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REVIEW

Association of All-Cause Mortality With Overweight and Obesity Using Standard Body Mass Index Categories

A Systematic Review and Meta-analysis

Katherine M. Flegal, PhD
Brian K. Kit, MD
Heather Orpana, PhD
Barry I. Graubard, PhD

Importance Estimates of the relative mortality risks associated with normal weight, overweight, and obesity may help to inform decision making in the clinical setting.

Objective To perform a systematic review of reported hazard ratios (HRs) of all-cause mortality for overweight and obesity relative to normal weight in the general population.

Data Sources PubMed and EMBASE electronic databases were searched through September 30, 2012, without language restrictions.

Study Selection Articles that reported HRs for all-cause mortality using standard body mass index (BMI) categories from prospective studies of general populations of adults were selected by consensus among multiple reviewers. Studies were excluded that used nonstandard categories or that were limited to adolescents or to those with specific medical conditions or to those undergoing specific procedures. PubMed searches yielded 7034 articles, of which 141 (2.0%) were eligible. An EMBASE search yielded 2 additional articles. After eliminating overlap, 97 studies were retained for analysis, providing a combined sample size of more than 2.88 million individuals and more than 270 000 deaths.

Data Extraction Data were extracted by 1 reviewer and then reviewed by 3 independent reviewers. We selected the most complex model available for the full sample and used a variety of sensitivity analyses to address issues of possible overadjustment (adjusted for factors in causal pathway) or underadjustment (not adjusted for at least age, sex, and smoking).

Results Random-effects summary all-cause mortality HRs for overweight (BMI of 25-<30), obesity (BMI of ≥30), grade 1 obesity (BMI of 30-<35), and grades 2 and 3 obesity (BMI of ≥35) were calculated relative to normal weight (BMI of 18.5-<25). The summary HRs were 0.94 (95% CI, 0.91-0.96) for overweight, 1.18 (95% CI, 1.12-1.25) for obesity (all grades combined), 0.95 (95% CI, 0.88-1.01) for grade 1 obesity, and 1.29 (95% CI, 1.18-1.41) for grades 2 and 3 obesity. These findings persisted when limited to studies with measured weight and height that were considered to be adequately adjusted. The HRs tended to be higher when weight and height were self-reported rather than measured.

Conclusions and Relevance Relative to normal weight, both obesity (all grades) and grades 2 and 3 obesity were associated with significantly higher all-cause mortality. Grade 1 obesity overall was not associated with higher mortality, and overweight was associated with significantly lower all-cause mortality. The use of predefined standard BMI groupings can facilitate between-study comparisons.

JAMA. 2013;309(1):71-82 www.jama.com

THE TOPIC OF THE MORTALITY differences between weight categories has sometimes been described as controversial.[1] The appearance of controversy may arise in part because studies of body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) and mortality have used a wide variety of BMI categories and varying reference categories, which can make findings appear more variable than when standard categories are used and also can make it difficult to compare and synthesize studies. A report[2] in 1997 from the World Health Organization Consultation on Obesity defined BMI-based categories of underweight, normal weight, preobesity, and obesity. The same cutoff BMI values were adopted by the National Heart, Lung, and Blood Institute in 1998.[3]

In this study, we used the National Heart, Lung, and Blood Institute's

For editorial comment see p 87.

CME available online at www.jamaarchivescme.com and questions on p 91.

Author Video Interview available at www.jama.com.

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terminology with categories of underweight (BMI of <18.5), normal weight (BMI of 18.5-<25), overweight (BMI of 25-<30), and obesity (BMI of ≥30). Grade 1 obesity was defined as a BMI of 30 to less than 35; grade 2 obesity, a BMI of 35 to less than 40; and grade 3 obesity, a BMI of 40 or greater. These standard categories have been increasingly used in published studies of BMI and mortality, but the literature reporting these results has not been systematically reviewed.

The purpose of this study was to compile and summarize published analyses of BMI and all-cause mortality that provide hazard ratios (HRs) for standard BMI categories. We followed the guidelines in the Meta-analysis of Observational Studies in Epidemiology (MOOSE) statement[4] for reporting of systematic reviews.

METHODS

Articles were identified by searches of PubMed and EMBASE through September 30, 2012. Details of search strategies appear in eTable 1 at http://www.jama.com. No language restrictions were applied. All articles were reviewed for inclusion by 1 reviewer (K.M.F.). An independent review of all articles was conducted by a second set of reviewers (B.K.K., H.O., and B.I.G.). The articles were reviewed to identify those that used standard BMI categories in prospective, observational cohort studies of all-cause mortality among adults with BMI measured or reported at baseline. Studies that addressed these relationships only in adolescents, only in institutional settings, or only among those with specific medical conditions or undergoing specific medical procedures were excluded. We included multiple articles from a given data set only when there was little overlap between articles by sex, age group, or some other factor.

In some cases, authors used standard BMI categories for overweight and obesity but had used a slightly broader reference BMI category of less than 25 or a slightly narrower reference BMI category of 20 to less than 25 rather than the standard normal BMI category of 18.5 to less than 25. We included these articles but have noted the cases in which the reference BMI category was less than 25 or 20 to less than 25. We classified studies that included a mix of self-reported and measured weight and height according to the preponderant type.

Abstracted items included sample size, number of deaths, age at baseline, length of follow-up, HRs and 95% confidence intervals, sex, age, type of weight and height data (measured or self-reported), country or region, source of study sample, adjustment factors, exclusion and inclusion criteria, and sensitivity analyses. Authors of screened articles were queried for additional information when necessary. In studies that only presented results stratified by smoking or health condition, we selected results for nonsmokers or never smokers or for those without the health condition. We selected the most complex model available for the full sample and used a variety of sensitivity analyses to address issues of possible overadjustment or underadjustment.

