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Anatomy of the Mediterranean Diet and Mortality among Older Women with Frailty

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Abstract

We examined individual components of the Mediterranean Diet (Med) and evaluated their relative contribution to mortality rates in older women with frailty. A sample (N=10,431) included Women's Health Initiative Observational Study participants aged 65-84 years with complete frailty diagnostic criteria and dietary data. Frailty was assessed with modified Fried's criteria and dietary data were collected by food frequency questionnaire. Over a mean follow-up of 12.4 years (range 3-21.0), 3,259 (31.2%) deaths occurred. Crude death rates demonstrated a decrease in mortality with higher intake of individual Med components. However, in the mutually adjusted models the majority of the Med components on their own were not significantly associated with mortality. Exceptions were vegetables, nuts and whole grains. A higher intake of vegetables, nuts and whole grains were associated with a significantly decreased hazard of mortality, by 8% ($p=0.04$), 13% ($p<0.001$) and 16% ($p<0.001$) respectively. The relative contribution of these components to diet mortality associations were 21%, 42% and 57% for vegetables, nuts and whole grains respectively. Subgroup analyses by chronic morbidity or smoking status or excluding women with early death did not substantially change these results.

Keywords

nutrition; dietary pattern; longitudinal; Women's Health Initiative; population

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INTRODUCTION

Current demographic trends indicate substantive growth in the older population; and women will continue to account for the majority of this changing demographic (1). Frailty, which is common in aging, is both a serious and potentially modifiable geriatric syndrome comprised of three of the following five characteristics: weight loss, slowness, weakness, inactivity and fatigue (2). Older persons with frailty are susceptible to adverse health outcomes including increased risk of death (3,4). A need to address the unfolding frailty epidemic led to efforts to elucidate factors that reduce risks of frailty and improve outcomes in frail individuals. Nutritional intakes are especially pertinent in that regard because they are modifiable and have been implicated in a transition to frailty and in its progression (5,6). Our previous work suggested independent and inverse association between overall adherence to healthy dietary patterns, and in particular Med and overall mortality in older women with frailty (7). Although these findings echoed compiling evidence that Med is beneficial in reducing the risk of morbidity and mortality (8,9), questions still exist about the relative importance of the individual components that comprise the Med that might account for this reduction in health risks. In the current study, we specifically evaluated the contribution of the nine widely accepted components of the Med (fruits, vegetables, nuts, legumes, whole grains, fish, red and processed meat, ratio of monounsaturated to saturated fats, and alcohol) in the diet mortality association in population-based cohort of older Women's Health Initiative (WHI) participants with frailty.

SUBJECTS AND METHODS

Analytic Sample

The WHI Observational Study (WHI OS) enrolled 93,676 women 50 to 79 years of age at baseline between 1993 and 1998 at 40 U.S. clinical centers. At baseline and then at the first follow-up clinic visit, which occurred three years after baseline (1996-2001), OS participants completed questionnaires on medical and psychosocial characteristics and provided weight and height measures. Since the sample used here was limited to those characterized as frail, the first follow-up visit was required to define the weight-loss component of the frailty phenotype. Thus, the eligible sample was participants 65 years old with a year 3 clinic visit (n=55,654). Participants with missing data on at least one of the frailty criteria (n=12,464) were further excluded. The analytical sample was further limited to 11,070 participants who screened positively for three or more of frailty scores (thoroughly defined below). Of these, a total of 623 women with extreme energy intake (i.e., <600 kcal/d or >5000 kcal/d) were excluded because these reports were judged to be implausible; 16 women with end-of-follow-up date that preceded frailty assessment also were excluded. The final analytical sample included data from 10,431 older, frail WHI OS study participants (Supplemental Figure 1) as in the previous study (7).

Frailty criteria

Frailty was operationally defined congruent with Fried's definition (3), as including the presence of three or more of the following five criteria: muscle weakness, slow walking speed, exhaustion, low physical activity, and unintentional weight loss (shrinking). For each

criterion, one or two points were assigned if the participant's assessment was below a criterion-specific cut-point (Supplemental Table 1). In the WHI RAND-36 Physical Function Scale scores below 75 indicated slowness and weakness (2 points); RAND-36 Vitality Scale scores below 55 indicated exhaustion (1 point); the lowest quartile on the WHI physical-activity questionnaire indicated low physical activity (1 point); and unintentional weight loss of more than 5% over 3 years indicated shrinking (1 point). Points were summed to provide a score ranging from zero to five. A score of three or more was used to characterize a woman as frail. This approach was adapted and validated in the WHI (10).

