### Title

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### Journal

Obesity, 28(1)



### Authors

Banack, Hailey
Bea, Jennifer
Stokes, Andrew
et al.



### Publication Date

2020

### DOI

10.1002/oby.22662

Peer reviewed

HHS Public Access

Author manuscript

*Obesity (Silver Spring)*. Author manuscript; available in PMC 2021 January 01.

Published in final edited form as:

*Obesity (Silver Spring)*. 2020 January ; 28(1): 171–177. doi:10.1002/oby.22662.

# It's absolutely relative: The effect of age on the body mass index-mortality relationship in postmenopausal women

**Hailey R. Banack**[1], **Jennifer W. Bea**[2], **Andrew Stokes**[3], **Candyce H. Kroenke**[4], **Marcia L. Stefanick**[5], **Shirley A. Beresford**[6], **Chloe E. Bird**[7], **Lorena Garcia**[8], **Robert Wallace**[9], **Robert A. Wild**[10], **Bette Caan**[11], **Jean Wactawski-Wende**[1]

[1]Department of Epidemiology and Environmental Health, School of Public Health and Health Professions, University at Buffalo, The State University of New York

[2]Department of Nutrition Sciences and University of Arizona Cancer Center, University of Arizona

[3]Department of Global Health and Center for Global Health and Development, Boston University School of Public Health

[4]Division of Research, Kaiser Permanente Northern California, Oakland, CA

[5]Division of Cardiovascular Medicine, Department of Medicine, Stanford, University School of Medicine, Stanford, CA, United States.

[6]Department of Epidemiology, School of Public Health, University of Washington, Seattle, Washington.

[7]RAND Corporation, Santa Monica, California.

[8]Department of Public Health Sciences, University of California Davis, Davis, CA, USA.

[9]Department of Epidemiology, College of Public Health, University of Iowa

[10]Department of Obstetrics and Gynecology, University of Oklahoma Health Sciences Center

[11]Division of Research, Kaiser Permanente Northern California, Oakland, CA

## Abstract

**Objective:** The use of relative and absolute effect estimates has important implications for the interpretation of study findings. Likewise, examining additive and multiplicative interaction can lead to differing conclusions about the joint effects of two exposure variables. The aim of this paper is to examine the relationship between BMI and mortality on the relative and absolute scales and investigate interaction between BMI and age.

**Methods:** We used data from 68,132 participants in the Women's Health Initiative (WHI). We estimated the risk ratio and risk difference of BMI on mortality. We also included a product term to examine interaction between BMI and age on the multiplicative scale and calculated the relative excess risk of interaction to measure additive interaction.

**Corresponding Author:** Hailey Banack, Department of Epidemiology and Environmental Health, School of Public Health and Health Professions, University at Buffalo, The State University of New York, 270 Farber Hall, Buffalo, NY 14214-8001, hrbanack@buffalo.edu.

**Conflicts of Interest:** The authors declare no conflict of interest

**Results:** Results demonstrated that the mortality risk ratio decreased as women aged but the mortality risk difference increased as women aged. We found evidence of additive and multiplicative interaction between age and BMI.

**Conclusions:** In postmenopausal women, the relative mortality risk associated with high BMI decreased with increasing age, but the absolute risk of high BMI increased with increasing age. This indicates the importance of considering the interaction between age and BMI to understand mortality risk in older women.

### Keywords

obesity; aging; risk ratio; risk difference; interaction

## Introduction

There is a substantial body of evidence demonstrating that the mortality risk due to obesity changes with aging.(1–7) The consistent change in associations between risk factors and outcomes with aging has long been recognized (2, 8). Understanding the changing association of obesity and mortality with aging is extremely relevant today given the increasing population prevalence of obesity (9) and rapid aging of our population(10). Over time, the proportion of older adults in the population has grown considerably: by 2030, more than 20% of American adults are expected to be over 65 years of age, while only 13% were above 65 years in 2010 and 9.8% in 1970.(10) At the same time, the prevalence of obesity among older adults (>60 years) has risen steadily; recent estimates indicate that 38.5% of men and 43.1% of women are obese in the United States.(9) This is a particular concern for older women as the prevalence of obesity is 3.7% higher for older men but 6.6% higher for older women compared to middle age men and women (40–59 years old)(9).

The effect of obesity on health outcomes in older adults is frequently of interest to researchers, clinician-scientists, and public health practitioners. By definition, the fact that the relationship between BMI and mortality differs across age categories is evidence of interaction between age and BMI. (3) Interaction can be assessed on either the additive or multiplicative scale.(11–13) Several authors have argued that additive interaction is more relevant than statistical or multiplicative interaction to understand disease etiology and for public health purposes.(12, 14–16) VanderWeele and Knol provide several clear examples of why additive interaction is the more relevant public health measure: in the real-world, additive interaction provides direct insight into the number of deaths that can be avoided by treating a high-risk group, but multiplicative interaction does not.(15) A null multiplicative effect between obesity and old age should not be used as evidence that weight management and intervention strategies are less important in older adults.(13, 17)

The aim of this paper is to examine the relationship between BMI and mortality on both the relative (risk ratio) and absolute (risk difference) scale in a large cohort of postmenopausal women. Additionally, we will investigate the presence of additive and multiplicative interaction between BMI and age. Understanding the interaction between BMI and age is important to identify groups at particularly high risk for mortality. Taken together, these

analyses will provide obesity researchers with a comprehensive understanding of age-related differences in the BMI- mortality relationship in older women.