We categorized HRs into 2 age groupings either as limited solely to people aged 65 years or older or as a mixed-age category (eg, aged 25-64 years or 40-80 years). We classified articles as adequately adjusted, possibly overadjusted, or possibly underadjusted. We categorized HRs by adjust-

Table 1. Summary Random-Effects Hazard Ratios (HRs) of All-Cause Mortality for Overweight and Obesity Relative to Normal Weight

	Self-reported or Measured Height and Weight			Height and Weight					
				Measured			Self-reported		
	No. of HRs	Summary HR (95% CI)	I^2, %	No. of HRs	Summary HR (95% CI)	I^2, %	No. of HRs	Summary HR (95% CI)	I^2, %
BMI of 25-<30									
All ages	140	0.94 (0.91-0.96)[a]	85.0	89	0.93 (0.89-0.95)[a]	75.8	51	0.96 (0.92-1.00)[a]	90.4
Mixed ages	107	0.95 (0.92-0.98)[a]	86.8	67	0.93 (0.89-0.96)[a]	79.6	40	0.98 (0.93-1.03)[a]	90.7
Age ≥65 y only	33	0.90 (0.86-0.94)[a]	51.2	22	0.90 (0.84-0.95)	31.2	11	0.90 (0.84-0.96)[a]	71.0
BMI of ≥30									
All ages	84	1.18 (1.12-1.25)[a]	86.7	56	1.13 (1.06-1.19)[a]	73.4	28	1.29 (1.18-1.41)[a]	89.7
Mixed ages	63	1.23 (1.16-1.31)[a]	87.2	41	1.16 (1.10-1.24)[a]	74.6	22	1.36 (1.25-1.48)[a]	86.1
Age ≥65 y only	21	1.03 (0.94-1.12)[a]	61.5	15	0.98 (0.86-1.12)[a]	61.1	6	1.09 (0.96-1.23)[a]	67.0
BMI of 30-<35									
All ages	53	0.95 (0.88-1.01)[a]	86.8	30	0.94 (0.86-1.03)[a]	80.5	23	0.95 (0.85-1.06)[a]	90.1
Mixed ages	42	0.96 (0.89-1.04)[a]	87.7	24	0.95 (0.86-1.06)[a]	83.2	18	0.97 (0.87-1.09)[a]	90.0
Age ≥65 y only	11	0.87 (0.72-1.05)[a]	76.3	6	0.89 (0.71-1.11)	56.2	5	0.83 (0.58-1.20)[a]	85.7
BMI of ≥35									
All ages	53	1.29 (1.18-1.41)[a]	81.7	30	1.25 (1.13-1.39)[a]	65.4	23	1.34 (1.16-1.55)[a]	88.3
Mixed ages	42	1.32 (1.19-1.45)[a]	82.8	24	1.28 (1.14-1.44)[a]	68.9	18	1.35 (1.16-1.58)[a]	89.0
Age ≥65 only	11	1.20 (0.94-1.52)[a]	70.6	6	1.10 (0.89-1.34)	25.1	5	1.29 (0.77-2.17)[a]	85.2

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a] Indicates significant heterogeneity ($P < .05$).

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ment level, by whether the data were measured or self-reported, by whether the analysis was performed separately for men and women or for both sexes combined, and by region (North America, Europe, and other).

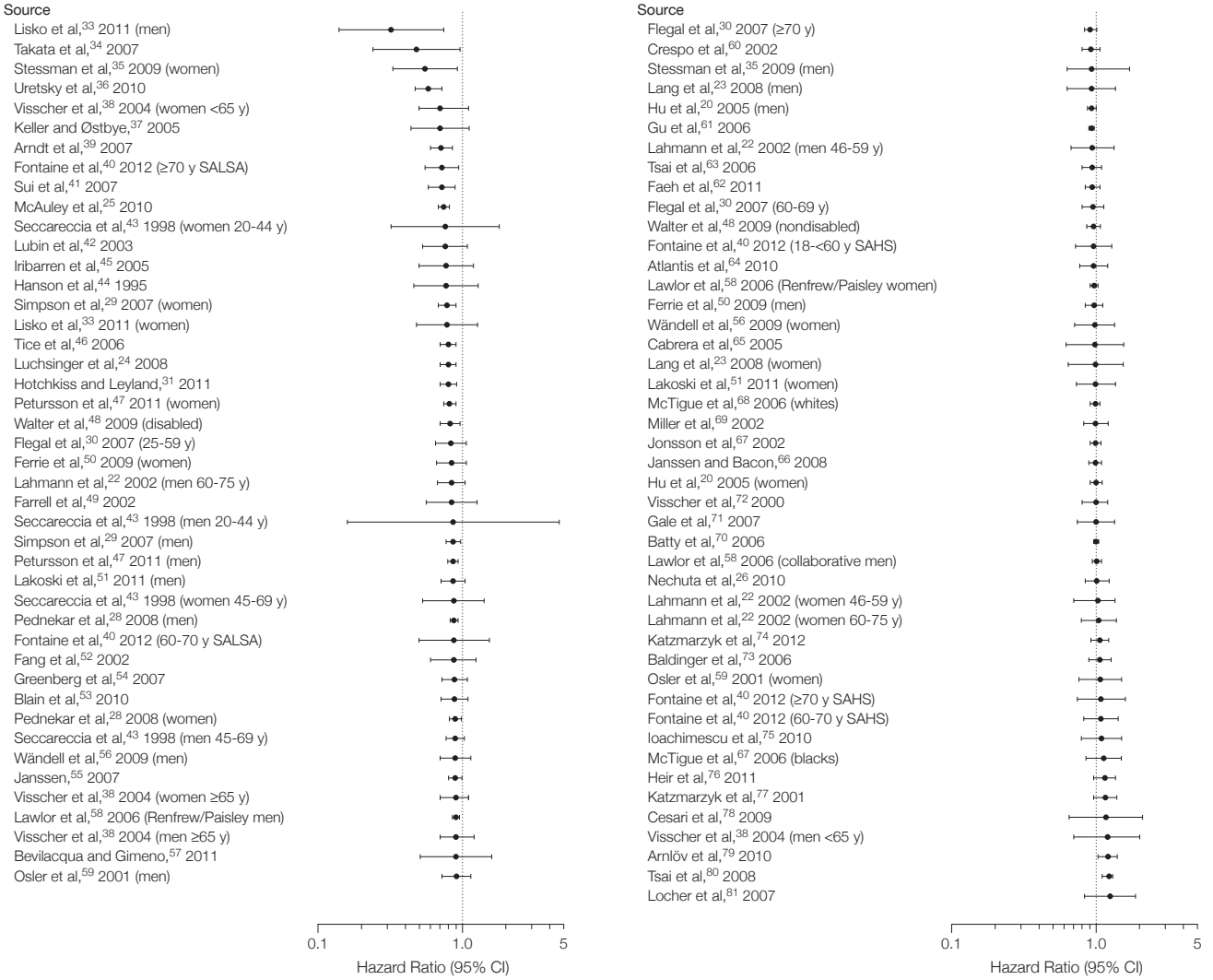
We used a random-effects model[5] to summarize the results overall and within subgroups and based statistically significant heterogeneity on a *P* value of less than .05. We calculated the quantity I^2 to describe the degree of heterogeneity with values of 25%, 50%, and 75% considered low, moderate, and high, respectively.[6] We also used a sequential approach similar to that described by Patsopoulos et al[7] to assess consistency of findings when heterogeneity was reduced. All analyses were performed with SAS version 9.3 (SAS Institute Inc).

