Socioeconomic Disparities in Health: The Role of Diet Cost

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Abstract

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Numerous studies have linked diet quality to all-cause mortality. Diet cost has been implicated as an important determinant of diet quality and has been linked to many of the dietary patterns and scores related to adverse health outcomes, such as weight gain, type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD) and all-cause mortality. However, few prospective studies have evaluated whether diet cost is associated with these adverse health outcomes. Therefore, this body of work sought to elucidate the relationship between diet cost and adverse health outcomes, while also examining the extent to which diet cost explains the association between socioeconomic status (SES) and health.

To address these aims, we used data on post-menopausal women (ages 49-64 years) included in the Women's Health Initiative (WHI). Participants' daily diet cost was estimated by linking a national food price database developed by the United States Department of Agriculture was linked to the participants' food frequency questionnaire. The four outcomes of this study were weight gain, T2DM, CVD and all-cause mortality. Adjusted linear regression models were used to evaluate the association between diet cost and weight change, whereas Cox proportional hazards regression models were used to evaluate the association between diet cost and T2DM, CVD and all-cause mortality. To evaluate the extent by which diet cost explained the

socioeconomic (income/education) gradient in outcomes, we evaluated the percent difference in the diet-cost adjusted income/education coefficients to the coefficients from models without the diet cost term.

The association between diet cost and diet cost was evaluated in 10,807 women from the control arm of the Dietary Modification (DM-C) trial. For weight change, a 50% increase in diet costs was associated with excess weight gain of 0.33 kg (95% CI 0.06, 0.59) over up-to seven years of follow-up, though the association was modified by weight change prior to baseline. Among women who previously gained weight or were weight stable there was no significant association between diet cost and weight change. For women who previously lost weight, a 50% increase in diet cost was associated with excess weight gain of 0.87 kg (95% CI 0.34, 1.40). Given the unexpected direction of the association between diet cost and weight change subsequent SES-mediation analyses were not conducted.

Over eight years of follow-up 2,174 new cases of T2DM were observed among 47,683 women from the DM-C and Observational Study (OS). A 50% increase in diet costs was associated with a 14% reduced risk of T2DM (hazard ratio [HR] 0.86; 95% CI 0.78, 0.94). In regression calibration models that incorporated estimated diet costs from the 4DFR, a 50% increase in diet cost was associated with a 22% reduced risk of diabetes (HR 0.78; 95% CI 0.67, 0.90). A strong social gradient in diabetes risk was observed for both education and income, with individuals of lower SES having an elevated risk of being diagnosed with T2DM. In mediation analyses, diet costs explained 15-19% ($p<0.05$ for all mediation analyses) of the association between income/education and T2DM.

With eight years of follow-up 1,208 cardiovascular events were observed among 42,632 women from the DM-C and OS. A 50% increase in diet costs was associated with a 19% reduced risk of CVD (HR 0.81; 95% CI 0.72, 0.92). In regression calibration models, a 50% increase in energy-

adjusted diet costs was associated with a 28% reduced risk of CVD (HR 0.72; 95% CI 0.58, 0.88). A strong social gradient in CVD risk was observed for both education and income, whereby individuals of lower SES experienced an elevated risk of CVD. In mediation analyses, diet costs explained 12-19% ($p<0.008$ for all mediation analyses) of social gradient in CVD.

Over 12 years of follow-up, 2,055 deaths were observed among 49,336 women from the DM-C and OS. Among the entire population, diet cost was not significantly associated with mortality (HR for 50% increase diet cost: 0.95; 95% CI 0.87, 1.04). When restricting the analysis to healthy never smokers, a 50% increase in diet costs was associated with a non-significant 15% reduced risk of death (HR 0.85; 95% CI 0.70, 1.03). Given the lack of a main effect between diet cost and mortality, subsequent SES-mediation analyses were not conducted.

This is the first systematic evaluation of the association between diet cost and adverse health outcomes in the United States. Contrary to the original hypothesis, higher diet costs were not associated with decreased weight gain. For T2DM and CVD, a significant inverse association between diet costs and risk of these outcomes was observed, and for mortality, there a suggestion of an association between higher diet costs and reduced mortality risk among healthy never smokers, but this association was not statistically significant. Diet cost accounted for 12-19% of the association between income/education and T2DM and CVD. The positive results observed for T2DM and CVD should be compared to results from other studies. Examining upstream factors associated with adverse health, including diet costs, expands our understanding of socioeconomic disparities in health, while also unpacking the consequences of the contemporary food environment on disease risk.

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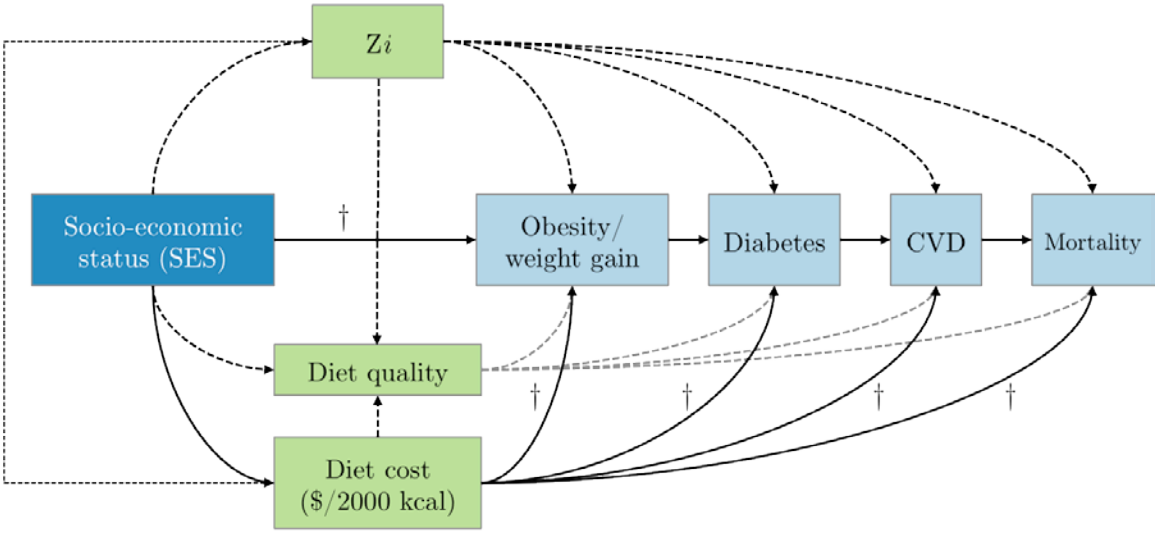
Introduction

Dietary factors have long been recognized as important determinants of chronic disease risk. Dietary factors, including nutrients, food groups, and diet quality scores/dietary patterns have been linked to numerous outcomes, including weight gain (1-5), type 2 diabetes (T2DM) (3, 6-8), cardiovascular disease (CVD) (8-15) and all-cause mortality (9, 11, 16-18). In the United States, 26% of deaths and 14% of disability-adjusted life years (DALYs) are due to dietary factors, with low intake of fruits, nuts/seeds, vegetables and high intakes of sodium, processed meat, and *trans* fats being particularly important (19). Dietary components are particularly important for morbidity and mortality related to cardiovascular and circulatory disease, but also cancer and diabetes.

Given the large burden of morbidity and mortality due to dietary factors, identifying the upstream determinants of food choices and diet composition is essential in developing interventions to improve the diet quality of the population. One upstream factor that has received little attention in relation to adverse health outcomes is food price and diet costs. Diet cost has been implicated as an important determinant of diet quality. Higher cost diets, particularly on a per-calorie basis, have been linked to many of the nutrients, food groups, and dietary patterns/scores related to weight change, T2DM, CVD and mortality (20-24). Following taste, food cost has been described as the most important factor in choosing foods (25). Data from 2007-2010 National Health and Nutrition Examination Survey show that 89% of US adults reported that food prices were “very important” or “important” in choosing foods at the grocery store, while only 11% said it was “not important” or “not too important” (26). Lower income adults were 2.8 times as likely to identify food cost as a “very important” consideration compared to higher income adults (26). Individuals with lower SES also tend to consume poorer quality and lower-cost diets (20), suggesting that diet costs may also play a role in contributing to socioeconomic differences in health (27-29).

While the population-wide burden of obesity and chronic disease including CVD and T2DM is considerable, this burden is not shared equally in the population. Specifically, individuals of lower socioeconomic status (SES), typically measured by family/household income or individual educational attainment, are more likely to be obese (particularly among women), be diagnosed with diabetes, experience a cardiovascular event (e.g., myocardial infarction or coronary heart disease death) or die prematurely (27, 29-36). Social disparities in these outcomes are often attributed to intermediate factors, including behaviors, such as smoking, physical activity or dietary composition (34, 35, 37). The possible role of diet costs as an upstream determinant of health disparities has not been evaluated.

Figure 1. Conceptual model guiding evaluation of diet cost and the role of diet cost in socioeconomic disparities in health



Zi represents other factors on the pathway from SES to health, such as tobacco use or physical activity. The dark paths are those directly under investigation and the daggers represent the novel pathways under study. CVD is cardiovascular disease.

Figure 1 details the conceptual model guiding this work. SES, measured by family income and education is directly associated with diet quality and diet cost. SES is hypothesized to be associated with weight gain, T2DM, CVD and mortality. Some of the social gradient for these

outcomes is through the pathway of traditional intermediates, such as smoking and physical activity. Given the association between SES and diet cost, the current studies evaluate whether diet cost may be a novel mediator of the social gradient in health.

Despite the consistent observation of an association between diet costs and diet quality (20-23, 38), a limited number of studies have evaluated the association between diet costs and health outcomes. One study conducted among Spanish university graduates observed that adults consuming more costly diets gained more weight than adults consuming cheaper diets, an unexpected finding given the previous observations of higher cost diets generally being healthier (23). In a representative sample of diabetic adults in the United States, increases in the prices of healthy foods was associated with higher fasting plasma glucose and hemoglobin HbA_{1c}, markers of diabetes control (39). Another prospective study, conducted among elderly Taiwanese, found that greater expenditures on fruits/vegetables were associated with a reduced risk of death (40). These results are not surprising given that expenditures on fruits/vegetables will be highly correlated with intakes of fruits/vegetables, which are also associated with reduced mortality risk. There is a need for focused research evaluating the association between diet costs and health.

