–1.81)	0.94 (0.66–1.34)	1.23 (0.64–2.37)	0.77 (0.51–1.15)	1.39 (0.59–3.29)	0.44 (0.11–1.69)
Good, fair, or poor health	2.41 (1.24–4.69)	1.50 (0.99–2.27)	0.77 (0.58–1.04)	0.86 (0.74–0.99)	0.74 (0.40–1.36)	0.85 (0.66–1.08)	1.15 (0.73–1.84)	0.85 (0.57–1.28)
Excellent or very good health, never smoked	–	1.30 (0.68–2.51)	0.49 (0.16–1.47)	0.97 (0.62–1.49)	0.54 (0.19–1.56)	1.12 (0.61–2.07)	1.11 (0.32–3.91)	0.35 (0.08–1.51)
Good, fair, or poor health; never smoked	9.61 (1.98–46.7)	1.22 (0.70–2.10)	0.94 (0.32–2.83)	0.93 (0.70–1.24)	0.54 (0.19–1.53)	0.98 (0.70–1.36)	1.24 (0.56–2.74)	0.71 (0.44–1.16)
Excellent or very good health, never smoked, first 3 years of deaths excluded	–	1.38 (0.69–2.75)	0.58 (0.15–2.19)	0.97 (0.59–1.58)	0.38 (0.15–0.94)	1.27 (0.68–2.39)	1.48 (0.38–5.70)	0.32 (0.06–1.72)
Good, fair, or poor health; never smoked; first 3 years of deaths excluded	2.00 (0.20–19.7)	1.26 (0.68–2.31)	0.58 (0.20–1.70)	0.92 (0.66–1.28)	0.50 (0.16–1.61)	1.04 (0.68–1.58)	1.07 (0.44–2.65)	0.65 (0.41–1.03)
Excellent or very good health, never smoked, less than 2.5 kg reported net weight loss in 10 years	–	3.68 (1.77–7.65)	0.88 (0.37–2.13)	0.92 (0.59–1.44)	1.12 (0.45–2.80)	1.05 (0.67–1.63)	1.55 (0.49–4.86)	0.19 (0.02–1.63)
Good, fair, or poor health; never smoked; less than 2.5 kg reported net weight loss in 10 years	1.45 (0.38–5.59)	1.84 (0.88–3.84)	0.91 (0.46–1.81)	0.86 (0.68–1.10)	1.26 (0.57–2.76)	0.93 (0.60–1.43)	1.76 (0.79–3.90)	1.03 (0.68–1.57)

– Quantity zero.

NOTES: Relative risks are adjusted for sex, smoking status, race–ethnicity group, and alcohol consumption. Body mass index is calculated as weight in kilograms (kg) divided by height in meters squared (m²). The reference category is body mass index 18.5–24.9.

SOURCE: NCHS, National Health and Nutrition Examination Survey, 1988–1994.

one survey, and the prevalence of underweight is quite low (2.2%); thus, for some subgroups of underweight persons under age 70, the relative risks could not be estimated very precisely. No deaths occurred among the 57 younger underweight nonsmokers with excellent or very good health, so the estimate of relative risk was 0.

In the NHANES III analyses for older people, underweight was associated with higher risk and overweight with lower risk. For younger people, overweight was generally associated with lower risk, with a single exception. These results,

based on physician-evaluated health status at baseline, did not suggest that the results were affected in any large or systematic way by residual confounding due to illness. Even when analyses were restricted to never smokers judged to be in excellent or very good health by the physician, and after eliminating the first 3 years of deaths, the relative risks were below 1 for overweight and greater than 1 for underweight.