For sensitivity analyses, we examined the effects on HRs of incorporating results from a recent large pooled study for overweight.[8] For comparative purposes, we also constructed approximate HRs relative to normal weight from several recent large studies[9-14] that had used finer BMI groupings and thus did not meet our inclusion criteria. To do this, we averaged HRs from the finer BMI groupings over groups corresponding to the standard BMI categories, weighting the HRs by the number of deaths.

RESULTS

As shown in the eFigure at http://www.jama.com, the primary search strat-

Figure 1. Hazard Ratios for All-Cause Mortality Relative to Normal Weight in Studies That Used Measured Data for Participants With a Body Mass Index of 25 to Less Than 30



Data markers indicate hazard ratios and error bars indicate 95% confidence intervals. SAHS indicates San Antonio Heart Study; and SALSA, Sacramento Area Latino Study on Aging.

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egy for PubMed yielded 4142 articles, of which 128 met our criteria. A second PubMed search yielded 2892 additional articles, of which 13 met our criteria. A search of EMBASE yielded 2 additional eligible articles. In total, 143 eligible studies were identified.

After exclusion of 41 articles with overlapping data sets and of 5 articles lacking sufficient information, 97 articles remained for analysis; all of which had been identified through systematic search procedures. The selected studies are shown in eTable 2 with additional information in eTable 3 regarding exclusions and adjustment factors. Regions of origin of participants included the United States or Canada (n=41 studies), Europe (n=37), Australia (n=7), China or Taiwan (n=4), Japan (n=2), Brazil (n=2), Israel (n=2), India (n=1), and Mexico (n=1). The tabulated studies included more than 2.88 million participants and more than 270 000 deaths.

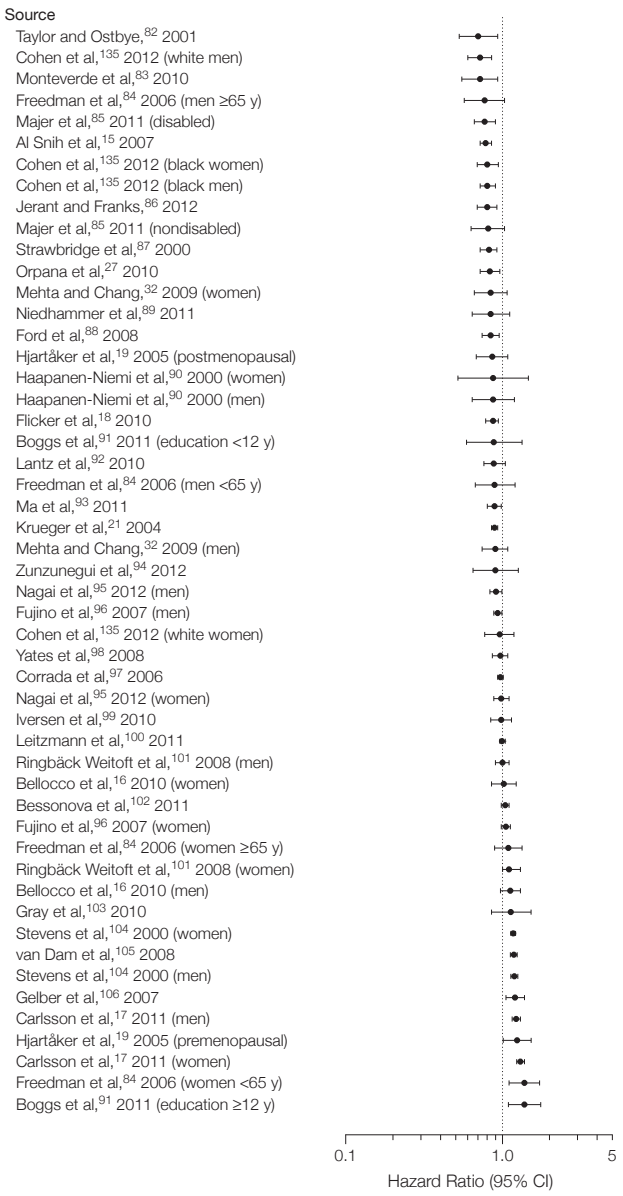
Not all studies reported the specific categories of interest. There were 93 studies for the BMI category of 25 to less than 30 (overweight), 61 studies for the BMI category of 30 or greater (obesity), and 32 studies for the BMI categories of 30 to less than 35 (grade 1 obesity) and 35 and greater (grades 2 and 3 obesity).