Traditionally, food expenditures have been evaluated at the household or family-level, whereas individual-level estimates of diet cost and food expenditures are needed to evaluate their association with health outcomes. The recent development of a representative national food price database by the Center for Nutrition Policy and Promotion at the United States Department of Agriculture allows for food prices to be merged with individual-level dietary assessment data permitting the examination of the potential association between diet cost and health. In this study, the association between diet cost and weight change, incidence of diabetes and cardiovascular disease, and all-cause mortality was evaluated using data from the Women's Health Initiative, a large-scale population-based randomized trial and observational

study of post-menopausal women. The extent by which diet cost explained the social gradient in these outcomes was also evaluated. This study represents the first evaluation of diet cost as it relates to weight change, incidence of diabetes and cardiovascular disease and all-cause mortality in the United States.

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Chapter 1: Diet cost and weight gain among post-menopausal women age 50-64y in the Women's Health Initiative

Abstract

Background: Diet cost has been implicated as an important determinant of diet quality. No studies in the United States have evaluated whether diet cost is associated with weight gain.

Methods: A prospective study among 10,807 post-menopausal women 50-64 years using data from the control arm of the Dietary Modification trial of the Women's Health Initiative was conducted to evaluate the association between diet cost and weight change. To estimate diet costs, a national food price database was linked to a food frequency questionnaire. Energy-adjusted diet costs were log-transformed to evaluate the impact of a relative increase in diet costs. Women were weighed at annual follow-up visits and the outcome was measured weight change over up-to 7 years of follow-up. Adjusted linear regression models evaluated the association between diet cost and weight after adjusting for covariates associated with diet cost and/or weight change.

Results: Overall, the average weight change was +0.89 kg (95% CI 0.77, 1.02) over up-to 7 years of follow-up. A 50% increase in diet costs was associated with excess weight gain of 0.33 kg (95% CI 0.06, 0.59), though the association was modified by weight change prior to baseline. Among women who previously gained weight or were weight stable there was no significant association between diet cost and weight change. For women who previously lost weight, a 50% increase in diet cost was associated with excess weight gain of 0.87 kg (95% CI 0.34, 1.40). Among non-obese women, there was no association between diet cost and weight change.

Conclusions: Studies relating behavioral factors to weight change are challenged by the difficulty in accounting for weight trajectories and changes in behaviors driven by prior weight changes or efforts to lose or maintain weight. Future studies should evaluate the impact of changes in diet cost as they relate to weight outcomes. In addition, studies conducted in

younger populations that incorporate information on weight management behaviors may better elucidate the association between diet cost and weight change.

Introduction

Preventing and reducing weight gain poses a major challenge to public health and individuals alike. Both diet and physical activity have received much attention for their potential role in promoting or hindering weight gain. Dietary factors associated with increased weight gain include increased consumption of sugar-sweetened beverages and processed foods, while increased consumption of fruits, vegetables, and whole grains tend to be associated with decreased weight gain (1-4). Beyond individual foods/food groups, dietary patterns also likely play a role in weight gain. For example, consumption of a Western dietary pattern, which includes foods such as red meats, processed meats, French fries, refined grains and sweets and desserts, among others, is associated with excess weight gain (5) On the other hand, consumption of a prudent dietary pattern, which includes foods such as green leafy vegetables, dark-yellow vegetables, fruit, cruciferous vegetables, tomatoes and legumes, among others, is associated with decreased weight gain (5). Consumption of a Mediterranean dietary pattern is also associated with decreased weight gain (6, 7), as are a wide array of diet quality scores (8, 9).

One upstream factor implicated for its potential role in obesity and weight gain is food and diet costs (10-12). On a per-calorie basis, at the food-level, many foods/beverages associated with the prudent or Mediterranean dietary pattern (and other healthful dietary patterns) are more costly than foods/beverages associated with less healthful dietary patterns (e.g., fruits, vegetables, lean meats compared to processed meats, refined grains, sweets or sugar-sweetened beverages) (13). At the diet-level, holding energy-intakes constant, improving the quality of the diet will generally result in higher diet costs (14, 15). Evaluations of NHANES data

linked to a national food price database, show that higher diet costs are associated with increased fruit and vegetable consumption and decreased intake of saturated fats and energy from solid fat, alcohol and added sugars. On the other hand, whole grain and oils consumption were not related to diet cost, indicating that increasing consumption of some healthful components may be possible without increasing costs (16). Gender appears to modify the association between diet cost and quality, with the diets of women being particularly sensitive to food costs (16, 17). Not only has diet cost been linked to diet quality but the cost of foods is an often-cited determinant of food choice or barrier to more healthful eating, particularly among individuals of lower socioeconomic status (SES) (18-20).

Given the association between diet cost and quality, it seems that diet cost may be an important factor in predicting weight gain. Limited cross-sectional studies have observed an association between higher diet cost and a lower BMI or reduced prevalence of obesity (21, 22). However, only one study, conducted in Spain, has prospectively evaluated the association between diet cost and weight change, surprisingly observing that higher cost diets were related to an increased likelihood of weight gain (23). Given the divergent results of cross-sectional and prospective studies, additional prospective studies are essential to better understand the consequences of diet cost on weight change. Further, since individuals of lower socioeconomic status (SES) generally consume lower cost diets (16) and are more prone to weight gain (24), diet costs may explain, in part, the association between SES and weight gain.

To evaluate the association between diet cost and weight change, a national food price database was merged with the food frequency questionnaire (FFQ) used in the control arm of the Dietary Modification (DM) trial in the Women's Health Initiative. Weights were measured objectively at annual study visits and the relation between diet cost and weight change was evaluated over up-to 7 years.

Methods

Data for this study came from the control arm of the Women's Health Initiative (WHI) Dietary Modification (DM-C) trial. The design of the WHI has been described previously (25, 26). Briefly, 48,835 generally healthy postmenopausal women aged 50-79y were randomly assigned to the DM trial at 40 clinical centers across the United States from 1993 and 1998. The DM trial investigated the effect of a low-fat dietary pattern on the incidence of breast and colorectal cancers and heart disease over an average of 8.1 years of follow-up (27, 28). The recommended dietary pattern emphasized increased intake of fruits, vegetables and grains, while reducing the percent of energy from total fat to less than 20% (25). This section describes the study population, the assessment and reliability of diet costs estimates, potential confounders of the diet cost and weight change association, outcomes and the statistical methods used.

Study Population

Given the emphasis of the current research on the relation between socioeconomic status (SES) and weight change, this study was restricted to women 50-64y at study baseline. Examining weight change in older populations can be particularly challenging due disease-related weight loss. In addition, with an emphasis on SES, the income variable is more meaningful in this age group than for older women. Women from the intervention arm of the DM trial were not included in the present study, as their diets changed dramatically over time due to the intervention effects. Data from other arms was not used due to lacking availability of dietary data and measured heights/weights. The following factors excluded participation in the DM: <32% energy from dietary fat, history of breast cancer, colorectal cancer in past 10 years, endometrial cancer in past 10 years, other cancer within the past 10 years, with the exception of non-melanoma skin cancer, stroke or acute myocardial infarction (MI) 6 months prior to

enrollment, body mass index (BMI)<18, hypertension (>200/>105 mm HG), ≥10 meals out per week, special low-fiber diet, special diet due to malabsorption, unintentional weight loss of >15 lb (6.8 kg) in the 6 months prior to baseline, self-reported diabetes prior to 21y.

To avoid truncation of percent of energy from dietary fat, this study used year 1 of the DM as baseline. Among participants age 50-64y in the DM-C, the analytic cohort was further restricted to those with complete data on variables of interest. Individuals missing data on diet cost, education, physical activity, smoking status, hormone use, social support and depression status were excluded. The primary sample size included 10,807 women 50-64y.

Assessing diet cost

The exposure of interest was estimated diet cost, which was assessed using the WHI FFQ. Food and beverage prices per 100g edible portion from a national food price database were linked to the underlying foods in the WHI FFQ. The food price database was created by the Center for Nutrition Policy and Promotion (CNPP) at the USDA and was contemporary with 2001-2002 food prices (29). The CNPP price database provided the prices for 6,680 foods and beverages, excluding alcoholic beverages and bottled water. This price database assumed that all foods/beverages are purchased at a store and prepared at home. The method we used for estimating alcohol prices has been described previously (16).

Diet costs were energy-adjusted using the residual method to account for differences in energy intake between individuals (30). This method estimates a residual value of diet cost based on the observed relation between energy intake and diet cost. A constant of 2000 kcal was then added to the estimated residual values to ease interpretation. For primary analyses, the diet cost variable was log-transformed to evaluate the impact of a percentage change in diet costs rather than an absolute difference. This was done because one would not expect a 1-dollar increase in diet costs to have the same impact for individuals consuming low vs. high cost diets.

For reporting purposes the change in weight associated with a 50% increase in diet cost is shown. For reference, a 50% increase in diet cost roughly corresponds to the difference between the 85th and 15th percentile values ($5.27 vs. $3.57/day).

In order to assess the measurement characteristics of the diet cost estimate from the FFQ and to utilize approaches to reduce the impact of measurement error, a reliability sub-study was conducted. In brief, we linked the USDA food price database (described above) and the MyPyramid Equivalents Database to 560 four-day food records (4DFR) completed by women enrolled in the DM-C, of whom 451 were eligible for inclusion in the weight change analysis. The MyPyramid Equivalents Database includes information on the number of servings of different foods groups and is needed to evaluate the HEI-2005 (31, 32).

The 4DFR were originally collected in order to evaluate adherence to the dietary modification trial and to complement data from the FFQ (25). To better measure long-term intake, avoid measuring correlated eating behaviors and include a weekend day, the 4DFR was completed on alternating days. Non-white women were over-sampled to participate in the 4DFR sub-study to more precisely evaluate dietary habits and adherence to the intervention among minority women. The correlation coefficient was 0.53 when comparing log-transformed energy adjusted diet costs and 0.51 for the HEI-2005 between the FFQ and 4DFR, comparable to values for saturated fat (0.56), niacin (0.54), or folate (0.52) for comparisons of FFQ and 4DFR data (33).