Biomarker-calibrated dietary energy and protein intake

Diet was measured at enrollment and at the year 3 visit among OS participants using a self-administered semi-quantitative food frequency questionnaire (FFQ) developed for and validated specifically in the WHI (11). The three sections of the WHI-FFQ included 122 composite and single-food line items asking about frequency of consumption and portion size, 19 adjustment questions related to type of fat intake, and four summary questions asking about the usual intake of fruits and vegetables and added fats for comparison with information gathered from the line items.

Calibrated energy intake estimates were calculated using previously published methods (7). Briefly, calibration equations were developed for the current study using linear regression models that used doubly labeled water (12) study to predict log-transformed calibrated intake of energy based on the log-transformed self-reported intake along with covariates related to characteristics of the study participants: body mass index (BMI), age, race-ethnicity, income, education, smoking and physical activity as metabolic equivalents (METs) per week.

Assessment of Mediterranean Diet

The alternative Mediterranean Diet (aMed) Index (13,14) was used to assess adherence to a Mediterranean dietary pattern according to consumptions of the following components: (1) fruit, (2) vegetables, (3) nuts, (4) legumes, (5) whole grains, (6) fish, (7) ratio of monounsaturated to saturated fat, (8) red and processed meats, and (9) alcohol. Participants whose intake was above the study sample median for fruits, vegetables, nuts, legumes, whole grains, fish, or ratio of monounsaturated to saturated fat received 1 point for each category. Consumption of red and processed meat below the median was awarded 1 point, and alcohol intake between 5 and 15 g/d was awarded 1 point; otherwise, women received 0 points. The total aMed index score was a tally of the components that took values from 0 (minimal adherence to the diet) to 9 (maximal adherence to the diet)

All-cause mortality

Medical updates were collected annually by mail. Participants' deaths were adjudicated by study physicians using hospital records, autopsy or coroner reports, and/or death certificates. Periodic checks of the National Death Index (NDI) for all participants, including those lost to follow-up, were performed. At the time of this analysis, the latest WHI data on mortality was available through December 2015.

Covariates

Baseline data on demographic and health variables, including age, race/ethnicity, family income, highest level of education completed, smoking status and history of common diseases related to body weight and mortality, such as cancer (excluding non-melanoma skin cancer), diabetes, emphysema, and cardiovascular disease (CVD) were obtained by self-report. Previous study have indicated smoking and the above-mentioned preexisting conditions confound the relationship between Med and mortality (9) and were found to be associated with prevalent and incident frailty (4). At the year-3 follow-up visit, trained staff performed anthropometric measurements in the clinic. Weight to the nearest 0.1 kilogram (kg) and height to the nearest 0.1 centimeter (cm) were measured and used to compute BMI (kg/m^2). Physical activity was also assessed at this visit by self-report of frequency and duration of walking and mild, moderate, and strenuous activities, with total expenditure of energy calculated in METs (15).

Statistical approach

First, chi-square and Wilcoxon-Mann-Whitney test for non- normally distributed variables, were used to evaluate proportion and median differences by all-cause mortality. Second, crude rates of mortality per 1000 person-years were calculated to express the number of deaths for each the aMed index component using median split for all but alcohol variables. Cox proportional hazard models were then used to estimate the association of separate aMed index components on the all-cause mortality rate while mutually adjusting for the other components in the aMed index and sequentially for other covariates. Specifically, using a staged approach models were first adjusted for age, total calibrated energy intake, and aMed index components (model 1) and then for race/ethnicity, income, education, BMI, physical activity, smoking and frailty score (model 2). The time-to-event was defined as number of years from the WHI year-3 follow-up visit to death from any cause, with censoring at the last known contact or the date of last available NDI search, whichever occurred later. Since the relationship of diet and mortality might be distorted by reverse causality of worse nutritional status due to prodromal disease symptoms and inadequate adjustment for the effects of smoking and chronic morbidity, regression models that stratified by the presence or absence of chronic conditions that included cancer, emphysema, CVD and diabetes and by smoking status also were performed. A sensitivity analysis that excluded women who died within three years after the year-3 follow-up period also was completed.