We considered the results adequately adjusted if they were adjusted for age, sex, and smoking and not adjusted for factors in the causal pathway between obesity and mortality, or if they had reported or demonstrated that adjustments or exclusions to avoid bias had shown little effect on their findings. A number of studies (for example[15-29]) reported qualitatively that such adjustments had little or no effect without showing quantitative details.

Other studies (for example[30-32]) demonstrated little effect through a series of sensitivity analyses. We considered the available full sample results from such studies to also be adequately adjusted. Otherwise, we considered studies as possibly overadjusted if they adjusted for factors such as hypertension that are considered to be in the causal pathway between obesity and mortality or as possibly underadjusted if they did not adjust for age, sex, and smoking. We classified 53 studies as adequately adjusted, 34 studies as possibly overadjusted, and 10 studies as possibly underadjusted.

Summary HRs are shown in TABLE 1 overall, by age group, and by whether data were measured or self-reported. The summary HRs were 0.94 (95% CI, 0.91-0.96) for overweight, 1.18 (95% CI, 1.12-1.25) for obesity (all grades), 0.95 (95% CI, 0.88-1.01) for grade 1 obesity, and 1.29 (95% CI, 1.18-1.41) for grades 2 and 3 obesity. Plots of HRs for these categories are shown in FIGURES 1-8.[33-110] Additional details are

Figure 2. Hazard Ratios for All-Cause Mortality Relative to Normal Weight in Studies That Used Self-reported Data for Participants With a Body Mass Index of 25 to Less Than 30



Data markers indicate hazard ratios and error bars indicate 95% confidence intervals.

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shown in eTables 4-7, which show summary HRs by age, sex, region, and measurement type.

Results for studies that we considered adequately adjusted are shown in TABLE 2. This more select group showed the same general pattern of overweight associated with reduced mortality, grade 1 obesity not significantly associated with increased mortality, and the higher grades of obesity significantly associated with increased mortality. The summary HRs were 0.94 (95% CI, 0.90-0.97) for overweight, 1.21 (95% CI, 1.12-1.31) for obesity (all grades), 0.97 (95% CI, 0.90-1.04) for grade 1 obesity, and 1.34 (95% CI, 1.21-1.47) for grades 2 and 3 obesity. For overweight, the results from possibly overadjusted studies and from adequately adjusted studies were similar (eTable 8). However, for obesity, the possibly overadjusted studies tended to have lower HRs than the adequately adjusted studies.

Between-study heterogeneity was statistically significant in most categories. According to Higgins et al,[6] this test may have "excessive power when there are many studies, especially when those studies are large." Heterogeneity (as indicated by the value of I^2) was less for studies with measured height and weight and was lower for studies limited to those older than 65 years. The value of I^2 was reduced by limiting findings to adequately adjusted studies with measured data.

Higher levels of heterogeneity, however, do not necessarily lead to dissimilar results that would affect the conclusions. For example, the summary HR for overweight for older ages (≥65 years) was identical (0.90) for measured height and weight (I^2=31.2%) and for self-reported height and weight (I^2=71.0%). For adequately adjusted studies, we sequentially excluded HRs within age and measurement categories as needed to reduce the I^2 value to below 25%. Within the 4 age-measurement groups, this required exclusion of 9% to 22% of studies for measured data and 14% to 39% of studies for self-reported data.

For overweight, excluding these studies led to a uniformly lower HR of 0.89 for both age groups and for both measured and self-reported data. For obesity, the effects of excluding these studies were more variable and led to an overall increase of the summary HR from 1.21 to 1.24. Corresponding values were from 0.97 to 1.05 (neither significantly different from 1) for grade 1 obesity and from 1.34 to 1.39 for grades 2 and 3 obesity. Thus, heterogeneity appeared to have had little

Figure 3. Hazard Ratios for All-Cause Mortality Relative to Normal Weight in Studies That Used Measured Data for Participants With a Body Mass Index of 30 or Greater