Outcome

At each annual follow-up visit women were weighed using standardized methods on beam scales (34). The outcome of this study was change in measured weight from baseline over up to 7 years of follow-up. Primary analyses used the latest weight data available over the 7 years of follow-up, though minor modifications were made to account for the impact of mortality and disease on weight. Specifically, analyses examined the impact that other diseases may have on

weight change. For example, one might expect individuals who die or are diagnosed with a severe disease (e.g., cancer) to lose weight as a result of disease or illness, both prior to and following disease-onset. Among individuals who died or had a new diagnosis of cancer we used their weight measure from 2 visits prior to the event. For individuals diagnosed with diabetes or who have another disease event (e.g., coronary heart disease or stroke) the most recently measured weight prior to that event was used. The goal of this approach is to account for weight loss due to subclinical disease or illness and for weight loss that is a consequence of poor health.

Potential Confounders

Key covariates were identified that are either associated with both diet cost or weight change. Variables and their coding are described below. All covariates, with the exception of weight/height measurements, were assessed via questionnaire at study baseline or at year 1 for some variables. Socio-demographic covariates included age group (50-54, 55-59, 60-64), race/ethnicity (American Indian/Alaskan Native, Asian/Pacific Islander, black, Hispanic, White not of Hispanic origin and unknown), family income (<10, 10-19, 20-34, 35-49, 50-74, 75-99, 100-149, and ≥150 in $1000 and a missing category), educational attainment (<high school, high school graduate/equivalent, some college, college degree/some post-graduate education and master's degree or higher) and having a partner (yes/no). While we did use a complete case approach for most analyses, a missing indicator was used. In analyses examining the association between SES variables and weight change, these variables were treated as continuous variables (e.g., <$10,000 = 1; $10,000-19,999 = 2, etc.).

Additional variables included quintiles of recreational physical activity (<0.75, 1-4.25, 4.33-10, 10.04-18.5, ≥18.58 MET [metabolic equivalents] hours/wk), smoking status (former, never or current), hormone therapy use (former, never or current), and depression status. Each of these

variables was modeled as a categorical variable. A summary variable quantifying social support was also included as a continuous covariate. As women in the DM-C could participate in the other WHI trials (i.e., the hormone therapy [HT] and Calcium and Vitamin D [CaD] trials) all analyses adjusted for study arm (25).

Statistical methods

Linear regression was used to assess the impact of diet cost and socioeconomic variables on weight change. A series of models were fit that accounted for an increasing number of variables. The first set of models (Model 1) adjusted for study arm (HT and CaD arm), age group, race/ethnicity, baseline weight and weight change prior to baseline. Model 2 adjusted for additional socio-demographic and behavioral factors associated with weight change and diet cost, including income, partner, education smoking status, hormone therapy use, recreational physical activity, a social support scale, and depression status. When diet cost was the independent variable of interest, Model 2 additionally adjusted for family income, having a partner and education. When income and education were the independent variables of interest the other SES variable was not included in the model, though all analyses evaluating the effect of family income included having a partner as a covariate. Because weight change and behaviors can be influenced by previous weight trajectories we examined whether the association between diet cost/SES and weight change was modified by weight trajectory. Specifically, the percent change in body weight from year 0 to year 1 (baseline for present study) was examined as a potential effect modifier. This variable was dichotomized as follows: one group represented the quartile of individuals experiencing the greatest proportion of weight loss from year 0 to year 1 (<-2.1% of body weight; inter-quartile range [IQR] -3.1% to -7.1%) and the remainder of individuals had stable weight or experienced weight gain (-2.1% to +54.3%; IQR 0 to +3.5). In addition to stratification by prior weight change, we evaluated whether the association between diet cost and weight change was modified by obesity

(dichotomized, BMI<30 and BMI≥30), in addition to prior weight change. The stratification by obesity status was done as some studies evaluating lifestyle factors related to weight change exclude obese subjects (1, 35).

Secondary analyses using an alternative approach were conducted to evaluate the association between diet cost and the incidence of obesity. Here, the outcome was becoming obese by the end of follow-up and the analysis was restricted to 6,715 women who were not obese at baseline. Specifically, a robust generalized linear model, with a log link from the Poisson family was used to estimate the relative risk of becoming obese associated with diet cost and other variables (e.g., family income) (36). For this analysis covariates included baseline BMI, weight change prior to baseline, age group, race/ethnicity, study arm and length of follow-up.

Because the estimate of diet cost is an error-prone measure, we used regression calibration to account for measurement error using the estimate of diet cost from the 4DFR as an “alloyed gold standard” (37, 38). An “alloyed gold standard” is a measure that is thought to better reflect the true value than the global instrument (37, 38). Here, the measurement properties of the 4DFR are considered better than the FFQ, which is supported by results on energy intake from studies using doubly-labeled water to compare self-report measures with objective measures of energy intake (39). The regression calibration approach reduces the bias from measurement error assuming that the errors in the two instruments are uncorrelated, though previous work has shown that even in the presence of modest correlated errors, the estimate from regression calibration should yield a less biased estimate of the observed exposure-outcome relationship using the error-prone measure (38). The %blinplus SAS macro was used to implement regression calibration (40).

Analyses were conducted using Stata 13.1 (College Station, TX), SAS 9.3 for Windows (Cary, NC 2013) for %blinplus macro (40).

Results

Population characteristics

Subject characteristics are provided in **Table 1**. Average diet costs by socio-demographic, anthropometric and behavioral characteristics are also provided. The mean age at study baseline was 59.0y (SD=3.8). The cohort was primarily non-Hispanic white, and had a wide range of family incomes. Nine percent of the cohort had family incomes less than $20,000/year, while nearly a quarter had family incomes greater than $75,000. A similarly broad distribution of education was observed, though only a small proportion of women had not graduated from high school. At baseline, 27% was healthy weight/underweight and 37.8% was considered obese. The average HEI-2005 score was 65.8 (SD=10.2) and the average number of MET hours from recreation physical activity per week was 10.7 (SD=12.3).

Diet cost

The average diet cost value was $4.42 (SD=$0.89; median=$4.31; 10^{th} percentile=$3.42; 90^{th} percentile=$5.54). Socio-demographic, anthropometric and behavioral characteristics were associated with diet costs. Older women consumed slightly more costly diets than women 50-54y. Non-Hispanic white women and Asian/Pacific Islander women consumed significantly more costly diets than black or Hispanic women (p-difference<0.001). Both education and income were positively associated with diet costs (p-trend<0.001). The diets of women with family incomes greater than $150,000 were 24% higher than women with incomes less than $10,000. A similar relationship was observed for education. Women with healthier diets as measured by both HEI-2005 and AHEI-2010 tended to have more costly diets, as did women who were more physically active (p-trend<0.001 for all).

Weight change

Women in the cohort were followed for an average of 5.6 years (median = 6 years). The average weight change was +0.89 kg (IQR -2.1 to +4.1 kg). Younger women (age 50-54) gained more likely to gain weight when compared to older women (p-trend<0.001). After adjusting for baseline weight, length of follow-up and previous weight change, black (+1.62 kg) and Hispanic (+1.38 kg) women gained more weight than non-Hispanic white women (+0.82 kg) (p-difference<0.001). A significant linear trend was also observed for family income, where lower income women gained significantly more weight than higher income women. Education was similarly associated with weight gain, with greater education associated with less weight gain (p-trend<0.001 for both income and education). Baseline diet quality, as measured by HEI-2005 and AHEI-2010, was not associated with weight change, though baseline physical activity was inversely related to weight gain (p-trend=0.003). On average, the small number of underweight women gained the most weight, while healthy weight, overweight and the moderately obese (BMI 30-34.9) gained between 0.89-1.22 kg. Overall, women with Class II obesity (BMI 35-39.9) gained little weight while the severely obese (BMI ≥40) lost weight (p-trend=0.066).

Diet cost & weight change

Overall, in minimally adjusted models, a 50% increase in diet cost was not associated with weight change (see **Table 2**). The association between diet cost and weight change was significantly modified by weight change prior to baseline (likelihood ratio test for interaction p-value < 0.001). Among women who lost weight prior to baseline, a 50% increase in diet cost was associated with excess weight gain of 0.59 kg (95% CI 0.09, 1.09, p-value = 0.01). Among women who had stable weight or gained weight prior to baseline, there was some evidence of an association between increased diet cost and weight loss. After adjusting for additional factors associated with diet cost and weight change the overall strength of the association between diet cost and weight change increased. Overall, a 50% increase in diet cost was associated with

weight gain of 0.33 kg (95% CI 0.06, 0.59, p = 0.015). Among women who previously lost weight, a 50% increase in diet cost was associated with excess weight gain of 0.87 kg (95% CI 0.34, 1.40; p-value < 0.001). There was no longer evidence of an association between diet cost and weight change among women who had stable weight or gained weight prior to baseline. In analyses that accounted for measurement error of the diet cost estimates, the association between diet cost and weight gain was strengthened. Specifically, in a fully adjusted model among women who previously lost weight, a 50% increase in diet cost was associated with weight gain of 1.44 kg (95% CI 0.37, 2.50; p-value = 0.008). In-line with uncorrected analysis, there was no longer any association between diet cost and weight change among the remaining 75% of women.

The association between diet cost and weight change was not only modified by prior weight change, but also by obesity status (see **Table 3**). Overall, among non-obese subjects there was no association between diet cost and weight change. In adjusted models among women who previously lost weight, there was a positive association between diet cost and weight change. In non-obese subjects who were weight stable or gained weight prior to baseline, a 50% increase diet cost was associated weight loss of -0.47 kg (95% CI -0.77, -0.18; p=0.002) though there was no longer any association after adjustment for confounders. Among obese women, overall and among those who previously lost weight, higher diet costs were associated with weight gain. There was no association between diet cost and weight change among obese subjects who had been weight stable or gained weight prior to baseline.