Additional exclusions of respondents who reported a net weight loss of 2.5 kg or more during the 10 years before baseline had little impact on relative risks. For the older

Table K. Adjusted relative risk (95% confidence interval) of mortality after stratifying by self-reported health status and excluding respondents with involuntary weight loss in 6 months prior to baseline: National Health and Nutrition Examination Survey, 1976–1980

Subgroup	Body mass index under 18.5		Body mass index 25–29.9		Body mass index 30–34.9		Body mass index 35 or over	
	Under 70 years	70 years and over	Under 70 years	70 years and over	Under 70 years	70 years and over	Under 70 years	70 years and over
All	1.17 (0.71–1.94)	1.50 (1.06–2.11)	0.77 (0.62–0.96)	0.86 (0.75–0.99)	0.84 (0.61–1.17)	1.11 (0.86–1.42)	1.30 (0.97–1.74)	0.98 (0.75–1.29)
Excellent or very good health	–	2.98 (1.72–5.17)	0.69 (0.43–1.10)	0.83 (0.63–1.09)	0.80 (0.41–1.57)	1.48 (1.04–2.10)	2.03 (1.08–3.82)	0.60 (0.20–1.74)
Good, fair, or poor health	1.49 (0.90–2.45)	1.16 (0.80–1.69)	0.81 (0.64–1.03)	0.86 (0.72–1.02)	0.80 (0.57–1.12)	0.99 (0.73–1.35)	1.04 (0.70–1.57)	1.03 (0.81–1.32)
Excellent or very good health, never smoked	–	2.40 (1.02–5.63)	0.64 (0.18–2.21)	0.68 (0.43–1.07)	1.32 (0.43–4.00)	1.20 (0.64–2.24)	3.39 (1.11–10.4)	0.72 (0.25–2.05)
Good, fair, or poor health, never smoked	2.10 (0.70–6.29)	1.17 (0.45–3.07)	0.52 (0.28–0.96)	0.90 (0.67–1.19)	0.78 (0.40–1.51)	1.03 (0.67–1.56)	1.00 (0.47–2.10)	1.19 (0.83–1.70)
Excellent or very good health, never smoked, first 3 years of deaths excluded	–	2.55 (1.12–5.84)	0.78 (0.22–2.79)	0.71 (0.45–1.13)	1.33 (0.33–5.27)	1.32 (0.69–2.52)	4.32 (1.38–13.50)	0.79 (0.27–2.29)
Good, fair, or poor health; never smoked; first 3 years of deaths excluded	2.34 (0.61–8.93)	1.22 (0.46–3.23)	0.58 (0.30–1.13)	0.90 (0.66–1.22)	0.77 (0.33–1.77)	0.91 (0.60–1.38)	1.17 (0.52–2.64)	1.16 (0.80–1.69)
Excellent or very good health, never smoked, first 3 years of deaths excluded, recent involuntary weight loss excluded	–	2.98 (1.37–6.45)	0.85 (0.23–3.09)	0.70 (0.44–1.11)	1.41 (0.33–5.97)	1.36 (0.70–2.67)	4.08 (1.29–12.9)	0.80 (0.28–2.26)
Good, fair, or poor health; never smoked; first 3 years of deaths excluded; recent involuntary weight loss excluded	–	0.74 (0.19–2.87)	0.62 (0.29–1.34)	0.94 (0.67–1.31)	1.05 (0.44–2.52)	0.99 (0.63–1.56)	1.43 (0.58–3.55)	1.25 (0.82–1.89)

– Quantity zero.

NOTES: Relative risks are adjusted for sex, smoking status, race–ethnicity group, and alcohol consumption. Body mass index is calculated as weight in kilograms (kg) divided by height in meters squared (m^2). The reference category is body mass index 18.5–24.9.

SOURCE: NCHS, National Health and Nutrition Examination Survey, 1976–1980.

group, underweight was still associated with a relative risk greater than 1, and for both age groups, overweight was still associated with a relative risk below 1.

For NHANES II only, these analyses were repeated, stratifying by self-reported baseline health status (Table K). Respondents who reported involuntary weight loss in the 6 months before baseline were excluded. In this survey, all four exclusionary criteria were used. Although the relatively small sample size in this single survey made it difficult to estimate relative risks precisely in the group under 70, the relative risks estimated after these exclusions did not suggest that residual confounding or illness-induced weight loss had caused any systematic bias in the relative risk estimates. For persons aged 70 and over who had never smoked, had excellent or very good health at baseline, did not report recent involuntary weight loss, and after excluding the first 3 years of deaths (i.e., after using all four exclusionary criteria), the relative risk was 2.98 for underweight, 0.70 for overweight, 1.36 for grade 1 obesity, and 0.80 for grades 2 and 3 obesity. The corresponding values before any exclusions were 1.50 for underweight, 0.86 for overweight, 1.11 for grade 1 obesity, and 0.98 for grades 2 and 3 obesity.