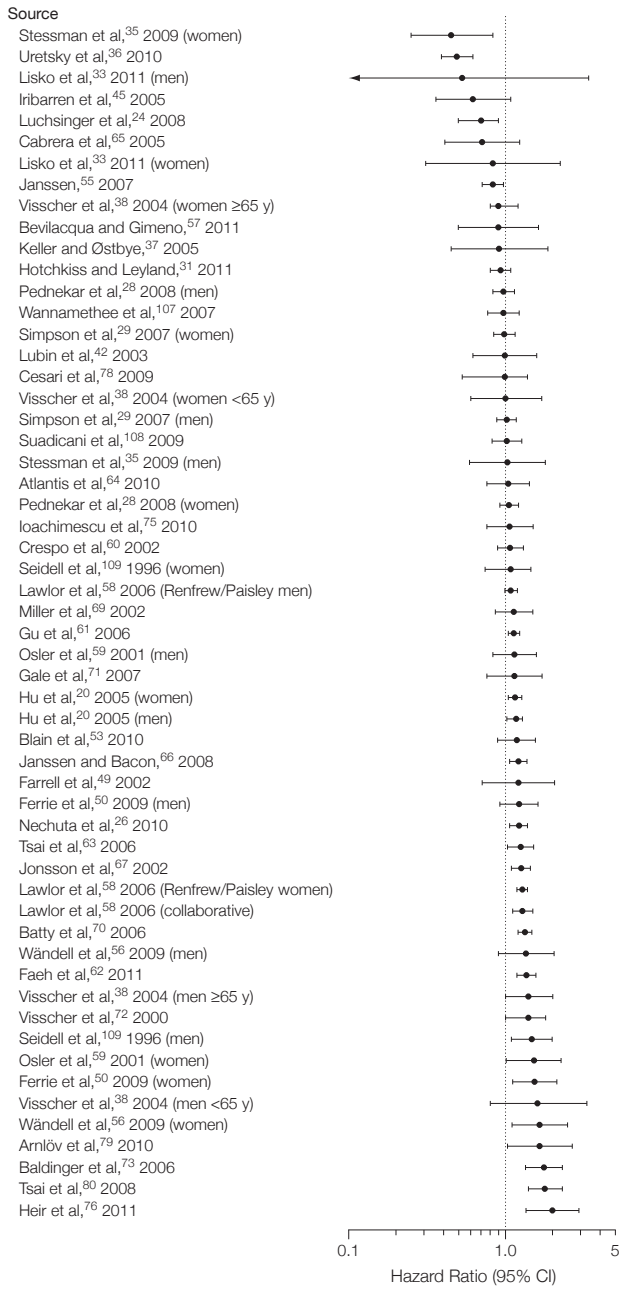

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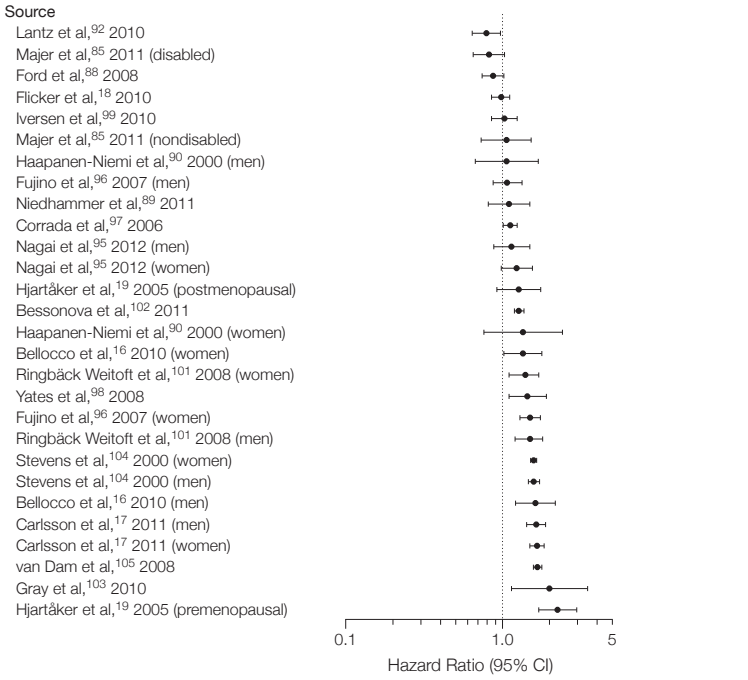
Figure 4. Hazard Ratios for All-Cause Mortality Relative to Normal Weight in Studies That Used Self-reported Data for Participants With a Body Mass Index of 30 or Greater



Data markers indicate hazard ratios and error bars indicate 95% confidence intervals.

effect on the conclusions of the meta-analysis.

The excluded studies varied across outcome categories; inspection of the excluded studies did not suggest specific reasons why they had contributed to heterogeneity. Taken together, the findings suggest that contributors to heterogeneity across all studies include adjustment levels, type of measurement data, and age group. Some degree of heterogeneity may also result from the variation in BMI levels within the broad BMI categories used, as well as from variations in the type of cohorts studied.

Sensitivity Analyses

For the overweight category only, we also repeated analyses including the results from a study that pooled data from 19 cohorts. After excluding ever smokers and those with a history of cancer or heart disease, Berrington de Gonzalez et al[8] found a HR of 1.11 (95% CI, 1.07-1.16) for men and 1.13 (95% CI, 1.09-1.16) for women with a BMI of 25 to 29.9 relative to those with a BMI of 20 to less than 25 (Amy Berrington de Gonzalez, DPhil, written communication, June 16, 2011).

Our analysis included published studies using 6 of the same cohorts, representing about 60% of the original Berrington de Gonzalez et al[8] sample. Excluding those studies from our analysis and substituting the above results from Berrington de Gonzalez et al did not change the summary HR for overweight.

We also repeated the analyses after excluding the studies that had used slightly different reference categories. Excluding studies with a reference BMI category of less than 25 had no effect on the HRs for overweight and decreased the HR for obesity by 0.02. Excluding studies with a reference BMI category of 20 to less than 25 increased the HR for overweight by 0.005 and had no effect on the HR for obesity.

Beyond these slight differences in the reference category, studies that used nonstandard BMI categories were excluded. However, we were able to construct approximate HRs from some recent large studies that had used nonstandard BMI categories (eTable 9). This approach does not allow for construction of appropriate standard errors or confidence intervals. The approximate HRs were consistent with our findings from our analyses of individual studies, showing similar minor variation.

COMMENT

This study presents comprehensive estimates (derived from a systematic review) of the association of all-cause mortality in adults with current standard BMI categories used in the United States and internationally. Estimates of the relative mortality risks associated with normal weight, overweight, and obesity may help to inform decision making in the clinical setting.