Socioeconomic status and weight change

The association between income and education and weight change is also described in **Table 2**. Overall, women with the lowest family incomes gained an excess of 1.01 kg (95% CI 0.44, 1.58; p-value < 0.001) compared to women with family incomes greater than $150,000. There was no association between income and weight change among women who previously lost

weight. Among women who were weight stable or gained weight, the difference between the two extreme income groups was 1.29 kg (95% CI 0.64, 1.95; p-value < 0.001). Adjustment for potential intermediates (e.g., physical activity) only modestly altered the association between income and weight change. Overall, women with less education gained significantly more weight than women with more education (+0.67 kg [95% CI 0.27, 1.08]). For education, there was no evidence that the association between education and weight change was modified by prior weight trajectories (likelihood ratio interaction p-value = 0.64). The association between income and education and weight change stratified by obesity status and prior weight change is provided in **Table 3**. There was no evidence that the association between income and education was modified by obesity status, but these data are presented for the purposes of consistency between the tables.

Table 4 shows the relative risk of becoming obese among 6,715 non-obese women at baseline. Over follow-up 12.4% of women became obese. A 50% increase in diet cost was not associated with an increased likelihood of becoming obese (RR 1.01, 95% CI 0.90, 1.15).

Discussion

The original hypothesis was that higher cost diets would be associated with decreased weight gain. Here, we observed that among the entire population there was a modest positive association between increased diet cost and increased weight gain, which was unexpected. The positive association between higher diet cost and increased weight gain was restricted to women who lost weight prior to study baseline. Among women who had gained weight or had stable weights there was a modest negative association between weight change and diet cost. As hypothesized, we did observe an association between lower SES and increased weight gain, though we did not examine diet cost as a potential mediator of this association given the unexpected direction of the diet cost and weight gain association.

In addition, obesity was identified as an additional effect modifier of the diet cost and weight change association. Among the non-obese subjects there was no evidence of a positive association between diet cost and weight gain overall and a weaker association among women who previously lost weight. In minimally adjusted analyses there was evidence of an association between higher diet costs and decreased weight change, though the relation did not hold upon adjustment for important covariates. On the other hand, among obese subjects, the positive association between diet cost and weight change was quite strong and was statistically significant in adjusted models among the entire population and the women who previously lost weight (21% of obese women). Among obese women who gained weight/lost weight (79% of obese women) there was no evidence of an association between diet cost and weight change.

Prospective studies of diet cost and anthropometric changes are few. To our knowledge, only one study has examined diet cost as it relates to changes in weight or BMI. This study was conducted in Spain and observed a modest positive association between higher diet costs and the likelihood of gaining 0.6 kg/year over up to 5 years of follow-up (23). However, this analysis did adjust for measures of diet (i.e., a Mediterranean vs. western dietary pattern score), which are on the potential pathway from diet cost to weight change or health outcomes. Despite the adjustment for factors on the pathway, the results of their adjusted analyses were comparable to those from age/sex-adjusted models. The results from the current study are generally consistent with the Spanish report, though this study was not able to stratify by weight changes prior to baseline.

Here, the association between diet cost and weight change was modified by previous weight change. Specifically, higher diet costs were associated with weight change among women who lost more than 2.1% of body weight in the year prior to baseline. This group of women gained significantly more weight over the subsequent period of follow-up than women who were weight stable or gained weight (average 3.02 kg of weight gain vs. 0.19 kg of weight gain when

adjusting for baseline weight, age group and length of follow-up). The women experiencing previous weight loss also consumed more costly diets ($4.53/d vs. $4.38/d) and had marginally healthier diets (HEI-2005: 67.1 vs. 65.4). One possible explanation for the unexpected association in this group, participants were making an effort to maintain their weight or lose additional weight, which included consuming a higher cost (and more healthful diet). Prior weight is among the strongest predictors of subsequent weight gain in the current data. Furthermore, weight loss, particularly short-term weight loss is particularly challenging to maintain (41). The addition of variables measuring weight intention or dieting behavior would be extremely useful in understanding the motivations or intention of weight change. Data on dieting behavior and long-term weight changes were collected at the WHI recruitment visit, but were not collected at the year 1 study visit.

Previous studies evaluating lifestyle factors, including physical activity and diet, likely face the same challenge regarding potential reverse causality. For example, studies linking consumption of diet soft drinks to subsequent weight gain have a difficult time disentangling the impact of prior weight changes and weight intention from a genuine effect (42). Surprisingly, given concerns regarding obesity, relatively few studies have examined how dietary patterns and factors influence weight change. The challenge of reverse causality and temporality are clear challenges to detecting diet-related influences on weight change. The strongest results have come from studies that include serial measurements of dietary habits, where change in intake of the dietary constituent or pattern is associated with weight gain/loss, but the impact of baseline consumption is not evaluated (1-5). Future work evaluating diet costs should evaluate changes in diet cost as they relate to subsequent changes in weight, though this will require a cohort with many years of follow-up for weight and serial dietary assessment.

Many studies of dietary factors on weight change are either restricted to the non-obese, or observe a stronger effect among the non-obese compared to the obese (1, 4, 5). In the current

study, the inverse association between diet cost and weight change among those who previously lost weight was much weaker in non-obese individuals, while a stronger negative association between diet cost and weight change was observed among non-obese individuals who gained weight or lost some weight.

Beyond evaluating the association between diet cost and weight change, an additional aim of the current research was to determine if differences in weight change by SES could be attributed to differences in diet cost. The observation that lower SES women experienced greater weight gain than women with higher SES was consistent with prior research (24, 43). However, while higher education and income were both associated with higher diet costs and higher SES was associated with reduced weight gain, diet cost was not negatively associated with weight gain as originally hypothesized. Relatively few studies have examined the determinants of the socioeconomic gradient in weight change, with most observing a residual association after accounting for physical activity, dieting or dietary factors (24, 44). Though not the emphasis of the current research, the inclusion of select intermediates (e.g., physical activity, social support and depression status) of the SES-weight change association (see Model 2 for income and education in **Table 2** and **Table 3**), resulted in very modest attenuation of the effect, suggesting that the intermediates included here were not important mediators of the SES-weight gain association in the current population. This could be partially attributed to error in measuring these intermediate variables or differences in the relative importance of mediators of the SES-weight association in different populations. To reduce SES disparities in weight gain, focused research is needed to identify the contributing factors, including both proximal (e.g., moderate physical activity or fruit/vegetable intake) and upstream factors (e.g., neighborhood walkability, food/diet costs or store availability).

The limitations of this study merit some discussion. The primary limitation of this study was the use of an FFQ instrument to estimate diet costs. Deriving diet costs using a national food price

database may not reflect the actual prices for food paid by individual WHI participants. This is similar to the weakness inherent in deriving nutrient intakes from nutrient composition databases, which do not reflect potential heterogeneity in the nutrient levels of foods actually consumed. In addition, the price database assumes that all foods are purchased at stores and consumed at home. Despite these limitations, data from a price database represents a meaningful source of information on food prices that can be linked to individual data on diets and health. Regression calibration approaches were used with data from a sub-set of 4DFRs to reduce the impact of measurement error from the FFQ-derived cost estimate. While the 4DFR is an imperfect measure of dietary intake, there is evidence that it performs better than an FFQ in studies assessing objective biomarkers (39). The primary source of error in the FFQ is fixed portions sizes and a restricted food list, both of which are remedied when using 4DFRs. Second, the study population may not be the ideal group in which to evaluate diet costs as they relate to weight change. The average age of this cohort was 59 years, while, among women, most weight gain occurs between ages 25-44y (45). Conducting a comparable study among younger women may be more likely to detect an association between diet cost and weight gain, though this may be challenging given the focus on middle-aged populations or older in most large prospective studies.

Conclusions

While previous studies have observed a strong association between diet cost and diet quality, few prospective studies have evaluated the association between diet cost and weight change. Overall, diet cost was associated with increased weight gain in a cohort of 10,807 post-menopausal women, though the association was driven by a strong effect observed among women who lost weight prior to baseline. Among women who were weight stable or gained weight prior to baseline, there was no association between diet cost and weight change. Studies of behavioral factors and weight change are challenged by the difficulty in accounting for weight

trajectories and changes in behaviors driven by prior weight changes or efforts to lose or maintain weight. Incorporating data on previous weight change was critical in better understanding the association between diet cost and weight change. Future studies in younger populations should evaluate diet cost as it relates to weight change.

Table 1. Diet cost ($/2000 kcal), obesity (body mass index [BMI] ≥ 30 kg/m^2) and weight change among (Women's Health Initiative analytic cohort (n=10,807)