## Methods

We used data from the Women's Health Initiative (WHI) clinical trials in this analysis. The WHI is a large longitudinal study of postmenopausal women across the United States focused on preventing heart disease, cancer, and osteoporotic fractures in older women.(18–20) Recruitment started in 1993 and the trials were all completed by 2005. Outcome ascertainment is still ongoing through the WHI extension studies I and II (2005–2010, 2010–2020). Information about recruitment and eligibility criteria have been published in detail elsewhere.(18) Briefly, postmenopausal women aged 50–79 were recruited to take part in partially overlapping randomized clinical trials: two hormone therapy (HT) trials testing either a combination of estrogen and progestin versus placebo or estrogen alone compared to a placebo, a dietary modification (DM) trial, and a vitamin (calcium and vitamin D; CaD) supplementation trial.(19, 21) Participants of the vitamin supplementation trial were recruited from the participants of the dietary modification trial and/or the HT trials; to be part of the CaD trial participants would have already consented to participate in the DM trial or HT trials at annual visits 1 or 2.(22)

The analytic cohort for this study consists of 68,132 women. In total, there were 27,347 women in the HT trials, 48,836 women in the DM trial, and 36,282 women in the CaD trial.(19, 21) In order to enhance recruitment effort, women were allowed to enroll in more than one clinical trial: for instance, of the participants in the HT trial, 29.4% also participated in the DM and 58.8% were part of the CaD trial.(23) After recruitment and randomization, clinic visits were required annually, and consisted of questionnaires, anthropometric measures, and clinical examinations.(18) The study protocol was reviewed by institutional review boards at each of the 40 WHI clinical centers as well as the WHI coordinating center and each participant provided informed consent.(22)

### Outcome ascertainment

All-cause mortality is the primary outcome of interest in this analysis, with follow-up until June 2017. The WHI coordinating center collects information on vital status through mail, telephone, searches of medical record and death certificates, and the National Death Index.(19, 22)

### Exposure variable and covariates

The exposure variable of interest is body mass index (BMI), an index of weight-for-height calculated as weight in kilograms (kg) divided by the square of height in meters ($m^2$). Height and weight were measured annually at clinic visits by trained examiners using standard procedures. For this analysis, we will categorize participants into standard BMI groups: BMI ≤18.5 kg/$m^2$, 18.5–24.9 kg/$m^2$, 25–29.9 kg/$m^2$, 30–34.9 kg/$m^2$, 35–39.9 kg/$m^2$, and ≥40 kg/$m^2$. Information on relevant confounding variables was collected through questionnaires or in-clinic measurements, and includes information on demographic

characteristics, personal and medical history, lifestyle habits, medication use, and physical measurements.

## Statistical Analysis

To illustrate the crude probability of survival according to baseline BMI category, the first step in this analysis was to create a Kaplan-Meier survival curve. We then estimated the relative and absolute effects of BMI on all-cause mortality, comparing the risk difference and risk ratio of mortality for each BMI category. Finally, we quantified interaction on the additive and multiplicative scales. To examine the influence of age at baseline, we present the main results stratified by baseline age group (50–59, 60–69, and 70–79).

To calculate the crude and multivariate adjusted relative risk (risk ratio) of mortality comparing women with a BMI of 25–29.9kg/$m^2$ to women with BMIs of <18.5., 18.5–24.9, 30–34.9 kg/$m^2$, 35–39.9 kg/$m^2$, and ≥40 kg/$m^2$, we used a generalized linear model with a log link and Poisson distribution.(16) BMI 25–29.9kg/$m^2$ was used as the referent group because it is the group associated with the lowest risk of mortality and less likely to be affected by illness-related weight loss than BMI 18.5–24.9.(24–26)

To calculate the risk difference by BMI category, we used a two-step process that involved obtaining the predicted probabilities from the generalized linear model and then using marginal standardization to obtain average marginal effects.(27) Average marginal effects are an absolute measure of effect, and can be interpreted similar to a risk difference (i.e., the difference in outcome risk comparing each BMI category to the referent group).(27) We adjusted for relevant confounding variables including: trial(s) and trial arm(s), race/ethnicity, education, marital status, health insurance status, self-rated health, smoking status and smoking history, personal hormone therapy use, baseline age, and alcohol use. In addition, in Supplementary Table 1, we present the rate ratio and rate difference results, also estimated from Poisson regression models but with an offset term to account for the log of the number of days of follow-up.