The most recent data from the United States show that almost 40% of adult men and almost 30% of adult women fall into the overweight category with a BMI of 25 to less than 30.[111] Comparable figures for Canada are 44% of men and 30% of women[112] and for England are 42% of men and 32% of women.[113]

According to the results presented herein, overweight (defined as a BMI of 25-<30) is associated with significantly lower mortality overall relative to the normal weight category with an overall summary HR of 0.94. For overweight, 75% of HRs with measured weight and height and 67% of HRs with self-reported weight and height were below 1. These results are broadly consistent with 2 previous meta-analyses[114,115] that used standard categories. In a pooled analysis of 26 observational studies, McGee et al[114] found summary relative risks of all-cause mortality for overweight of 0.97 (95% CI, 0.92-1.01) for men and 0.97 (95% CI, 0.93-0.99) for women relative to normal weight.

Recent estimates for the prevalence of obesity (defined as a BMI of ≥30) among adults are 36% in the United States,[111] 24% in Canada,[112] and 26% in

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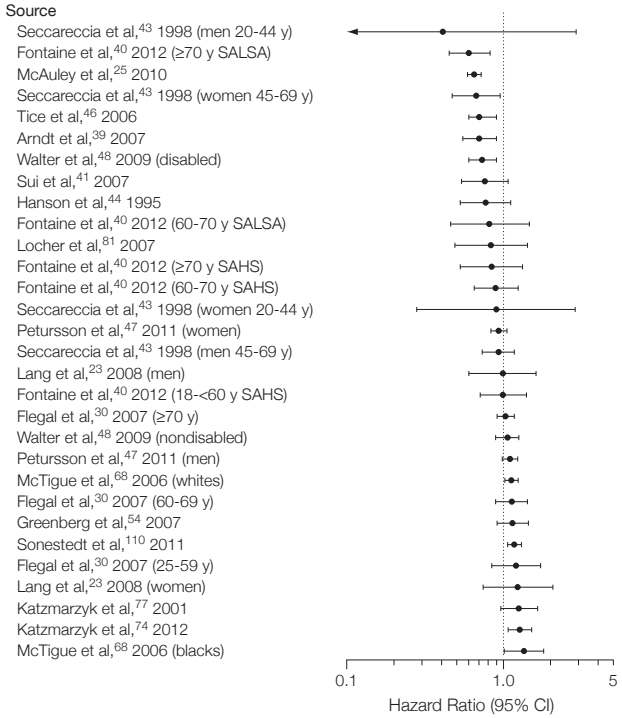
England.[113] Obesity was associated with significantly higher all-cause mortality relative to the normal weight BMI category with an overall summary HR of 1.18. Corresponding estimates for obesity from McGee et al[114] were 1.20 (95% CI, 1.12-1.29) for men and 1.28 (95% CI, 1.18-1.37) for women. In the United States and Canada, more than half of those who are obese fall into the grade 1 category (BMI of 30-<35). We did not find significant excess mortality associated with grade 1 obesity, suggesting that the main contribution to excess mortality in obesity comes from higher levels of BMI.

Our findings are consistent with observations of lower mortality among overweight and moderately obese patients.[116-119] Possible explanations have included earlier presentation of heavier patients,[120] greater likelihood of receiving optimal medical treatment,[121-123] cardioprotective metabolic effects of increased body fat,[124,125] and benefits of higher metabolic reserves.[118]

The results presented herein provide little support for the suggestion[126] that smoking and preexisting illness are important causes of bias. Most studies that addressed the issue found that adjustments or exclusions for these factors had little or no effect. However, overadjustment for factors in the causal pathway appears to decrease HRs for obesity but not for overweight.

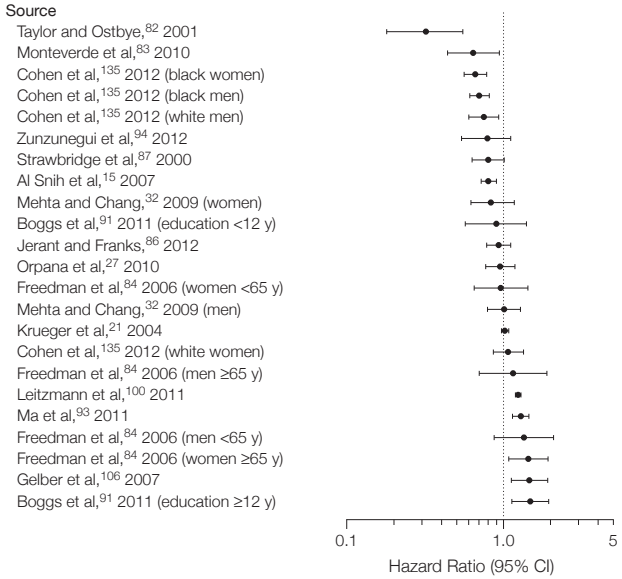
An important source of bias appears to be the errors in self-reported weight and height data. Such errors have been shown to vary by age, sex, race, measured values, and data collection method.[127,128] The systematic error of self-reported data rather than measured data can result in substantial misclassification of individuals into incorrect BMI categories,[129] create errors that are difficult to correct,[130] and lead to upward bias in the estimates.[131] We found a generally lower summary HR and less heterogeneity in studies using measured data than in studies using self-reported data. The differences were more pronounced in analyses stratified by sex than in analy-

Figure 5. Hazard Ratios for All-Cause Mortality Relative to Normal Weight in Studies That Used Measured Data for Participants With a Body Mass Index of 30 to Less Than 35



Data markers indicate hazard ratios and error bars indicate 95% confidence intervals. SAHS indicates San Antonio Heart Study; and SALSA, Sacramento Area Latino Study on Aging.