The relative importance of each of the aMed index component was modeled as follow. First the association of a one unit increase in aMed index score with mortality was modeled using fully adjusted Cox regressions. Then, component specific modified aMed indexes were created by subtracting alternately one component at a time from the original index (thus reducing the 9-point score to eight-point score). Next, Cox models were used to estimate the nine mortality ratios associated with a one unit increase in the aMed index minus fruits, aMed index minus vegetables, aMed index minus whole grains, aMed index minus nuts, aMed index minus legumes, aMed index minus fish, aMed index minus red and processed meat, aMed index minus ratio of monounsaturated to saturated fats, and aMed index minus alcohol, similarly to the method described in details in Trichopoulou et al., (16) paper. To preserve comparability, the logarithm of the estimated nine mortality ratios was multiplied

by 8/9 before exponentiation. Lastly, two components in descending order of their importance (as assessed from the models in which these components were individually subtracted from the aMed index) were jointly removed to evaluate their synergetic impact on mortality ratios. Comparability with the original model was preserved by multiplying log coefficients by 7/9 before exponentiation. In addition to other adjustment variables alternate subtraction models were also adjusted for the corresponding subtracted aMed index component. Schoenfeld residuals were used to test proportionality. Statistical analyses were completed using Stata version 14.

RESULTS

Among the 10,431 WHI OS frail older women, 31.2% ($n = 3,259$) died over a mean follow-up of 12.4 years (range 3.0–21.0). The mean (SD) age at death was 81.8 (6.2) years, whereas the mean (SD) age at this study baseline was 73.7 (4.5) years. At the Year 3 clinical visit, women who died were older, were more likely to smoke, had lower BMI and higher frailty score ($p < 0.001$ for all [Table 1]).

Furthermore, frail participants with a subsequent death had lower total calibrated energy intake ($P < 0.001$). Differences in aMed components were observed for fruits, nuts, whole grains, and ratio of monounsaturated to saturated fats ($P < 0.01$, for all).

In general, crude death rates, expressed in number of deaths per 1000 person-years, demonstrated a decrease in mortality with above median intake of all aMed index components, but fruits, legumes and red and processed meat (Table 2). However, in the mutually adjusted models the majority of the aMed index components on their own were not significantly associated with mortality. Exceptions were vegetables, nuts and whole grains (Models 1 and 2, Table 2). A higher intake of vegetables, nuts and whole grains were associated with a significantly decreased hazard of mortality, by 8% ($p = 0.04$), 13% ($p < 0.001$) and 16% ($p < 0.001$), respectively. Noteworthy, a borderline and direct association with increased mortality rates was also observed for legumes ($p = 0.06$).

The associations between higher vegetables, nuts and whole grains consumption and mortality rates were sustained in a subgroup of women with no early death (defined as death within 3 years after the year-3 follow-up visit [Figure 1]). Similarly, these associations were preserved in women with and without chronic morbidity and in ever smokers.

Table 3 shows the mortality ratio associated with a one unit increment in the aMed index score, as well as how this ratio changes with alternate exclusion of each of the nine components from the index. The table also shows the percentage change in the apparent effect of the aMed index score with the alternate subtraction of its individual components. For example, when whole grains are excluded from the aMed index, the mortality ratio, properly adjusted for the change from a 9 point to eight-point score, changes from 0.964 to 0.984— that is, the beneficial effect of the aMed index is reduced from $1 - 0.964 = 0.036$ to $1 - 0.984 = 0.016$ or by 56.6%. Similarly, removal of nuts from the aMed index yielded 42% reduction in beneficial effects of the diet, whereas removal of legumes resulted in almost

30% increase in benefits of the diet. Successful removal of both the whole grain and nuts components from the aMed index yielded mortality ratio around the null value of 1.

DISCUSSION

In the current study, we examined components of the aMed index to evaluate their relative importance and independent association with mortality in older women with frailty. Our results show that over an average 12.4 years of follow-up, controlling for the effect of the other components, significant inverse associations with mortality were observed for vegetables, nuts and whole grain components. These associations were sustained after adjustment for many potential confounders, importantly including estimates for total calibrated energy intake that is not routinely available in nutrition studies. Furthermore, stratifying by chronic morbidity, smoking status, or excluding women with early death did not substantially change our results, further reinforcing the validity of the findings. Alternate subtraction of each of dietary component from the total aMed index score also showed relative importance of higher consumption of vegetables, nuts and whole grains that contributed 21%, 42% and 57% to the benefits of the diet. Interestingly, these models indicated that low consumption of legumes might have favourable effect on mortality ratio estimates.