The prevalence of underweight was low, and in the group under 70, death rates were also low. In the group of 67 persons under 70 with a BMI less than 18.5 who reported excellent or very good health, no deaths occurred during follow-up, yielding an estimated relative risk of 0.

Effects of Age at Measurement

The age group 70 and over included both persons whose weight and height had been measured at younger ages and had survived to age 70, and persons whose weight and height had been measured at age 70 or over. Additional analyses were performed to evaluate whether the relative risks for the age group 70 and over differed according to whether the original measurements of weight and height had been made under age 70 or at age 70 or over. The majority of deaths in the sample occurred in persons whose BMI had been measured before age 70. Data were stratified according to whether BMI was based on measurements made before age 70 or at age 70 or over, with results by survey for the age group 70 and over as presented in Table M.

Table M. Adjusted relative risk (95% confidence interval) of mortality for persons aged 70 and over, by survey, body mass index category, and age at measurement of weight and height: National Health and Nutrition Examination Survey, 1971–1994

Survey and age at weight and height measurements	Body mass index			
	Under 18.5	25–29.9	30–34.9	35 and over
NHANES I				
All ages	2.01 (1.42–2.84)	0.99 (0.86–1.14)	1.20 (1.02–1.41)	1.92 (1.44–2.56)
Measured under age 70	2.16 (1.40–3.34)	1.03 (0.85–1.25)	1.23 (0.98–1.53)	1.91 (1.33–2.74)
Measured at age 70 or over	1.69 (1.05–2.69)	0.90 (0.75–1.08)	1.15 (0.89–1.49)	1.98 (1.14–3.43)
NHANES II				
All ages	1.50 (1.06–2.11)	0.86 (0.75–0.99)	1.11 (0.86–1.42)	0.98 (0.75–1.29)
Measured under age 70	1.53 (1.03–2.27)	0.88 (0.75–1.04)	1.16 (0.86–1.57)	1.03 (0.73–1.44)
Measured at age 70 or over	1.30 (0.63–2.68)	0.81 (0.66–0.99)	0.95 (0.67–1.36)	0.92 (0.56–1.49)
NHANES III				
All ages	1.67 (1.21–2.30)	0.89 (0.74–1.06)	0.91 (0.74–1.11)	0.98 (0.66–1.46)
Measured under age 70	2.07 (0.97–4.41)	0.70 (0.44–1.12)	0.67 (0.42–1.09)	0.84 (0.40–1.77)
Measured at age 70 or over	1.56 (1.14–2.14)	0.94 (0.79–1.12)	1.01 (0.80–1.27)	1.04 (0.68–1.59)

NOTES: NHANES is National Health and Nutrition Examination Survey. Relative risks are adjusted for sex, smoking status, race–ethnicity group, and alcohol consumption. Body mass index is calculated as weight in kilograms (kg) divided by height in meters squared (m²). The reference category is body mass index 18.5–24.9.

SOURCE: NCHS, NHANES, 1971–1994.

Table N. Percentage of sample and percentage of deaths remaining before and after selected exclusionary criteria were applied, by age group and survey: National Health and Nutrition Examination Survey, 1971–1994

Subgroup	NHANES I, II, and III combined		NHANES II		NHANES III	
	Under 70 years	70 years and over	Under 70 years	70 years and over	Under 70 years	70 years and over
Sample						
All	100.0	100.0	100.0	100.0	100.0	100.0
Excellent or very good health	51.9	36.7	49.6	35.0	49.7	37.9
Excellent or very good health, never smoked	28.5	19.7	30.4	19.5	27.5	20.4
Excellent or very good health, never smoked, first 3 years of deaths excluded	28.2	19.1	30.1	19.3	27.2	19.4
Excellent or very good health, never smoked, first 3 years of deaths excluded, weight stable	–	–	26.8	17.6	23.4	15.6
Deaths						
All	100.0	100.0	100.0	100.0	100.0	100.0
Excellent or very good health	28.6	26.7	29.2	25.4	24.6	26.2
Excellent or very good health, never smoked	20.7	15.4	21.8	15.9	18.1	14.9
Excellent or very good health, never smoked, first 3 years of deaths excluded	18.1	13.2	19.7	14.9	14.1	11.9
Excellent or very good health, never smoked, first 3 years of deaths excluded, weight stable	–	–	17.4	13.9	10.9	8.2

– Quantity zero.