		Diet Cost ($/2000 kcal)		Obesity prevalence	Weight Change (**Δ** kg)[1]	
	n	Mean	95% CI	%	Mean	95% CI
Total cohort	10,807	4.42	4.40, 4.44	37.9	0.89	0.77, 1.02
Age						
50-54	1,933	4.34	4.30, 4.38	35.2	1.75	1.48, 2.03
55-59	4,062	4.43	4.40, 4.46	37.8	1.21	1.02, 1.40
60-64	4,812	4.44	4.42, 4.47	39.0	0.28	0.11, 0.46
P-trend			<0.001	<0.001		<0.001
Race/ethnicity						
American Indian/Alaskan Native	40	4.23	3.92, 4.55	50.0	1.93	0.03, 3.84
Asian/Pacific Islander	335	4.54	4.43, 4.65	17.9	-0.22	-0.88, 0.45
Black	1,117	4.00	3.95, 4.05	55.6	1.62	1.26, 1.99
Hispanic	422	4.04	3.95, 4.12	39.6	1.38	0.79, 1.97
White, not Hispanic	8,765	4.49	4.47, 4.50	36.1	0.82	0.69, 0.94
Unknown (incl. other)	128	4.48	4.33, 4.62	47.6	0.98	-0.09, 2.04
P-difference			<0.001	<0.001		<0.001
Family Income						
<$10,000	282	3.97	3.89, 4.06	53.2	1.71	0.99, 2.43
$10,000-19,999	707	4.03	3.97, 4.09	48.5	1.72	1.27, 2.18
$20,000-34,999	2,011	4.20	4.17, 4.24	43.7	1.10	0.83, 1.37
$35,000-49,999	2,231	4.35	4.32, 4.38	40.4	1.02	0.76, 1.27
$50,000-74,999	2,653	4.48	4.44, 4.51	36.5	0.84	0.61, 1.08
$75,000-99,999	1,343	4.64	4.59, 4.68	31.0	0.57	0.24, 0.90
$100,000-149,999	932	4.80	4.74, 4.86	26.1	0.23	-0.17, 0.63
≥$150,000	421	4.91	4.82, 5.01	23.0	0.20	-0.39, 0.79
Don't know	227	4.33	4.21, 4.45	41.4	0.82	0.02, 1.62
P-trend			<0.001	<0.001		<0.001
Education						
<High school	353	3.85	3.76, 3.93	55.8	1.89	1.25, 2.54
High school/equivalent	1,662	4.21	4.17, 4.25	43.6	0.95	0.65, 1.24
Some college	4,166	4.38	4.35, 4.4	40.6	1.04	0.86, 1.23
College graduate	1,252	4.52	4.47, 4.58	32.8	0.85	0.51, 1.19
≥Master's degree	3,374	4.59	4.56, 4.62	31.7	0.60	0.39, 0.80
P-trend			<0.001	<0.001		<0.001
HEI-2005						
Q1 (29.3-57.1) [Poor diet]	2,162	4.08	4.04, 4.12	44.3	1.04	0.78, 1.30
Q2 (57.2-63.6)	2,161	4.29	4.25, 4.32	40.0	0.82	0.56, 1.08
Q3 (63.7-69.1)	2,162	4.40	4.36, 4.43	37.3	0.53	0.28, 0.79
Q4 (69.2-75.1)	2,161	4.58	4.54, 4.61	34.5	0.98	0.72, 1.24
Q5 (75.2-91.8) [Better diet]	2,161	4.75	4.72, 4.79	33.3	1.10	0.84, 1.36
P-trend			<0.001	<0.001		0.52

AHEI-2010						
Q1 (15-34.2) [Poor diet]	2,162	4.01	3.98, 4.04	43.3	1.03	0.77, 1.29
Q2 (34.3-40.4)	2,161	4.21	4.17, 4.24	39.8	0.89	0.63, 1.15
Q3 (40.4-46.1)	2,162	4.41	4.37, 4.44	37.8	0.73	0.47, 0.99
Q4 (46.2-52.8)	2,161	4.6	4.57, 4.64	35.5	1.00	0.74, 1.26
Q5 (52.9-92.2) [Better diet]	2,161	4.87	4.83, 4.91	33.0	0.81	0.55, 1.07
P-trend			<0.001	<0.001		0.43
Rec. physical activity (MET-hrs/wk)						
Q1 (0-0.75)	2,341	4.15	4.12, 4.19	53.6	1.13	0.88, 1.39
Q2 (1-4.25)	1,982	4.30	4.26, 4.34	46.2	0.98	0.71, 1.25
Q3 (4.33-10)	2,258	4.41	4.38, 4.44	35.5	0.93	0.68, 1.18
Q4 (10.04-18.5)	2,077	4.55	4.51, 4.59	30.8	0.84	0.58, 1.11
Q5 (18.58-113.2)	2,149	4.70	4.66, 4.74	23.4	0.57	0.31, 0.83
P-trend			<0.001	<0.001		0.003
Body mass index (kg/m^2)						
Underweight: <18.5	41	4.34	4.08, 4.61	-	2.07	0.13, 4.01
Healthy weight: 18.5-24.9	2,871	4.54	4.50, 4.57	-	0.89	0.55, 1.23
Overweight: 25-29.9	3,803	4.46	4.43, 4.48	-	1.22	1.02, 1.43
Class I obesity: 30-34.9	2,455	4.35	4.31, 4.38	-	0.94	0.66, 1.21
Class II obesity: 35-39.9	1,097	4.27	4.22, 4.32	-	0.36	-0.13, 0.85
Class III obesity: ≥40	540	4.15	4.09, 4.22	-	-0.58	-1.37, 0.21
P-trend			<0.001			0.066

[1] Adjusted for age group, baseline weight, length of follow-up and weight change from time^{-1} to time^{0}.

Table 2. Association between 50% increase in diet cost, income and education and weight change over up to 7 years of follow-up in Women's Health Initiative analytic cohort (n=10,807)

	Overall (n=10,807)			Lowest quartile of weight change from time^{-1} to time^{0} (n=2,702)			Other three quartiles of weight change from time^{-1} to time^{0} (n=8,105)		
	Δ kg	95% CI	p-value	Δ kg	95% CI	p-value	Δ kg	95% CI	p-value
Diet cost (per 50% increase)									
Model 1[1]	0.05	-0.20, 0.31	0.70	0.59	0.09, 1.09	0.01	-0.27	-0.56, 0.02	0.064
Model 2[2]	0.33	0.06, 0.59	0.015	0.87	0.34, 1.40	<0.001	-0.02	-0.33, 0.28	0.88
Diet cost (per 50% increase); corrected									
Model 1[1]	0.20	-0.32, 0.48	0.69	1.02	0.09, 1.96	0.03	-0.42	-0.88, 0.03	0.069
Model 2[2]	0.54	0.09, 0.97	0.017	1.44	0.37, 2.50	0.008	-0.04	-0.45, 0.88	0.88
Income (<$10,000 vs. ≥$150,000)									
Model 1[1]	1.01	0.44, 1.58	<0.001	0.17	-1.00, 1.35	0.77	1.29	0.64, 1.95	<0.001
Model 2[2]	0.91	0.33, 1.50	0.002	0.00	-1.21, 1.21	0.99	1.15	0.48, 1.82	<0.001
Education (<HS vs. ≥master's)									
Model 1[1]	0.67	0.27, 1.08	0.001	0.68	-0.14, 1.50	0.11	0.59	0.13, 1.05	0.012
Model 2[2]	0.60	0.19, 1.00	0.004	0.61	-0.22, 1.45	0.15	0.53	0.06, 0.99	0.026

[1] Adjusted for age group, baseline weight, length of follow-up, race/ethnicity, HT study arm, CaD study arm and weight change from time^{-1} to time^{0}.
2 Adjusted for factors from Model 1, in addition to family income, partner, education, quintiles of recreational physical activity, smoking status, HT use, social support, depression status, history of diabetes, history of cancer and history of cardiovascular disease. Income models do not adjust for education and education models do not adjust for income or having a partner.

P-interaction for diet cost was <0.001 for both models. P-interaction for income was 0.14 for Model 1 and Model 2. P-interaction for education was 0.64 for Model 1 and 0.65 for Model 2.

Table 3. Association between 50% increase in diet cost and weight change over up to 7 years of follow-up in Women's Health Initiative analytic cohort among women stratified by obesity status (obese vs. non-obese)[1] (n=10,807)

	Overall			Lowest quartile of weight change from time^{-1} to time^{0}			Other three quartiles of weight change from time^{-1} to time^{0}		
	Δ kg	95% CI	p-value	Δ kg	95% CI	p-value	Δ kg	95% CI	p-value
Non-obese (BMI<30)[a]									
Diet cost (per 50% increase)									
Model 1[2]	-0.17	-0.42, 0.09	0.21	0.41	-0.10, 0.91	0.12	-0.47	-0.77, -0.18	0.002
Model 2[3]	0.10	-0.17, 0.37	0.45	0.59	0.06, 1.14	0.029	-0.19	-0.50, 0.12	0.221
Income (<$10,000 vs. ≥$150,000)									
Model 1[2]	0.82	0.23, 1.41	0.006	-0.23	-1.43, 0.96	0.70	1.18	0.51, 1.84	0.001
Model 2[3]	0.63	0.03, 1.22	0.04	-0.49	-1.73, 0.73	0.43	1.01	0.34, 1.69	0.003
Education (<HS vs. ≥master's)									
Model 1[2]	0.81	0.39, 1.22	<0.001	0.38	-0.47, 1.22	0.38	0.86	0.38, 1.34	<0.001
Model 2[3]	0.67	0.25, 1.10	0.002	0.25	-0.61, 1.11	0.57	0.72	0.24, 1.21	0.003
Obese (BMI≥30)[b]									
Diet cost (per 50% increase)									
Model 1[2]	0.35	-0.17, 0.67	0.19	0.70	-0.43, 1.83	0.22	0.06	-0.53, 0.64	0.85
Model 2[3]	1.60	0.25, 2.95	0.020	1.29	0.05, 2.53	0.041	0.26	-0.35, 0.88	0.40
Income (<$10,000 vs. ≥$150,000)									
Model 1[2]	1.37	0.19, 2.55	0.023	1.06	-1.65, 3.78	0.44	1.39	0.10, 2.70	0.035
Model 2[3]	1.46	0.26, 2.65	0.017	1.04	-1.73, 3.82	0.46	1.46	0.14, 2.79	0.03
Education (<HS vs. ≥master's)									
Model 1[2]	0.50	-0.31, 1.31	0.23	1.47	-0.37, 3.31	0.12	0.21	-0.69, 1.11	0.65
Model 2[3]	0.46	-0.36, 1.27	0.27	1.41	-0.44, 3.26	0.13	0.18	-0.76, 1.09	0.70

[a] Sample size for non-obese was 6,716 (4,880 weight stable/gain prior to baseline and 1,835 weight loss prior to baseline). [b] Sample size for obese was 4,092 (3,225 for weight stable/gain prior to baseline and 867 weight loss prior to baseline).

[1] P-value for 3-way interaction between obesity, weight change prior to baseline and diet cost was 0.0023 for Model 1 and 0.003 for Model 2. There was no evidence of a 3-way interaction between obesity, weight change prior to baseline and either SES variable, though the results are stratified by obesity status for purposes of comparison.

[2] Adjusted for age group, baseline weight, length of follow-up, race/ethnicity, HT study arm, CaD study arm and weight change from time^{-1} to time^{0}.

3 Adjusted for factors from Model 1, in addition to family income, partner, education, quintiles of recreational physical activity, smoking status, HT use, social support, and depression status. Income models do not adjust for education and education models do not adjust for income or having a partner.