Med has been defined as “primarily a plant-based diet characterized by a high ratio of monounsaturated to saturated fatty acids, with total fat accounting for 30-40% of daily energy consumption” (17). More specifically, Med is characterized by a high intake of olive oil as the main source of added fat, vegetables, fruits and nuts, legumes, whole grains, fish and seafood; a low intake of dairy products, meat and meat products; and a moderate alcohol intake. The Med has been proven to confer health benefits in older populations with chronic disease and conditions (7,13,14). Likewise, selected studies provided insights into components within the Med that were associated with lower mortality (18), but these were mainly in younger and non-frail populations.

Consumption of vegetables has been associated with reduced risk of all-cause and CVD mortality (19). Vegetables may exert beneficial effect through the high content of vitamins and polyphenols (20). Indeed, in the Prevention with Mediterranean diet trial, total urinary polyphenol excretion, as a surrogate of vegetable intake, was associated with decreased inflammatory biomarkers and improved CVD risk factors (21). Another mechanism to explain the protective role of vegetables may be the vegetable-derived nitrate intake, which improves markers of vascular health via formation of nitric oxide and other bioactive nitrogen oxides. Indeed, among elderly women higher vegetable nitrate intake was independently associated with a lower risk of an ischemic cerebrovascular disease (22). Given preponderance of cardiovascular morbidity and mortality in persons with frailty, it is plausible that cardioprotection might confer health benefits in this at-risk population.

The mechanisms through which whole grains intake is beneficial for health are diverse. In general, whole grains are richer than their refined counterparts in fibers and in several phytochemicals (23). Whole grains also beneficially influence gut microbiota composition (24). Additionally, there is evidence that whole grains consumption increases the levels of

bacteria that produce short-chain fatty acids such as butyrate and propionate from fermentation of carbohydrates (25). Butyrate and propionate are metabolites with anti-inflammatory properties and insulin sensitizing effects (26). Inflammatory and insulin pathways are highly disrupted in older adults and even to a greater extent in those with frailty suggesting role in its pathophysiology and progression (2). In addition, whole grains have higher content of many phytochemicals that are lost or markedly reduced after refining. One phytochemical is betaine that is contained in wheat, rye and quinoa which is instrumental in protein synthesis (27). Nuts are rich in unsaturated fatty acids, fiber, vitamins and antioxidants (28), and have been demonstrated to improve endothelial markers involved in blood pressure control (29). Among women in the Nurses' Health Study and men in the Health Professionals Follow-up Study, nut consumption was inversely associated with total mortality, and inverse associations were observed between nut consumption and deaths due to cancer, CVD, and respiratory disease (30). This protective association has been replicated in other cohorts indicating consistency across different ethnic and mixed age groups (18). Pending further research, one cautious interpretation is that in person with frailty, in concert with other populations, nuts might confer vascular benefits.

Borderline direct association between legume consumption and mortality rates does not have clear explanation and need to be viewed in light of a low legume intake observed in this population. Legumes are a rich source of protein, dietary fiber and have low glycemic index (GI(31)). Low GI foods provide a slower release of glucose into the blood and thus, decrease after meal peaks in blood glucose levels. One speculative explanation that ought to be tested in future studies is that the nutrients in beans, peas, and lentils coupled with low glycemic index may slow the rate of digestion of the starch and absorption of glucose. Given that persons with frailty have disrupted glucose regulation (32) and have low energy reserves, availability of energy metabolites might be important in this population.

We acknowledge that our study has limitations. First, measurement bias may have occurred since reported dietary intake and aMed index relied on FFQ data; however, measurement error was minimized by using calibrated energy estimates. Furthermore, we had no measurement of change in diet over the course of the study period. However, due to the prospective nature of this study, any information bias is non-differential. Second, given a preponderance of White female participants in our study sample, our results may not be widely generalizable. Lastly, a greater intake of nuts, whole grains and vegetables may be a marker for a generally healthier lifestyle. We have therefore adjusted for other major nutritional variables including other Med components as well as lifestyle parameters, but as with any observational study, unmeasured and residual confounding cannot be ruled out.