To estimate interaction on the additive and multiplicative scales, we included product interaction terms between BMI categories, as dummy variables, and age as a continuous variable (age per 5 year increase) in a generalized linear model with log link and Poisson distribution. Age was scaled to 5 year increments by dividing continuous age by 5.(12) In this analysis, we first created dummy variables for BMI categories compared to the referent group. We then created product terms by multiplying the BMI dummy variables by age, and included them in a Poisson regression model:

$$\log(E(Y|X,Z)) = \beta_0 + \beta_1 BMI_1 + \beta_2 BMI_2 + \beta_3 BMI_4 + \beta_4 BMI_5 + \beta_5 BMI_6 + \beta_6 Age + \beta_7 BMI_1 xAge + \beta_8 BMI_2 xAge + \beta_9 BMI_4 xAge + \beta_{10} BMI_5 xAge + \beta_{11} BMI_6 xAge + \beta_k Z$$

Where $BMI_1$ represents the dummy variable for BMI<18.5 compared to the referent group, 25–29.9, $BMI_2$ represents the dummy variable for BMI 18.5–24.9 compared to the referent group, $BMI_4$ represents the dummy variable for BMI 30–34.9 compared to the referent group, $BMI_5$ represents the dummy variable for BMI35–39.9 compared to the referent group, and $BMI_6$ represents the dummy variable for BMI>40 compared to the referent

group. We again controlled for all of the aforementioned confounding variables, noted by the vector Z.

The value of the coefficients and 95% confidence intervals from the product terms between BMI category and age ($\beta_7$ to $\beta_{11}$) provide information about multiplicative interaction. In a logistic regression model, or other exponential models, a non-zero value for the coefficient of the product term indicates deviation from exact multiplicativity (i.e., the presence of sub- or super-multiplicative interaction).

To quantify the magnitude of additive interaction, we used the results from the regression model to calculate the relative excess risk of interaction (RERI)(12, 28) for each BMI category:

RERI for BMI $_{<18.5}$ = $\exp(\beta_1 BMI_1 + \beta_6 Age + \beta_7 BMI_1 xAge) - \exp(\beta_1 BMI_1) - \exp(\beta_6 Age) + 1$

RERI for $BMI_{18.5–24.9}$ = $\exp(\beta_2 BMI_2 + \beta_6 Age + \beta_8 BMI_2 xAge) - \exp(\beta_2 BMI_2) - \exp(\beta_6 Age) + 1$

RERI for $BMI_{30–34.9}$ = $\exp(\beta_3 BMI_4 + \beta_6 Age + \beta_9 BMI_4 xAge) - \exp(\beta_3 BMI_4) - \exp(\beta_6 Age) + 1$

RERI for $BMI_{35–39.9}$ = $\exp(\beta_4 BMI_5 + \beta_6 Age + \beta_{10} BMI_5 xAge) - \exp(\beta_4 BMI_5) - \exp(\beta_6 Age) + 1$

RERI for $BMI_{\geq 40}$ = $\exp(\beta_5 BMI_6 + \beta_6 Age + \beta_{11} BMI_6 xAge) - \exp(\beta_5 BMI_6) - \exp(\beta_6 Age) + 1$

An RERI value of 0 indicates the joint effects of age and BMI are exactly additive, meaning the combined effect of BMI and age on mortality is exactly equal to the sum of the individual effects and there is no additive interaction. An RERI value less than 0 indicates sub-additivity, when the combined effect of BMI and mortality are less than the sum of the individual effects on mortality. An RERI value greater than 0 indicates the combined effects of BMI and age are larger than the sum of the individual effects, or super additivity.(28) We estimated 95% confidence intervals for the RERI using bootstrapping.(12)

## Results

Demographic characteristics of the study population (n=68,132) at baseline are presented in Table 1. Over the total WHI study follow-up, 17,785 deaths occurred. At baseline, the average age of study participants was 62.2 years (± 6.9). The majority of women had BMI 25–29.9 kg/m$^2$ at baseline (36%), followed by 18.5–24.9 kg/m$^2$ (27%), 30–34.9 kg/m$^2$ (22%), 35–39.9 kg/m$^2$ (10%), ≥40 kg/m$^2$ (4%), and <18.5 kg/m$^2$ (0.4%). The mean BMI of the study sample was 28.9 kg/m$^2$ (SD=5.9).

Figure 1 depicts a Kaplan Meier (unadjusted) survival curve by baseline BMI. In the early years of follow-up, having very low BMI (<18.5 kg/m$^2$) was associated with the lowest survival probability. However, over the entire study period, having a BMI ≥40 kg/m$^2$ or 35–39.9 kg/m$^2$ was associated with the lowest survival. The cumulative probability of survival

for women with BMI 34–39.9kg/m$^2$ was 0.60 (0.55, 0.63) and 0.57 (0.53, 0.61) for the ≥40 category. The probability of survival was very similar among women who have BMI 25–29.9kg/m$^2$ and 18.5–24.9kg/m$^2$. In Supplementary Figure 1, we present Kaplan Meier survival curves stratified by age group at baseline (50–59, 60–69, and 70–79).