Table 4. Factors associated with relative risk (RR) of becoming obese among non-obese women at baseline (n=6,715)

Variables	RR	95% CI	p-value
Diet cost (per 50% increase)	1.01	0.90, 1.15	0.82
Energy (per 1131 kcal increase)[2]	0.87	0.78, 0.98	0.017
HEI-2005 (per 20 point increase)[2]	1.01	0.90, 1.13	0.83
AHEI-2010 (per 22 point increase)[2]	1.03	0.92, 1.15	0.63
Recreational physical activity (MET-hr/wk)			
Q1 (least recreational PA)	1.22	1.02, 1.44	0.026
Q2	1.12	0.94, 1.35	0.21
Q3	1.00	0.83, 1.20	0.99
Q4	0.96	0.80, 1.16	0.70
Q5 (most recreational PA)	ref		
P-trend			0.006
Family Income[3]			
<$10,000	1.38	0.89, 2.15	0.16
$10,000-19,999	1.22	0.83, 1.78	0.31
$20,000-34,999	1.29	0.93, 1.79	0.13
$35,000-49,999	1.28	0.93, 1.76	0.13
$50,000-74,999	1.07	0.78, 1.47	0.68
$75,000-99,999	1.01	0.72, 1.40	0.98
$100,000-149,999	0.87	0.59, 1.28	0.49
≥$150,000	ref		
Don't know	1.86	1.19, 2.89	0.006
P-trend			0.001
Education			
<High school	1.44	1.08, 1.93	0.014
High school/equivalent	1.22	1.02, 1.45	0.025
Some college	1.07	0.93, 1.22	0.36
College graduate	1.07	0.89, 1.30	0.47
≥Master's degree	ref		
P-trend			0.014

[1] All analyses adjusted for baseline BMI (continuous), age group (5-year bands), weight change prior to baseline (continuous percentage), length of follow-up, race/ethnicity and study arm.

[2] Corresponds to 2-standard deviation increase.

[3] Additionally adjusted for having a partner.

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Chapter 2: Diet cost and risk of type 2 diabetes: does diet cost mediate the association between socioeconomic status and diabetes risk?

Abstract

Background: Diet cost has been implicated as an important determinant of diet quality. No studies have evaluated whether diet cost is associated with diabetes risk.

Methods: A prospective cohort study among 47,683 post-menopausal women 49-64 years using data from the Observational Study and the control arm of the Dietary Modification trial of the Women's Health Initiative was conducted to evaluate the association between diet cost and diabetes risk. This study had two aims: 1) to examine the association between diet cost and diabetes and; 2) to determine the extent by which the socioeconomic gradient in diabetes was explained by diet cost. To estimate diet costs, a national food price database was linked to a food frequency questionnaire. Energy-adjusted diet costs were log-transformed to evaluate the impact of a relative increase in diet costs. The outcome was treated type 2 diabetes. Cox proportional hazards models examined the association between diet cost and diabetes after adjusting for covariates associated with diet cost and/or diabetes (e.g., age, smoking, family history, physical activity, body mass index, and income among others).

Results: Over 8 years of follow-up, 2,174 new cases of diabetes were observed. After adjusting for covariates, a 50% increase in energy-adjusted diet costs (e.g., from $4/d-$6/d) was associated with a 14% reduced risk of diabetes (hazard ratio (HR) 0.86; 95% CI 0.78, 0.94). In regression calibration models that incorporated estimated diet costs from a four-day food record, a 50% increase in energy-adjusted diet costs was associated with a 22% reduced risk of diabetes (HR 0.78, 95% CI 0.67, 0.90). In models adjusting for established intermediates of the income and diabetes association (e.g., physical activity or smoking), women with incomes of less than $10,000/year had a 1.4-fold increased risk of diabetes (95% CI 1.15, 1.78). Diet cost explained 15-19% of the association between income/education and diabetes.

Conclusions: As the first report to observe an association between diet cost and diabetes these results need to be compared to other studies. Examining upstream factors in diabetes risk, including diet costs, expands our understanding of socioeconomic disparities in health, while also exploring the consequences of the contemporary food environment on health.

Introduction

Type 2 diabetes mellitus (T2DM) is among the leading causes of morbidity and mortality in the United States (1). In the US, the prevalence of diagnosed diabetes has increased from 3.8% to 8.5% from 1990 to 2011 (2). T2DM has been characterized by dramatic disparities, including those by socioeconomic status (SES) and race/ethnicity (3, 4). Adults with lower incomes or less education have a significantly higher prevalence, and incidence and mortality rate of diabetes when compared to individuals with higher SES (5-10). Proximal lifestyle factors including diet, physical activity, and smoking, account for some, but not all, of the observed differences in T2DM by SES (5, 6, 8).

Differences in diet quality account for about 10% of the observed socioeconomic gradient in diabetes (6, 11). However, considering measurement error in evaluating diet, the extent of diet in accounting for disparities in diabetes is likely greater than 10%. Among dietary factors associated with a lower risk of diabetes are consumption of fruit and vegetables, whole grains, low-fat dairy, and moderate consumption of alcohol (12-17). Among dietary factors associated with a higher risk of diabetes are elevated consumption of processed meats and sugar-sweetened beverages, among others (18, 19).

It has been noted that on a per-calorie basis, numerous components of a diabetes-protective diet are more costly (e.g., fruits and vegetables), whereas many foods associated with an increased risk of diabetes are much less costly. Specifically, lower SES individuals are more likely to consumed processed meats and sugar-sweetened beverages and are also at higher

risk of diabetes (8, 20). One upstream factor that has not been previously examined in relation to the incidence of T2DM is the role of food prices and diet costs.

Numerous cross-sectional studies, conducted in a number of countries, have shown that higher quality diets are associated with higher diet costs (21-26). However, no US based studies have evaluated whether the consumption of a higher cost diet is associated with a reduced risk of diabetes. Using data from the Women's Health Initiative (WHI) Dietary Modification (DM) Trial and Observational Study (OS), we conducted an observational study to examine the association between diet cost and incident diabetes. Furthermore, the extent by which differences in diet cost explains the observed association between SES and diabetes was evaluated.

Methods

Data for this study came from the WHI comparison arm of the DM trial and the OS. The design and baseline descriptions of the WHI studies have been previously described (27). Briefly, 48,835 and 93,676 generally healthy postmenopausal women aged 50-79y were randomly assigned to the DM trial or enrolled in the OS, respectively, at 40 clinical centers across the United States between 1993 and 1998. The DM trial investigated the effect of a low-fat dietary pattern on the incidence of breast and colorectal cancers and heart disease over an average of 8.1 years of follow-up (28, 29). The recommended dietary pattern emphasized increased intake of fruits, vegetables and grains (27). The OS offered opportunities for investigating a broad range of epidemiologic questions. Many women not eligible for the DM trial entered the OS.

This section describes the study population, the assessment and reliability of diet costs estimates, potential confounders and intermediates of the diet cost and diabetes association, outcomes and the statistical methods used. The approach used to evaluate the extent by which diet cost explained socioeconomic disparities in diabetes incidence is also described.

Study Population

Given the emphasis of the current research on the relation between socioeconomic status (SES), as measured by family income and education, and diabetes, this study was restricted to women 49-64y at study baseline. Women from the intervention arm of the DM trial were not included in the present study, as their diets changed dramatically over time due to the intervention. We created an analytic cohort by combining data from two study arms (OS and DM-C). This was done to increase the available sample size and make use of measurement error correction techniques, which required the availability of date from four-day food records (4DFRs) for a sub-set of participants (described in detail below).

The first step in creating the analytic cohort was to make the two study arms as similar to each other as possible (30, 31). Because eligibility for the DM trial depended on consuming a high-fat diet (32), we treated year-1 as baseline for DM-C participants to avoid the complete truncation of dietary intakes based on data from year-0. For the OS, year-0 was baseline. In addition to using different baseline periods, the exclusion criteria for the dietary modification trial were applied to the WHI Observational Study (OS). This resulted in the exclusion of women with a history of breast cancer, colorectal cancer in past 10 years, endometrial cancer in past 10 years, other cancer within the past 10 years, with the exception of non-melanoma skin cancer, stroke or acute myocardial infarction (MI) 6 months prior to enrollment, body mass index (BMI)<18, hypertension (>200/>105 mm HG), food frequency questionnaire (FFQ) reported daily energy intake of <600 kcal or >5000 kcal, ≥10 meals out per week, special low-fiber diet, special diet due to malabsorption, unintentional weight loss of >15 lb (6.8 kg) in the 6 months prior to baseline, self-reported diabetes at age ≤ 21 (a proxy measure for history of type 1 diabetes). For both OS and DM-C participants, those without a diet cost estimate were excluded. Those with prior history of diabetes (either type 1 or type 2 diabetes), but not gestational diabetes, were also excluded.

Among these individuals, the analytic cohort was further restricted to those with complete data on variables of interest. Individuals missing data on physical activity, body mass index, hormone use, history of cardiovascular disease, education, smoking status, hypertension, depression status, social support and Healthy Eating Index-2005 (HEI-2005) were excluded. Given the delay in baseline for participants in the DM-C, women diagnosed with treated diabetes from baseline to year 1 were also excluded. The final sample size included 47,683 women 49-64y (36,227 from the OS and 11,456 from the DM-C).

Assessing diet cost

The exposure of interest was estimated diet cost, which was assessed using the WHI FFQ. Food and beverage prices per 100g edible portion from a national food price database were linked to the component foods in the WHI FFQ. The food price database was created by the Center for Nutrition Policy and Promotion (CNPP) at the USDA and was contemporary with 2001-2002 food prices (33). The CNPP price database provided the prices for 6,680 foods and beverages, excluding alcoholic beverages and bottled water. This price database assumed that all foods/beverages are purchased at a store and prepared at home. The method used for estimating alcohol prices has been described previously (21).