In conclusion, our results emphasized that the dominant components of the aMed index as a predictor of lower mortality are higher consumption of whole grains, nuts and vegetables. These findings might also be relevant to other frail populations that are prone to nutritional deficits due to poor appetite accompanied by lower consumption of healthy foods. Although our study is prospective and allows temporal inference, clinical trials addressing causal relationship and implementation of nutritional recommendations are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TAKE AWAY POINTS

- The dominant components of the Mediterranean Diet as a predictor of lower mortality in older women with frailty are higher consumption of whole grains, nuts and vegetables
- A higher consumption of whole grains, nuts and vegetables are important for older women with frailty regardless of their concurrent morbidity and life style factors
- Among Mediterranean Diet components whole grains has the strongest indirect association with mortality outcomes

Figure 1:

Basic and subgroup analyses for Hazard Ratios for all-cause mortality according to alternative Mediterranean diet (aMed) index components in the frail and older Women's Health Initiative Observational Study participants (n=10,431). Chronic disease include cancer, emphysema, cardiovascular disease, diabetes. Early mortality is defined as death within 3 years of this study follow up. Basic and subgroup models are adjusted for age, calibrated dietary energy intake, calibrated protein intake, race/ethnicity, income, education,

body mass index, physical activity, smoking, and frailty score. Never and ever smokers models are not adjusted for smoking.
95% CIs for calibrated HRs are based on log-estimated HR $\pm$ 1.96 bootstrap SE (1000 bootstrapped samples)

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Table 1.

Baseline and Year 3 characteristics of the 10431 Women's Health Initiative Observational Study frail older women by mortality

Characteristics	Died (n = 3,259)	Censored (n = 7,172)	P value
Baseline measures			
White, n (%)	2,946 (90.76)	6,062 (84.78)	<0.0001
Black, n (%)	181 (5.58)	587 (8.21)	<0.0001
Hispanic, n (%)	52 (1.60)	184 (2.57)	0.002
Other race, n (%)	67 (2.06)	317 (4.43)	<0.001
Income, n (%)			0.416
\$20000	807 (32.58)	1,666 (31.43)	
\$20000–\$35000	941 (37.99)	1,977 (37.29)	
\$50000–\$75000	422 (17.04)	968 (18.26)	
>\$75000	307 (12.39)	690 (13.02)	
Education, n (%)			<0.001
High school or less	208 (9.18)	561 (12.04)	
College	2,059 (90.82)	4,100 (87.96)	
Cardiovascular disease, n (%)	1,233 (38.71)	2,003 (28.65)	<0.001
Treated diabetes, n (%)	342 (10.50)	415 (5.79)	<0.001
Cancer, n (%)	652 (20.19)	1,110 (15.60)	<0.001
Emphysema, n (%)	341 (10.66)	440 (6.26)	<0.001
Year 3 measures			
Age, yr (SD)	73.74 (4.53)	71.97 (4.47)	<0.001
BMI, kg/m ² (SD)	29.02 (6.81)	29.53 (6.28)	0.002
Smoker, n (%)	214 (6.62)	298 (4.18)	<0.001
Physical activity, MET (SD)	5.48 (8.85)	5.83 (9.08)	0.07
Frailty score, n (%)			<0.001
3	1,743 (53.48)	4,367 (60.89)	
4	1,276 (39.15)	2,551 (35.57)	
5	240 (7.36)	254 (3.54)	
Total calibrated energy intake, kcal/d (SD)	1945.82 (177.62)	1979.28 (171.60)	<0.001
Total calibrated protein intake, g/d (SD)	66.64 (10.34)	68.80 (10.41)	<0.001
Fruits, cup/d ^a (IQR)	1.41 (1.37)	1.32 (1.32)	0.002
Vegetables, cup/d ^a (IQR)	0.94 (0.80)	0.95 (0.78)	0.49
Nuts, oz/d ^a (IQR)	0.40 (0.62)	0.43 (0.62)	0.01
Legumes, oz/d ^a (IQR)	0.21 (0.35)	0.21 (0.35)	0.37
Whole grains, oz/d ^a (IQR)	0.84 (0.95)	0.89 (1.00)	0.009
Fish, oz/d ^a (IQR)	0.42 (0.54)	0.44 (0.56)	0.41
Red and processed meats, oz/d ^a (IQR)	1.53 (1.76)	1.55 (1.75)	0.22

Characteristics	Died (<i>n</i> = 3,259)	Censored (<i>n</i> = 7,172)	<i>P</i> value
Monounsaturated to saturated fat, ratio ^a (IQR)	1.13 (0.30)	1.15 (0.30)	<0.001
Alcohol, g/d ^a (IQR)	0.06 (2.38)	0.06 (2.10)	0.35

^aMedian value; med = Median; IQR = Interquartile range

Table 2.