Table 2 contains relative (risk ratio) and absolute (risk difference) estimates and 95% confidence intervals for the effect of BMI category on mortality, stratified by age at baseline. Consistent with previous research, examination of the stratified relative risk results demonstrates that the relative risks of high BMI are attenuated in the oldest group of women (70–79) compared with the youngest group (50–59). In the youngest women, the mortality risk ratios are 1.08 (0.98, 1.18) for BMI 30–34.9kg/m$^2$, 1.38 (1. 24, 1.53) for BMI 35–39.9 kg/m$^2$, and 1.74 (1.54, 1.96) for women with BMI ≥40 kg/m$^2$, whereas in the oldest women, the mortality rate ratios were 1.02 (0.98, 1.07) for BMI 30–34.9kg/m$^2$, 1.08 (1.02, 1.15) for BMI 35–39.9 kg/m$^2$, and 1.18 (1.07, 1.30) for women with BMI greater than 40 kg/m$^2$. These results represent a decrease in the risk ratio of 5.9% in the 30–34.9kg/m$^2$ category, 27.8% in the 34–39.9 category, and 47% in the ≥40 category comparing the oldest (70–79) and youngest women (50–59). Rate ratio results demonstrate a similar trend (presented in Supplemental Table 1).

The risk difference results presented in Table 2 demonstrate differences in the BMI-mortality relationship by baseline age cohort, but in the opposite direction from the rate ratio results. In contrast to the risk ratio results, the mortality risk difference increased in women who were older at baseline. In 50–59 year old women, the risk difference (per 10,000) was 74 (38,111), 212 (159, 264), and 432 (349,515) for women who had BMI of 30–34.9, 35–39.9, or >40kg/m$^2$, compared to the referent group. In 60–69 year old women, the risk difference results for the same categories were 177 (91, 264), 504 (379, 1227), and 1030 (832, 1364), and in 70–79 year old women, the results were 384 (197, 572), 1093 (362, 1226) and 2231(1799, 2663). These results strongly suggest that the absolute risk of mortality increases with increasing age and BMI. Rate difference results are presented in Supplemental Table 1. The difference between relative and absolute effect estimates is illustrated in Figure 2 comparing the risk ratio and risk difference results for the youngest (50–59) and oldest (70–79) year old age groups.

Interaction results are presented in Table 3. The coefficients (95% CI) for the product terms for BMI<18.5, 30–34.9, 35–39.9, and >40kg/m$^2$ per 5 year age increase were −0.09 (−0.24, 0.05), −0.03 (−0.06, 0.003), −0.08 (−0.12, −0.04) and −0.13 (−0.19, −0.08), suggesting negative interaction on the multiplicative scale, also called sub-multiplicative interaction. The relative excess risk of interaction results (RERI) and 95% confidence intervals for the high BMI categories (30–34.9, 35–39.9, and >40kg/m$^2$) strongly indicated the presence of super-additive interaction between age and BMI. The RERI values for each of the high BMI categories per 5 year age increase were 0.26 (0.02, 0.50), 0.99 (0.46, 1.52), and 2.51 (1.17, 3.85). Results for the interaction between BMI 18.5–24.9 and age were qualitatively different than for the other BMI categories, suggesting sub-additive interaction (RERI= −0.02; 95% CI: −0.17, 0.14) and super-multiplicative interaction (β= 0.004; 95% CI: −0.03, 0.03). However, the confidence intervals for both the RERI and interaction term are quite wide, making it difficult to draw a definitive conclusion for this category.

## Discussion

Using prospectively collected data from the WHI clinical trials, we examined the joint effects of BMI and age on mortality in a cohort of postmenopausal women. We compared risk difference and risk ratio results and quantified interaction between age and BMI on the additive and multiplicative scales. We found evidence to support the frequently reported pattern of attenuation of obesity-related mortality risk across age cohorts, but only on the relative scale. The opposite pattern was seen when considering the absolute scale (risk differences); there was a clear increase in the number of excess deaths due to high BMI in older compared to younger women. These conclusions were also supported by the results of the interaction analysis, we found evidence of a sub-multiplicative and super-additive interaction between increasing age and BMI category.

Prior work examining the relationship between BMI and mortality in older adults in the general population and in the WHI has consistently reported that the relative risks associated with high BMI decline with age.(1, 4, 13, 29, 30) For example, in a study of 13,451 male and female participants in the Leisure World Cohort Study (mean age=73.5 years), Corrada and colleagues reported that obese participants only had increased mortality up to age 75. (29) A similar pattern of attenuation has been reported in other studies from the WHI cohort: compared to BMI 18.5–24.9, for women with BMI of 30–34.9, Chen and colleagues reported hazard ratios (HR) of 1.08 (0.95 −1.23) for 50–59 year old women and 0.98 (0.92, 1.06) for women aged 70–79, for women with BMI of 35–39.9 they reported HRs of 1.61 (1.39, 1.87) for 50–59 year olds and 1.11 (1.00, 1.23) for 70–79 year olds, and for women with BMI ≥40, the HRs were 1.82 (1.55, 2.15) for 50–59 year olds and 1.08 (0.92, 1.26) for 70–79 year olds.(31) Using data from a sub-cohort of WHI women, Bea et al. also reported a consistent pattern of age-attenuation in analyses stratified by age group at baseline.(3) These results support previous work on the differing effects of relative and absolute estimates when studying obesity in older men and women (8). Similar to the results presented herein, Stevens and colleagues (1999) demonstrated that the relative age-related mortality risks of obesity (BMI ≥30 kg/m$^2$) decrease while the absolute age-related mortality risk increased. (8)