Diet costs were energy-adjusted using the residual method to account for differences in energy intake between individuals (34). This method estimates a residual value of diet cost based on the observed relation between energy intake and diet cost. A constant of 2000 kcal was then added to the estimated residual values to ease interpretation and comparability with other studies. For primary analyses, the diet cost variable was log-transformed to evaluate the impact of a percentage change in diet costs rather than an absolute difference. This was done for two reasons. First, the diet cost exhibited some positive skew. Second, one would not expect a 1-dollar increase in diet costs to have the same impact for individuals consuming low versus high

cost diets. For reporting purposes the relative risk of diabetes associated with a 50% increase in diet costs is reported. A 50% increase in diet cost roughly corresponds to the difference between the 85th and 15th percentile values ($5.51 vs. $3.62/day/2,000 kcal). A 50% increase was selected as it roughly corresponds to the difference between extreme quintiles if participants were grouped into five categories. In addition, a 50% increase is comparable to a two standard deviation increase (+$1.95) from the 25th%ile estimate of diet cost (i.e., from $3.90 to $5.85).

In order to assess the measurement characteristics of the diet cost estimate from the FFQ and to utilize approaches to reduce the impact of measurement error, a reliability sub-study was conducted. Briefly, the USDA food price database (described above) and the MyPyramid Equivalents Database Version 2.0 was merged with 560 four-day food records (4DFR) completed by women enrolled in the DM-C. Of these 560 women, 456 were included in the diabetes analysis. The MyPyramid Equivalents Database includes information on the number of servings of different foods groups and is needed to evaluate the HEI-2005 (35, 36).

The 4DFR were originally collected in order to evaluate adherence to the dietary modification trial and to complement data from the FFQ (27). To better measure long-term intake, avoid measuring correlated eating behaviors and include a weekend day, the 4DFR was completed on alternating days. Non-white women were over-sampled to participate in the 4DFR sub-study to more precisely evaluate dietary habits and adherence to the intervention among minority women. The correlation coefficient was 0.53 for a comparison of log-transformed energy adjusted diet costs and 0.51 for the HEI-2005 between the FFQ and 4DFR, comparable to values for saturated fat (0.56), niacin (0.54), or folate (0.52) for nutrients between the FFQ and 4DFR (37).

Potential Confounders

Key covariates were identified that are associated with both diet cost and the risk of diabetes. These variables and their parameterization are described below. All covariates, with the exception of body mass index, were assessed via questionnaire at baseline (or at year 1 for DM-C participants). Socio-demographic covariates included age group (49-54, 55-59, 60-64), race/ethnicity (American Indian/Alaskan Native, Asian/Pacific Islander, non-Hispanic white, black, Hispanic/Latina and unknown [including other/mixed race]), family income (<10, 10-19, 20-34, 35-49, 50-74, 75-99, 100-149, and ≥150 in $1000 and a missing category), educational attainment (<high school, high school graduate/equivalent, some college, college degree/some post-graduate education and master's degree or higher) and having a partner (yes/no). While we did use a complete case approach for most analyses, a missing indicator was used since income was missing for 5.5% of respondents.

Additional variables included recreational physical activity (<1.67, 1.75-6.75, 6.83-12.83, 12.87-22.92, ≥23 metabolic equivalents [MET] hours/wk), family history of diabetes (yes, no and don't know), smoking status (former, never or current), use of pills or patches for hormone therapy (former, never or current), history of cardiovascular disease and hypertension (yes/no), body mass index category (<25 [underweight/healthy weight], 25-29.9 [overweight], 30-34.9 [class I obese], 35-39.9 [class II obese], and ≥40 [class III obese] kg/m^2), a social support scale and depression status. Each of these variables was modeled as a categorical variable, with the exception of social support, which was treated as a continuous variable.

Finally, given the inclusion of participants from both the OS and DM-C we adjusted for study arm (OS vs. DM-C) and arm of the hormone trial (HT) as participants in the DM-C could also participate in the HT trial (38). No adjustment was conducted for participation in the Calcium and Vitamin D (CaD) trial arm, as there was no relation between CaD arm and diabetes risk (39).

Potential Intermediates

To de-compose the relation between diet cost and diabetes a number of variables that are consequences of diet cost, but likely associated with diabetes risk, were also assessed. Additional variables included alcohol servings per week (none, 0.21-1.9, 2-6.9, 7-13.9 and ≥14), Healthy Eating Index-2005 (HEI-2005), Alternative Healthy Eating Index-2010, glycemic load and glycemic index (36, 40). For analysis, the later four were treated as continuous variables. The methods for calculating HEI-2005 and AHEI-2010 have been described in detail elsewhere (36, 41). While alcohol is included as part of the HEI-2005, we opted to evaluate an additional variable because the HEI-2005 groups alcohol with added sugars and solid fat, as a dietary constituent to avoid. This is important, because there is an inverse association between moderate alcohol use and type 2 diabetes, necessitating the separation of alcohol intake from the global measures of diet quality (13, 16). Dietary covariates were assessed via food frequency questionnaire (FFQ). The development and measurement characteristics of the WHI FFQ have been previously described (37).

Outcome

Diagnosis of diabetes prior to study participation was documented by self-report prior to randomization. Previous gestational diabetes was not included in the definition of prior diabetes. New cases of treated diabetes (i.e., by insulin or pills) were identified by self-report at each semiannual contact. While the outcome of treated diabetes is dependent on seeing a medical professional, 93.6% of participants reported having a regular health care provider at baseline and 86% reported seeing their provider within the past year. Objective outcome data (i.e., data on fasting plasma glucose or oral glucose tolerance test) was only available for a subset of participants in the DM-C. Given the age of the population, all new cases of diabetes were assumed to be T2DM. Events were enumerated after at least 1-year of follow-up to avoid

including prevalent cases as incident cases. Outcomes were assessed over 8 years of follow-up.

Statistical methods

Cox proportional hazards regression was used to estimate the relative risk of incident treated diabetes associated with a 50% increase in diet cost. A series of models were fit that accounted for an increasing number of variables. The first set of models (Model 1) adjusted for study arm, age group, and race/ethnicity. Model 2 additionally adjusted for additional socio-demographic and behavioral factors associated with diabetes risk and diet cost, including family household income, educational attainment, having a partner, family history of diabetes, smoking status, hormone use, recreational physical activity, BMI, social support, depression status and history of cardiovascular disease and hypertension. In models evaluating the effect of income/education on diabetes risk, the other SES measure was excluded.

Because the estimate of diet cost is an error-prone measure, regression calibration was used to account for measurement error in the estimate of diet cost, treating data from the 4DFR as an alloyed gold standard (42, 43). An “alloyed gold standard” is a reference measure that is not a perfect gold standard, but rather a measure that captures the true exposure of interest better than the primary instrument (i.e., the FFQ). While clearly, the 4DFR is an imperfect measure of diet as shown by studies of doubly labeled water, it has been shown to have better measurement characteristics than an FFQ (44). This approach reduces the bias from measurement error assuming that the errors in the two instruments are uncorrelated, though previous work has shown that even in the presence of modest correlated errors, the estimate from regression calibration should yield a less biased estimate of the observed exposure-disease relationship using the error-prone measure (43). The %blinplus SAS macro was used to

implement regression calibration (45). The coefficients for HEI-2005 and AHEI-2010 were also included in separate calibration models.

Mediation Framework

We further evaluated the extent to which the association between socioeconomic status (SES) and diabetes is mediated or explained by diet cost. We included the same covariates from the previous Model 2, but did not include the other SES variable in the assessment of mediation (i.e., education was not included as a covariate in the assessment of diet cost mediating the relation between income and diabetes). To facilitate estimation of a summary measure of mediation we coded both SES variables as continuous variables (e.g., income <$10,000 = 1; $10-19,999 = 2, etc.). We compared the functional form of each SES variable by comparing continuous coding and categorical coding to determine whether treatment of these variables as continuous appropriately captured the SES-diabetes association. Mediation was quantified by calculating the percentage change in the regression coefficients (log hazard ratio) for income and education in two models, one that omits diet cost and a second that includes diet cost (46). The %mediate SAS macro was used to assess the extent to which diet cost mediated the association between the two SES measures and diabetes, the confidence interval of the proportion explained and a p-value for mediation (47). The formula used to derive standard errors of the mediated effect was derived from Equation 5 in Lin *et al* (46). Exploratory analyses examined the extent to which the SES-diabetes association was mediated after accounting for measurement error in the diet cost estimate using the same approach. The same approach was used to assess the impact of dietary intermediates (e.g., HEI-2005 and AHEI-2010) of the association between diet cost and diabetes.

The proportional hazards assumption was evaluated for all primary analyses by evaluating the Schoenfeld residuals. Analyses were conducted using Stata 13.1 (College Station, TX), SAS 9.3 for Windows (Cary, NC 2013), for the %mediate and %blinplus macros (45, 47).

Results

Population characteristics

Subject characteristics are provided in **Table 1**. Average diet costs by socio-demographic, anthropometric and behavioral characteristics are also provided. The mean age at study baseline was 58.1y (SD=4.1). The cohort was primarily non-Hispanic white, and had a wide range of family incomes. About nine percent of the cohort had family incomes less than $20,000/year, while more than a quarter had family incomes greater than $75,000. A similarly broad distribution of education was observed, though only a small proportion of women had not graduated from high school. About 40% of the cohort was healthy weight/underweight and 27% were considered obese. The average HEI-2005 score was 68.3 (SD=10.5) (out of 100 possible) and the average number of MET hours from recreation physical activity per week was 13.5 (SD=14.4).

The average energy-adjusted diet cost was $4.58 (SD=$0.98; median=$4.47; 10^{th} percentile=$3.45; 90^{th} percentile=$5.82). Socio-demographic, anthropometric and behavioral characteristics were associated with diet costs. Older women consumed slightly more costly diets than women 49-54y (p-trend<0.001). Non-Hispanic white women consumed significantly more expensive diets than non-Hispanic black and Hispanic/Latina women (p-difference<0.001). Both education and income were positively associated with higher diet costs (p-trend<0.001 for both). The diets of women with family incomes greater than $150,000 were 29% higher than women with incomes less than $10,000. A similar relationship was observed for education. Women with healthier diets as measured by HEI-2005 tended to have more costly

diets, as did women who were more physically active (p-trend<0.001 for both). Those with lower BMIs consumed less costly diets than heavier participants (p-trend<0.001).