NOTE: NHANES is National Health and Nutrition Examination Survey.

SOURCE: NCHS, NHANES, 1971–1994.

Proportions Excluded

The proportion of the total sample remaining after sequential exclusions is shown in [Table N](#). For the combined data set, after excluding smokers and those in poor health, about 28%

of participants under age 70 and about 19% of participants aged 70 and over remained in the analytic sample. The additional exclusion of those who died in the first 3 years after baseline had only a slight effect. For NHANES II, when smokers; those in good, fair, or poor health; those who

died within the first 3 years after baseline; and those who reported recent involuntary weight loss were all excluded from the analytic sample, about 27% of those under age 70 and 18% of those aged 70 and over remained in the analytic sample. Similar but slightly lower results were seen for NHANES III when similar criteria were applied.

The weighted proportions of deaths in the analytic sample after exclusions are shown in the bottom half of [Table M](#). After all exclusions in the combined data set, approximately 18% of deaths in those under age 70 and 13% among those aged 70 and over remained in the analytic sample. After further exclusions for weight instability in NHANES II and NHANES III, the proportion of deaths remaining in the analytic sample fell even lower. For the older group in NHANES III, after all exclusions, only 8.2% of deaths remained in the analytic data set.

Discussion

The purpose of the analyses described above is to examine the impact of excluding study participants with potential confounding characteristics on the magnitude and direction of estimates of mortality relative risk in various BMI categories. Estimates of the population attributable fraction and the resulting absolute number of excess deaths use the point estimates of relative risk, regardless of their statistical significance. However, the variance of the relative risk estimates is incorporated into the overall variance of the estimated excess deaths. The discussion that follows refers to the point estimates and not to the statistical significance of the relative risks themselves.

The object of these analyses is not to make statistical comparisons between subgroups, which are not independent of each other, nor to assess the statistical significance of the relative risk within a small subgroup. Rather, the object is to examine trends in the relative risks for indications that the estimates of excess deaths might be affected by systematic biases, such as those potentially due to illness-induced weight loss or residual confounding by smoking or prevalent illness. These relative risks based on exclusions would not be appropriate to use to estimate excess deaths in the entire population. Relative risks that are adjusted for confounding factors need to be used in conjunction with the risks associated with those confounding factors.

Relative Risk of Mortality Associated With Underweight

The original analyses found that people who were underweight (BMI less than 18.5) had an elevated risk of mortality relative to persons of normal weight (BMI 18.5–24.9). This observation persisted in virtually all analyses reported here. The prevalence of BMI less than 18.5 is quite low in the population, and in several categories of persons under age 70, in which the death rates are also lower, no

deaths occurred. The analyses of NHANES I data for persons whose measured weight had changed by less than 2 kg over the preceding 10 years showed that underweight was still associated with an increased relative risk of mortality. The relative risk for underweight was also greater than 1 for people who had never smoked. When the analyses were further confined to people who had never smoked and reported having excellent or very good health at baseline, the relative risk for underweight was still greater than 1. Additional exclusions of early deaths and weight loss did not change the direction of the relative risk for underweight. For those aged 70 and over, the relative risk for underweight was always greater than 1. For younger ages, except for the small subgroups with no deaths, the risk was also greater than 1. When analyses of mortality in those aged 70 or over were restricted to participants whose weight and height had been measured before age 70, the relative risks in the underweight category increased, rather than decreased.