Relative risks are often reported in the literature because they are familiar to researchers and easily interpreted. However, it is important to keep in mind that relative risks can potentially obscure actual differences in the risk between groups.(2, 8, 32–35). For instance, using an example of a study looking at the relationship between obesity and mortality, reporting a risk ratio (RR) of 2.0 would be interpreted as a two-fold increase in mortality risk in the exposed group (obese) relative to the unexposed group (non-obese).(36) This may appear to be a meaningful increase in mortality risk, but it could result from having exceedingly low risks in both the exposed and unexposed group, such as 0.0002% in the exposed (obese) group and 0.0001% in the unexposed (non-obese) group (RR = $Risk_{exposed}$ /$Risk_{unexposed}$). Reporting an absolute risk difference (RD) of 0.0001% (RD = $Risk_{exposed}$ - $Risk_{unexposed}$) is less likely to be interpreted as a meaningful difference, either clinically or from a population health perspective, but gives a true indication of the low mortality risk due to exposure.(32, 36)

In studies of older adults, the mortality risk difference comparing obese and non-obese may still be the same (or greater) in older individuals compared to younger individuals owing to the increased mortality risk associated with aging.(8, 33) If the risk in the unexposed group increases with time, the same observed risk ratio in different age groups would correspond with a larger change in absolute risk in older individuals than younger individuals.(8, 33, 37) Consider this example of a study exploring the relationship between BMI and heart failure: if the hazard ratio for a 5-unit change in BMI was 1.20 in 40 year old individuals, but 1.10 in 80 year old individuals, it might appear as though the increase in risk associated with a 5-unit change in BMI is 50% greater (20% risk increase vs 10% risk increase) in 40-year olds compared with 80-year olds. However, it is necessary to also consider the risk of the outcome in each group. If the incidence of heart failure is 3 per 100,000 in younger adults (40 year olds) but 19 per 100,000 in older adults (80 year olds), the absolute difference of a 5-unit reduction in BMI would be approximately 3 times greater at age 80 than age 40.(35)

It is important to note that both relative and absolute estimates can be valid measures of effects in cohort studies, choosing one over the other has important implications for the interpretation of study findings.(32, 33) The same is true of additive and multiplicative interaction.(13) The absolute effect estimates directly indicate the excess number of deaths that can be attributed to each BMI category, whereas relative effect estimates can only inform how much more (or less) likely an individual is to experience the outcome, relative to those in the referent group. Since the baseline risks are different in younger and older individuals, the risk ratios are difficult to compare. Similarly, it has long been recognized that additive interaction is more relevant for clinicians, public health practitioners, and policymakers because it highlights the individuals in the population who would benefit most from an intervention.(15, 38) Based on the interpretation of super additive interaction from our results, the number of deaths in aging women who have high BMI values is greater than the number of deaths expected from either high BMI or increasing age independently.(13, 28, 39) Ultimately, whether additive or multiplicative interaction is most relevant depends on the question that the researchers are trying to answer. Some authors have suggested it is good practice to examine both types of interaction in an analysis.(15, 40)

Although there are many articles focused on the relationship between obesity and mortality in older adults, several pertinent questions remain unanswered. We have presented an analysis in a large, well-characterized cohort, but this type of analysis does not answer questions about the effect of specific interventions (e.g., diet, exercise, pharmacotherapy (41)) on mortality risk among older women with high BMI. These are questions best answered in the context of a rigorously conducted randomized controlled trial. We used baseline BMI to simplify the analysis and interpretation for the purpose of demonstrating the differences between relative and absolute effect estimates. Another limitation of this analysis is the use of BMI categories as the primary exposure, as it may not adequately represent body composition in postmenopausal women(42). We considered the BMI-mortality relationship in our analyses, however it would be interesting to examine the interaction between age and other anthropometric indices (e.g., waist circumference, body surface area) in future work. Finally, it is important to note that all of the participants in the WHI are women, which has important implications for the generalizability of our study findings.

## Conclusion

The objective of this manuscript was to investigate the effect of BMI on mortality in postmenopausal women on the relative and absolute scales and examine interaction between aging and BMI on the additive and multiplicative scales. Our results provide an important reminder of the different interpretations of relative and absolute effect estimates and highlight the need for future research exploring obesity in older adults.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements:

We thank Dr. Noel Weiss for his thoughtful comments on an initial version of this analysis.

We also acknowledge the Women's Health Initiative (WHI): Program Office: (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Jacques Rossouw, Shari Ludlam, Joan McGowan, Leslie Ford, and Nancy Geller Clinical Coordinating Center: (Fred Hutchinson Cancer Research Center, Seattle, WA) Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg Investigators and Academic Centers: (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn E. Manson; (MedStar Health Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, CA) Marcia L. Stefanick; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University of Arizona, Tucson/Phoenix, AZ) Cynthia A. Thomson; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende; (University of Florida, Gainesville/Jacksonville, FL) Marian Limacher; (University of Iowa, Iowa City/Davenport, IA) Jennifer Robinson; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker; (University of Nevada, Reno, NV) Robert Brunner Women's Health Initiative Memory Study: (Wake Forest University School of Medicine, Winston-Salem, NC) Mark Espeland.