Hazard ratios for all-cause mortality per adherence to alternative Mediterranean Diet (aMed) index components

	Crude rate per 1000 persons years	Model 1 ^a		Model 2 ^b	
		HR (95% CI)	P value	HR (95% CI)	P value
Fruits					
< Median	24.62	Ref		Ref	
Median	25.93	1.01 (0.93-1.09)	0.82	1.04 (0.96-1.13)	0.32
Vegetables					
< Median	25.81	Ref		Ref	
Median	24.52	0.91 (0.84-0.98)	0.02	0.91 (0.84-0.99)	0.02
Nuts					
< Median	26.79	Ref		Ref	
Median	23.54	0.88 (0.82-0.95)	<0.001	0.87 (0.80-0.94)	<0.001
Whole grains					
< Median	26.61	Ref		Ref	
Median	23.82	0.85 (0.79-0.91)	<0.001	0.83 (0.77-0.90)	<0.001
Red and processed meat					
< Median	24.64	0.97 (0.90-1.05)	0.47	1.03 (0.95-1.11)	0.46
Median	26.00	Ref		Ref	
Fish					
< Median	26.11	Ref		Ref	
Median	24.19	0.98 (0.91-1.06)	0.62	1.01 (0.93-1.09)	0.83
Legumes					
< Median	25.01	Ref		Ref	
Median	25.50	1.09 (1.01-1.18)	0.02	1.08 (0.99-1.16)	0.06
Monounsaturated to saturated fats					
< Median	26.43	Ref		Ref	
Median	23.98	0.96 (0.89-1.03)	0.24	0.98 (0.91-1.06)	0.61
Alcohol					
Low/High ^c	25.37	Ref		Ref	
Moderate ^d	24.24	0.91 (0.81-1.02)	0.91	0.94 (0.83-1.05)	0.25

^a adjusted for age, total calibrated energy intake and Mediterranean diet components

^b adjusted for Model 1 + race/ethnicity, income, education, body mass index, physical activity, smoking, frailty score

^c Intake below 5 or more than 15 g/d

^d Intake between 5 and 15 g/d

Hazard ratios (HRs) for all-cause mortality according to alternative Mediterranean diet (aMed) index and after alternate subtraction of its components^a

Table 3.

Dietary variable	HR ^b (95% CI)	P value	Change in apparent effect (%) ^c
aMed overall	0.964 (0.943-0.985)	0.001	0
aMed minus fruits	0.958 (0.937-0.979)	<0.001	-15.0
aMed minus vegetables	0.971 (0.949-0.993)	0.011	-20.9
aMed minus nuts	0.979 (0.958-1.000)	0.05	-42.0
aMed minus legumes	0.953 (0.933-0.975)	<0.001	28.1
aMed minus whole grains	0.984 (0.963-1.01)	0.146	-56.6
aMed minus fish	0.962 (0.942-0.983)	<0.001	3.3
aMed minus red and processed meat	0.962 (0.943-0.982)	0.001	3.9
aMed minus monounsaturated to saturated fat ratio	0.968 (0.948-0.989)	0.006	-12.5
aMed minus alcohol	0.968 (0.949-0.987)	0.003	-13.1
aMed minus whole grains and nuts ^d	1.001 (0.981-1.021)	0.917	-103.0

^aOriginally estimated logarithms of mortality ratios were multiplied by 8/9 and then exponentiated to correct for eight point scale

^bAdjusted for age, total calibrated energy intake, race/ethnicity, income, education, body mass index, physical activity, smoking, frailty score, and corresponding subtracted component

^cEstimated from original numbers

^dOriginally estimated logarithms of mortality ratios were multiplied by 7/9 and then exponentiated to correct for seven-point scale