These observations are consistent with findings in several other large samples. For example, in a prospective study with 10,858 participants, Thorogood et al. (34) found an increased mortality risk in those with BMI less than 18 and those with BMI 18 to less than 20 relative to BMI 20–22 after 18 years of follow-up, even after excluding ever smokers and the first 5 years of deaths. These associations also persisted when the sample was restricted to participants who were under age 60 at baseline. Calle et al. (22) similarly found elevated mortality at low BMI levels in the large Cancer Prevention Study (CPS) II study relative to those with BMI 23–25, even after excluding ever smokers and those with prevalent disease.

Relative Risk of Mortality Associated With Overweight

Analyses for the combined data set also showed a modestly reduced risk of mortality in the overweight category relative to the normal weight category. This reduction was observed in all surveys and age groups. A similar reduction was observed in analyses limited to weight-stable respondents in NHANES I, indicating that overweight that had persisted for at least 10 years was still associated with reduced risk. When data from the combined data set were stratified by self-reported health status, the relative risks for overweight continued to be less than 1 for both age groups. Additional exclusions of ever smokers and the first 3 years of deaths did not change the direction of the association; overweight was still associated with reduced mortality relative to the normal weight category. Similar results were observed in the NHANES III data when stratified by physician-evaluated health status. For respondents in excellent or very good health, the relative risk was slightly above 1 (1.04), but when analyses were additionally limited to never smokers, the relative risks dropped below 1. Additional exclusions of the first 3 years of deaths in NHANES III and of respondents reporting more than 2.5 kg of net weight loss in 5 years

still resulted in relative risks less than 1 for the overweight category. Similar exclusions in NHANES II, including the exclusion of participants reporting recent involuntary weight loss, still resulted in relative risks less than 1 for the overweight category. This observation is also consistent with other studies. A meta-analysis of 26 cohorts found a relative risk of 0.97 for overweight relative to the normal weight category (19).

Relative Risk of Mortality Associated With Obesity

Slight but not systematic changes in relative risks, in both directions, were observed for both grade 1 and grades 2 and 3 obesity, when data were stratified by health status, smoking, and weight change, and when early deaths were excluded. The relative risks sometimes increased and sometimes dropped below 1 for both obesity categories.

Proportions Excluded

The exclusionary approach resulted in the majority of the participants being excluded from the analytic sample. After exclusions on the basis of health status, smoking, early death, and weight stability, less than 30% of the original sample remained among participants under age 70, and less than 20% remained in those aged 70 and over. The proportion of deaths remaining was even lower. This high proportion of exclusions is comparable with that seen in other studies. In the Nurses' Health Study, after limiting the sample to those without cardiovascular disease or cancer at baseline, exclusions on the basis of smoking and weight stability resulted in 88.8% of the deaths in the sample (4,195 of 4,726 deaths) being excluded (24). The total proportion of excluded deaths in the cohort may have been higher, because participants with cancer or cardiovascular disease at baseline had previously been excluded. In the CPS II study, almost 82% of men and 63% of women in the analytic sample were excluded from further analysis (22).

An examination of 15 epidemiologic cohorts demonstrated that results similar to those obtained by excluding smokers from the analytic sample were obtained by randomly deleting the same number of respondents (35). Those researchers concluded that, "The belief that smoking is responsible for the quadratic relation between BMI and mortality or that it explains the excess of mortality among the leanest groups is not supported by empirical observation or quantitative testing" (35).

Conclusions

These analyses of the effects of exclusions and stratification by health status for the combined data set do not suggest that the analyses on the full sample in the paper by Flegal et al. (3) were affected in any important or systematic way

by residual confounding due to smoking, prevalent illness at baseline, or illness-induced weight loss. These analyses do not suggest that Flegal et al. (3) had overestimated the risks associated with underweight, or underestimated the risks associated with overweight or obesity. Even when analyses were restricted to a subset of healthy individuals who had never smoked and deaths occurring in the first part of the study were excluded, the relative risks were still elevated for underweight respondents and under 1 for overweight respondents, and the relative risks for obesity did not show an increase. Thus, these analyses do not suggest that biases due to illness-induced weight loss or residual confounding by smoking and prevalent illness explain the findings of Flegal et al. (3).

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