**Sources of Funding:** The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts HHSN268201600018C, HHSN268201600001C, HHSN268201600002C, HHSN268201600003C, and HHSN268201600004C. HRB is supported by the Banting Postdoctoral Fellowship Program from the Canadian Institutes of Health Research (CIHR)

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### Study Importance Questions

- Using data from a large sample of postmenopausal women in the Women's Health Initiative, in this paper we examine relative (e.g., risk ratio, rate ratio) and absolute (e.g., risk difference, rate difference) effect estimates for the BMI-mortality relationship.
- We report on interaction between age and BMI on mortality risk on both the additive and multiplicative scales. We found evidence of super-additive and sub-multiplicative interaction between age and high BMI. Super-additive interaction implies that the number of deaths due to the combination of obesity and aging is greater than the sum number of deaths that would be due to either exposure independently, whereas sub-multiplicative interaction indicates that the product of the joint effects of obesity in aging is less than the product of the two exposures individually.
- Obesity in older adults is an important topic; as life expectancies continue to rise and given the high population prevalence of obesity, there is a need for clinical, epidemiologic and public health research on effective policies and intervention programs specifically aimed at older adults with high BMI

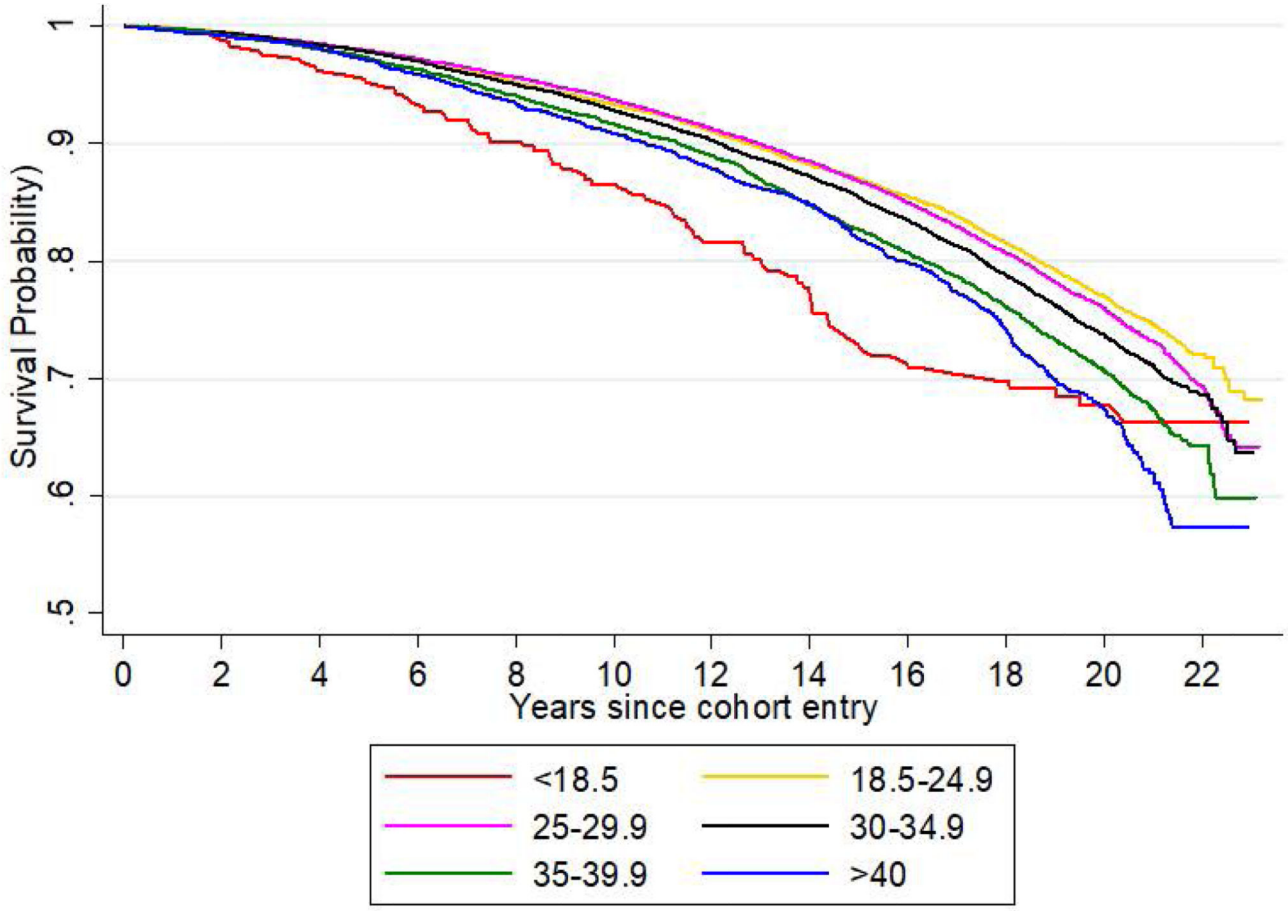


**Figure 1.**
Kaplan Meier survival curve by BMI categories

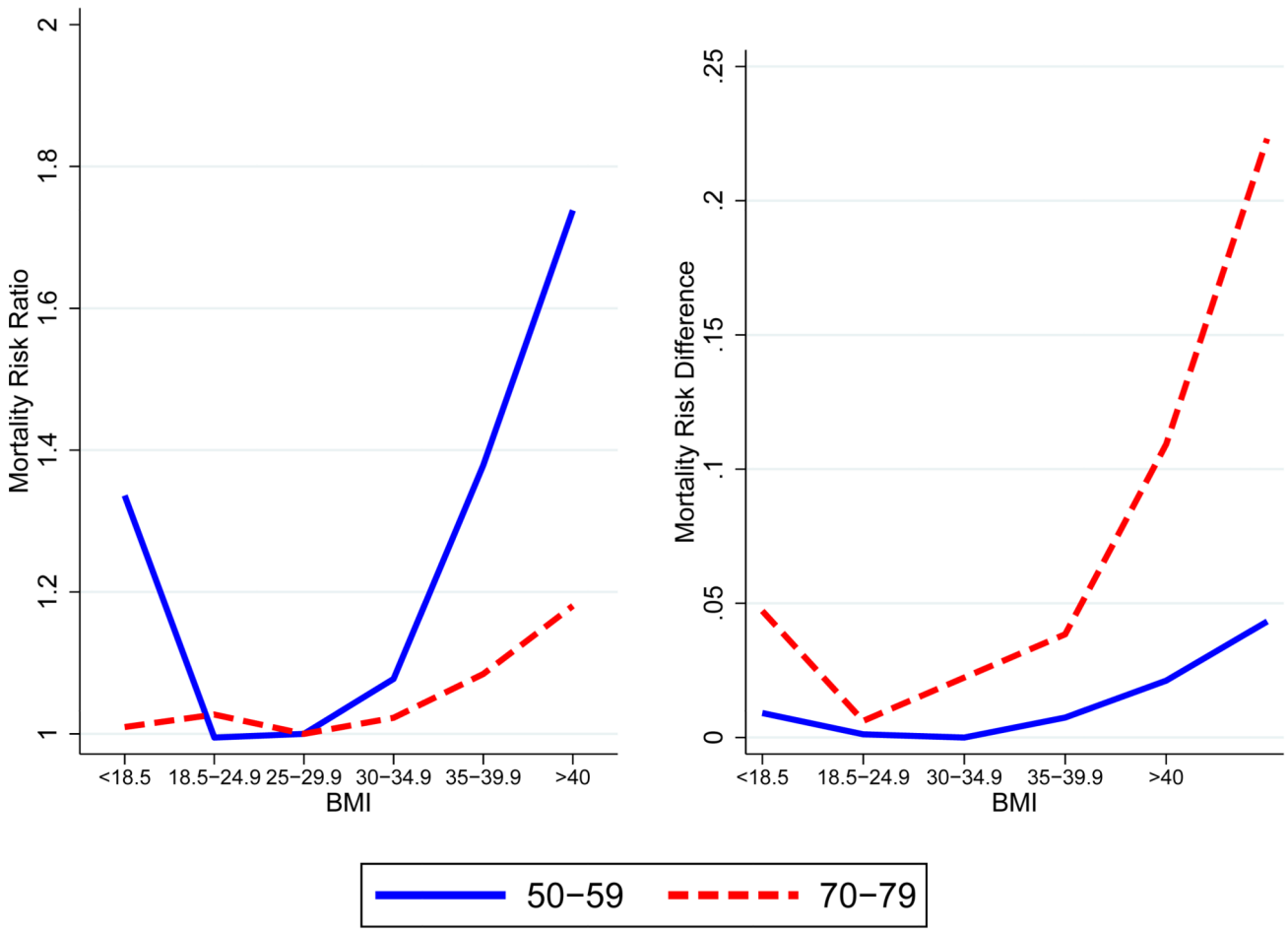


**Figure 2.**

Graphical comparison of risk ratio and risk difference results for the effect of BMI on mortality among women who were 50–59 at baseline and 70–79 at baseline