Figure 6. Hazard Ratios for All-Cause Mortality Relative to Normal Weight in Studies That Used Self-reported Data for Participants With a Body Mass Index of 30 to Less Than 35



Data markers indicate hazard ratios and error bars indicate 95% confidence intervals.

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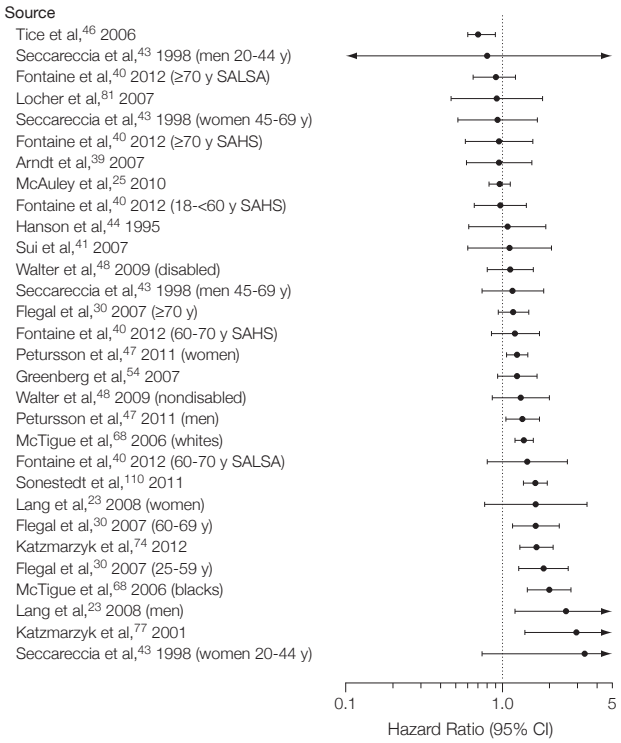
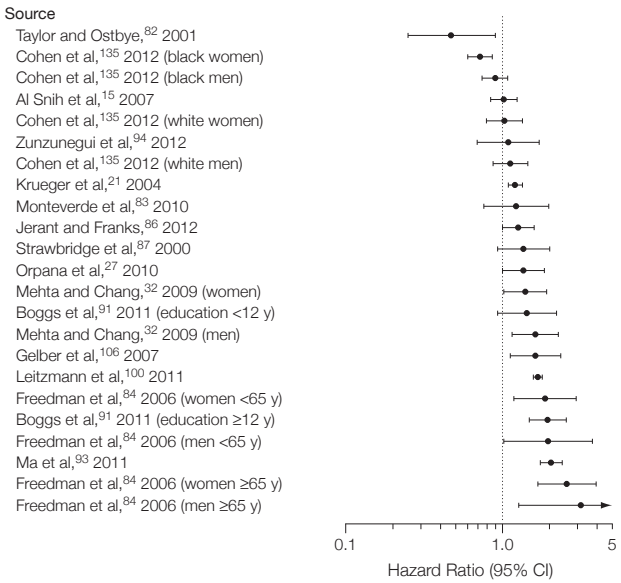
Figure 7. Hazard Ratios for All-Cause Mortality Relative to Normal Weight in Studies That Used Measured Data for Participants With a Body Mass Index of 35 or Greater



Data markers indicate hazard ratios and error bars indicate 95% confidence intervals. SAHS indicates San Antonio Heart Study; and SALSA, Sacramento Area Latino Study on Aging.

Figure 8. Hazard Ratios for All-Cause Mortality Relative to Normal Weight in Studies That Used Self-reported Data for Participants With a Body Mass Index of 35 or Greater



Data markers indicate hazard ratios and error bars indicate 95% confidence intervals.

ses that combined both men and women. Because the errors in self-reported data tend to differ by sex, there may be an offsetting effect when analyses combine men and women.

Publication bias can potentially affect systematic reviews. Studies that find little or no association of overweight or obesity with mortality risk sometimes only mention these results in passing without providing details. For example, He et al[132] did not include terms for overweight or obesity in their models, reporting only that overweight and obesity were not associated with increased mortality. Studies of BMI and mortality sometimes selectively report analyses of certain subgroups, an approach that can lead to bias.[133,134]

The study by Berrington de Gonzalez et al[8] and the overlapping study by Adams et al[1] found results similar to ours in their full sample but based their final results on a subgroup with less than half of their original sample, arguing that this subgroup provided more valid results than the full sample. The validity of this assertion has not been demonstrated, and such large-scale exclusions may introduce additional bias, particularly when using self-reported data. Other studies* have shown little or no effect of similar exclusions.

Strengths and Limitations

One of the strengths of our study is the large sample size and number of studies included, which make the findings robust to the effects of any single study. Additionally, we used a comprehensive search strategy and prespecified standard categories. Although standard BMI categories were developed by the World Health Organization and by the National Institutes of Health in the 1990s, not all studies of BMI and mortality use standard categories as part of their analyses. The combination of flexible categorization and selective reporting can lead to wide variations in HRs even within a single data set.[136] Categorization of BMI has both advantages and disadvantages.[137,138] How-

*References 15, 16, 18, 19, 22-25, 27, 28, 30-32, 135.

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ever, the use of predefined standard groupings avoids issues of post hoc and ad hoc selection of categories and reference categories.

Our study also has limitations. It addresses only all-cause mortality and not morbidity or cause-specific mortality. It addresses only findings related to BMI and not to other aspects of body composition such as visceral fat or fat distribution. Our census of these articles may be incomplete. Our coding and data abstraction procedures may have introduced errors. Our information on age was limited. Because of publication bias and selective reporting, null or negative HRs may have been less likely to be published. Geographical coverage was limited.