**Table 1.**

Demographic characteristics of the WHI clinical trial cohort at baseline (n=68132)

| | WHI clinical trial cohort (n=68132) |
|---|---|
| **Age, years (mean ± SD)** | 62.1 ± 7.0 |
| **Age category at baseline (n; (%)** | |
| 50-59 | 27,408 (40.2) |
| 60-69 | 30,193 (44.3) |
| 70-79 | 10,531 (15.5) |
| **Race/ethnicity (n; %)** | |
| Non-Hispanic White | 55,631 (81.7) |
| Non-Hispanic Black | 7,000 (10.3) |
| Hispanic | 2,876 (4.2) |
| Other | 2,601 (3.8) |
| **Education (n; %)** | |
| Some high school | 3,795 (5.6) |
| High school diploma or GED | 12,502 (18.5) |
| Post-secondary school | 33,871 (50.0) |
| Post-graduate school | 17,515 (25.9) |
| **Smoking status (n; %)** | |
| Current smoker | 5,352 (7.9) |
| Former smoker | 27, 596 (41.0) |
| Never smoker | 34, 409 (51.1) |
| **Marital status (n; %)** | |
| Married | 41,340 (60.9) |
| Widowed | 11,588 (17.1) |
| Divorced | 11,076 (16.3) |
| **Has health insurance (n; %)** | 63,320 (93.8) |
| **Employed (n; %)** | 23,822 (39.4) |
| **History of CVD (%)** | 12,959 (19.0) |
| **BMI categories (kg/m$^2$; n; %)** | |
| <18.5 | 294 (0.43) |
| 18.5-24.9 | 18,333 (26.9) |
| 25-29.9 | 24,310 (35.7) |
| 30-34.9 | 15,240 (22.3) |
| 35-39.9 | 6,757 (9.9) |
| >40 | 3,171 (4.7) |

| | WHI clinical trial cohort (n=68132) |
|---|---|
| **Body mass index (mean ± SD)** | 28.9 ± 5.9 |
| **Years since menopause (mean ± SD)** | 14.4 ± 9.0 |

**Table 2.**

Comparison of relative (risk ratio) and absolute (risk difference) estimates from multivariate adjusted models stratified by baseline age cohort (50–59, 60–69, 70–79)

| | Mortality Risk Ratio (95% CI) | Mortality Risk Difference (95% CI) per 10,0000 |
|---|---|---|
| **Age 50–59** | | |
| **<18.5 kg/m$^2$** | 1.34 (0.86, 2.08) | 91 (−78, 261) |
| **18.5–24.9 kg/m$^2$** | 0.99 (0.91, 1.09) | 12 (−22, 46) |
| **25–29.9 kg/m$^2$** | -ref- | -ref- |
| **30–34.9 kg/m$^2$** | 1.08 (0.98, 1.18) | 74 (38,111) |
| **35–39.9 kg/m$^2$** | 1.38 (1.24, 1.53) | 212 (159, 264) |
| **>40 kg/m$^2$** | 1.74 (1.54, 1.96) | 432 (349, 515) |
| **Age 60–69** | | |
| **<18.5 kg/m$^2$** | 1.13 (0.91, 1.40) | 218 (−187, 622) |
| **18.5–24.9 kg/m$^2$** | 1.01 (0.96, 1.05) | 29 (−52, 109) |
| **25–29.9 kg/m$^2$** | -ref- | -ref- |
| **30–34.9 kg/m$^2$** | 1.09 (1.04, 1.15) | 177 (91, 264) |
| **35–39.9 kg/m$^2$** | 1.18 (1.11, 1.25) | 504 (379, 1227) |
| **>40 kg/m$^2$** | 1.29 (1.19, 1.40) | 1030 (832, 1364) |
| **Age 70–79** | | |
| **<18.5 kg/m$^2$** | 1.01 (0.84, 1.21) | 471 (−404, 1347) |
| **18.5–24.9 kg/m$^2$** | 1.03 (0.99, 1.07) | 62 (−112, 236) |
| **25–29.9 kg/m$^2$** | -ref- | -ref- |
| **30–34.9 kg/m$^2$** | 1.02 (0.98, 1.07) | 384 (197, 572) |
| **35–39.9 kg/m$^2$** | 1.08 (1.02, 1.15) | 1093 (362, 1226) |
| **>40 kg/m$^2$** | 1.18 (1.07, 1.30) | 2231 (1799, 2663) |

**Table 3.**

Interaction results on the additive and multiplicative scale for the effect of BMI category on mortality per 5 year age increase

| | Relative Excess Risk of Interaction (95% CI) | Additive Interaction | Interaction (β) Coefficient | Multiplicative Interaction |
|---|---|---|---|---|
| **Per 5-year age increase** | | | | |
| **<18.5 kg/m$^2$** | 1.15 (−1.37, 3.67) | Super-additive | −0.09 (−0.24, 0.05) | Sub-multiplicative |
| **18.5–24.9 kg/m$^2$** | −0.02 (−0.17, 0.14) | Sub-additive | 0.004 (−0.03, 0.03) | Super-multiplicative |
| **25–29.9 kg/m$^2$** | --- | -- | -- | -- |
| **30–34.9 kg/m$^2$** | 0.26 (0.02, 0.50) | Super-additive | −0.03 (−0.06, 0.003) | Sub-multiplicative |
| **35–39.9 kg/m$^2$** | 0.99 (0.46, 1.52) | Super-additive | −0.08 (−0.12, −0.04) | Sub-multiplicative |
| **>40 kg/m$^2$** | 2.51 (1.17, 3.85) | Super-additive | −0.13 (−0.19, −0.08) | Sub-multiplicative |