CONCLUSIONS

Relative to normal weight, obesity (all grades) and grades 2 and 3 obesity were both associated with significantly higher all-cause mortality. Grade 1 obesity was not associated with higher mortality, suggesting that the excess mortality in obesity may predominantly be due to elevated mortality at higher BMI levels. Overweight was associated with significantly lower all-cause mortality. The use of predefined standard BMI groupings can facilitate between-study comparisons.

Author Contributions: Dr Flegal had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Flegal, Kit, Graubard.
Acquisition of data: Flegal, Kit, Orpana, Graubard.
Analysis and interpretation of data: Flegal, Kit, Orpana, Graubard.
Drafting of the manuscript: Flegal.
Critical revision of the manuscript for important intellectual content: Flegal, Kit, Orpana, Graubard.
Statistical analysis: Flegal, Graubard.
Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.
Funding/Support: There was no external funding for this work. The Centers for Disease Control and Prevention and the National Cancer Institute reviewed and approved the manuscript before submission.
Disclaimer: The findings and conclusions in this report are those of the authors and not necessarily the official views of the Centers for Disease Control and Prevention or the National Cancer Institute.
Online-Only Material: The Author Video Interview, eTables 1 through 9, eFigure, and eReferences are available at http://www.jama.com.
Additional Contributions: We thank Amy Berrington de Gonzalez, DPhil (National Cancer Institute), Marselle Bevilacqua (Universidade Federal de São Paulo, Brazil), Michael Bursztyn, MD (Hadassah-Hebrew University Medical Center), Sarah Cohen, PhD (International Epidemiology Institute), Jane Ferrie, PhD (University College, London), Trond Heir, MD (Oslo University Hospital), Heather Keller, PhD (University of Waterloo), Patrick Krueger, PhD (University of Colorado), Petra Lahmann, PhD (Queensland Institute of Medical Research), Iain Lang, MD (Peninsula College of Medicine and Dentisty), Malena Monteverde, PhD (National Council of Scientific and Technical Research, Argentina), Mangesh Pednekar, PhD (Sekhsaria Institute for Public Health), Julie Simpson, PhD (University of Melbourne), and Joachanan Stessman, MD (Hadassah-Hebrew University Medical Center), for providing additional information about their studies; Yinong Chong, PhD (Centers for Disease Control and Prevention), for assistance with an article in Chinese; Eduardo Simoes, MD (Centers for Disease Control and Prevention), for assistance with an article in Portuguese; and David Check, BS (National Cancer Institute), for assistance with the figures. No financial compensation was provided to any of these individuals.

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Table 2. Summary Hazard Ratios (HRs) of All-Cause Mortality for Overweight and Obesity Relative to Normal Weight From Studies Considered Adequately Adjusted

	Self-reported or Measured Height and Weight			Height and Weight					
				Measured			Self-reported		
	No. of HRs	Summary HR (95% CI)	I^2, %	No. of HRs	Summary HR (95% CI)	I^2, %	No. of HRs	Summary HR (95% CI)	I^2, %
BMI of 25-<30									
All ages	86	0.94 (0.90-0.97)[a]	87.6	45	0.92 (0.88-0.96)[a]	74.8	41	0.95 (0.90-1.01)[a]	91.0
Mixed ages	68	0.95 (0.91-0.99)[a]	89.3	34	0.93 (0.88-0.98)[a]	79.2	34	0.96 (0.91-1.02)[a]	91.8
Age ≥65 y only	18	0.90 (0.86-0.95)	27.9	11	0.90 (0.84-0.96)	23.4	7	0.91 (0.84-0.98)	42.9
BMI of ≥30									
All ages	42	1.21 (1.12-1.31)[a]	89.3	22	1.11 (1.03-1.20)[a]	67.1	20	1.33 (1.21-1.47)[a]	88.0
Mixed ages	33	1.26 (1.16-1.37)[a]	89.7	16	1.13 (1.04-1.23)[a]	66.7	17	1.39 (1.27-1.53)[a]	84.3
Age ≥65 y only	9	1.05 (0.92-1.21)[a]	63.9	6	1.02 (0.81-1.29)[a]	73.1	3	1.08 (0.93-1.25)	39.7
BMI of 30-<35									
All ages	42	0.97 (0.90-1.04)[a]	83.8	21	1.00 (0.92-1.09)[a]	64.2	21	0.94 (0.84-1.05)[a]	89.6
Mixed ages	33	0.98 (0.91-1.06)[a]	84.8	16	1.03 (0.94-1.12)[a]	64.8	17	0.95 (0.85-1.07)[a]	90.3
Age ≥65 y only	9	0.88 (0.69-1.12)[a]	78.0	5	0.90 (0.70-1.16)[a]	64.1	4	0.82 (0.46-1.47)[a]	88.1
BMI of ≥35									
All ages	42	1.34 (1.21-1.47)[a]	81.2	21	1.32 (1.20-1.46)[a]	46.6	21	1.35 (1.16-1.57)[a]	88.7
Mixed ages	33	1.35 (1.22-1.50)[a]	82.2	16	1.37 (1.24-1.52)	40.4	17	1.34 (1.14-1.57)[a]	89.6
Age ≥65 y only	9	1.28 (0.93-1.76)[a]	75.2	5	1.12 (0.89-1.43)	37.8	4	1.40 (0.64-3.07)[a]	86.8

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a]Indicates significant heterogeneity ($P < .05$).

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The test of intelligence [is] not how much we know how to do, but how we behave when we don't know what to do. Similarly, any situation, any activity, that puts before us real problems, that we have to solve for ourselves, problems for which there are no answers in any book, sharpens our intelligence.

—John Holt (1923-1985)

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