Association between diet cost and diabetes

The average length of follow-up was 7.6 years and 2,174 new diagnoses of diabetes were observed. The incidence rate of diabetes was 59.8 per 10,000 person-years. The association between diet cost, income and education as they relate to risk of diagnosed diabetes is provided in **Table 2**. In minimally adjusted models, a 50% increase in diet costs was associated with a 38% reduced risk of being diagnosed with diabetes (95% CI 33-43%). After adjusting for potential confounders, a 50% increase in diet cost was associated with a 14% reduced risk of diabetes (95% CI 6-22%). In analyses accounting for measurement error in the diet cost estimate, a 50% increase in diet cost was associated with a 22% reduced risk of diabetes (hazard ratio [HR] 0.78; 95% CI 0.67, 0.90). For reference, a 50% increase in diet cost roughly corresponds to the difference between the 85th and 15th percentile values ($5.49 vs. $3.60/day/2,000 kcal). The effect of alternative parameterizations of diet cost (e.g., sextiles and continuous) on the risk of diabetes is provided in **Table 5**.

The extent of the association between diet cost and diabetes was also compared to other dietary factors (see **Figure 1**). A 2-standard deviation increase in diet costs ($1.95) was associated with a 17% reduced risk of diabetes (HR 0.83; 95% CI 0.75, 0.91), while a 2-standard deviation increase in HEI-2005 (21-points) was associated with a 6% reduced risk of diabetes (HR 0.94; 95% CI 0.86, 1.03). For AHEI a 23-unit increase was associated with a 9% reduced risk of diabetes (HR 0.91; 95% CI 0.83, 1.00). From fully adjusted regression calibration models diet cost had the strongest relation to diabetes risk (HR 0.78; 95% CI 0.67, 0.90) than either AHEI-2010 (HR 0.84; 95% CI 0.71, 1.00) or HEI-2005 (HR 0.91; 95% CI 0.78, 1.07).

Formal mediation analyses evaluated the following potential intermediates of the observed diet cost and diabetes association: HEI-2005, AHEI-2010, glycemic index, glycemic load, and alcohol intake (see **Table 3**). These variables were considered intermediates of the diet cost and diabetes association, not confounders. In adjusted models, HEI-2005 accounted for none of the observed association between diet cost and diabetes. Adjustment for AHEI-2010 accounted for 10% (95% CI -11, 30%) of the observed association between diet cost and diabetes. Neither glycemic load nor glycemic index explained the association between diet cost and diabetes. Alcohol intake accounted for 67% of the association between diet cost and diabetes, with the association between diet cost and diabetes no longer statistically significant after accounting for alcohol (HR 0.96; 95% CI 0.86, 1.05). In regression calibration models that accounted for measurement error in the HEI-2005 and AHEI-2010 scores, HEI-2005 did not account for the association between diet cost and diabetes, though AHEI-2010 accounted for 14% of the association in fully adjusted models.

Diet cost as a mediator of the socioeconomic gradient in diabetes

A secondary aim of this study was to assess the extent by which differences in diet cost may account for the socioeconomic gradient in diabetes. In minimally adjusted models, both income and education were strongly and negatively associated with diabetes risk (see **Table 2**). Compared to individuals with incomes greater than $150,000/year women with incomes less than $10,000 had a 3.4-fold increased risk of diabetes (HR 3.44; 95% CI 2.78, 4.25). A similar association was observed for education. After accounting for additional covariates, compared to high-income women, those incomes less than $10,000 had a 43% increased risk of being diagnosed with diabetes (HR 1.43; 95% CI 1.15, 1.78).

Mediation analyses suggested that diet cost accounted for some of the observed association between income and diabetes (18.8% [95% CI 0.8, 36.8%]), after accounting for numerous

covariates (see **Table 4**). The mediating effect was generally similar in adjusted and unadjusted models. We conducted secondary analysis the extent to which the SES-diabetes association was mediated by diet cost after accounting for measurement error in the diet cost estimate. For income, 34.2% of the association between income and diabetes was explained by diet cost, while a quarter of the education gradient in diabetes was explained by diet cost.

In primary analyses, there was some evidence that the proportional hazards assumption was violated (Schoenfeld residuals global test $p<0.05$ for analyses treating diet cost, education and income as the main effects). The variables responsible for the violation of the assumption were identified and subsequent analyses stratified on these variables allowing the baseline hazards to vary. Comparing the results of the simple Cox model to the stratified Cox model revealed that the main effect coefficients of interest were qualitatively unchanged (<2.5% change in log hazard ratio of interest). Therefore, violation of the proportional hazards assumption was not considered a major threat to the validity of the estimated hazard ratios of interest.

Discussion

Association between diet cost and diabetes

In this prospective cohort study of 47,683 post-menopausal women, a 50% increase in diet costs was associated with a significantly reduced risk of incident treated diabetes (HR 0.86; 95% CI 0.78, 0.94). In analyses accounting for measurement error in the estimate of diet cost, a 50% increase in diet cost was associated with a 22% reduced risk of being diagnosed with diabetes (HR 0.78; 95% CI 0.67, 0.90).

Systematic mediation analyses were conducted to evaluate what dietary variables explained the observed association between diet cost and diabetes risk. In adjusted models, HEI-2005 and glycemic index and glycemic load had little impact on the association between diabetes and diet

cost, while alcohol consumption explained much of the observed association. AHEI-2010 explained a modest amount of the association between diet cost and diabetes. While both HEI-2005 (r=0.32) and AHEI-2010 (r=0.38) were both correlated with diet cost, HEI-2005 was not associated with diabetes risk after accounting for covariates, a finding consistent with previous research (41). Moderate alcohol intake has previously been identified as being inversely associated with diabetes risk (13, 16). In the present study, alcohol intake was also strongly and inversely related to diabetes risk. After accounting for all covariates, women consuming 14 or more alcoholic drinks per week had a 43% reduced risk of diabetes (HR 0.57; 95% CI 0.42, 0.77) compared to women consuming no alcohol. Alcohol consumption was strongly related to diet cost. Non-drinkers had an average diet cost of $4.17/d compared to $6.45/d for those consuming 14+ drinks per week. Some previous work has omitted alcohol from calculations of diet cost, contending that they are disproportionately costly and that consumers may respond to alcohol prices differently than other foods/beverages (23, 48). Here, we opted to include alcoholic beverages in the estimates of diet cost in order to capture the complete cost of the diet and its relation to diabetes.

Comparing the observed association between diet cost and diabetes in context with other factors associated with diabetes is informative. Compared to the effect of AHEI-2010 on diabetes risk, the effect of diet cost was somewhat weaker. A 2-standard deviation increase in diet costs was associated with a 17% reduced risk of diabetes compared to 9% for AHEI. These results suggest that diet cost may be more strongly related to diabetes risk than frequently used diet quality measure.

The primary analyses here evaluated diabetes risk associated with a 50% increase in daily diet cost. The average daily cost observed here was $4.58, which would correspond to an increase of $2.29 to $6.87. This corresponds to $836/year based on 2001-2002 prices or $1087 in 2013 dollars after accounting for inflation. Whether this amount poses a true barrier to individuals is

an open question, though there is considerable evidence that individuals are highly sensitive to food costs. After taste, food cost was the most important factor in choosing foods (49). In 2007-2010, 40% of US adults reported that food prices were “very important” in choosing foods at the grocery store, while only 11% said it was “not important” or “not too important” (49, 50). As one would expect, lower income adults were 2.8-times as likely to identify food cost as a “very important” consideration compared to higher income adults (50).

Prospective studies evaluating diet cost and health are few. To our knowledge, this is the first prospective study evaluating the association between diet cost and diabetes incidence, though one recent observed that higher prices of healthy foods were associated with increased blood glucose level among individuals with type 2 diabetes (51). One prior prospective study evaluating diet cost was conducted in Spain and found that lower diet costs were not associated with an increased risk of weight gain, though this study did not evaluate any other health outcomes (52). To date, most research focused on diet costs have been cross-sectional studies describing the relation between cost and diet quality (21-24, 26, 52). It has also been suggested that socioeconomic disparities in diet quality are partially attributed to diet cost (53, 54). In relation to health outcomes, a limited number of cross-sectional studies have observed an inverse association between diet cost and body mass index (26, 55). The present study fills an important gap in the literature and represents the first prospective evaluation of diet cost and diabetes incidence.

Diet cost as a mediator of the SES-diabetes association

Given the dramatic socioeconomic gradient in diabetes and diet cost, we also attempted to quantify the extent by which the socioeconomic gradient in diabetes could be attributed to differences in diet cost. Mediation analyses revealed that about 15-19% of the association

between SES and diabetes could be attributed to diet cost after accounting for numerous covariates.

The socioeconomic gradient in diabetes has been attributed to proximal factors, including chronic systemic inflammation (i.e., c-reactive protein and interleukin-6), and lifestyle and anthropometric factors, including smoking, diet quality, physical activity, moderate alcohol use and body mass index/obesity (6-8, 11, 56). Individually, factors such as smoking, physical activity, and dietary factors explain between 1-12% of the association between SES and incident diabetes, while BMI/obesity explains approximately 20% of the SES-diabetes relationship in other studies (6, 11). The present study included the standard behavioral and anthropometric intermediates, but includes diet cost as a novel, upstream intermediate of the social gradient in diabetes risk. Here, we observed that a modest amount of the association between income/education and diabetes incidence was explained by differences in diet cost (see **Table 3**). The quantitative impact of diet cost as a mediator was greater than the impact of hypertension (14.5%) or AHEI-2010 (10.1%), comparable to the impact of physical activity (18.0%), but less than the effect of BMI alone (48.4%). When mediation approaches were applied to the regression coefficients from measurement-error correction models, the extent by which the association between income and education and diabetes was explained by diabetes increased from 18.8% and 14.8% to 34.2% and 25.3%, respectively. Given the qualitative difference between the corrected and uncorrected estimated mediation effects, future work should formalize how to incorporate methods to correct for measurement error in evaluating mediation. Differences in the extent of measurement error for potential intermediates complicate the ranking of intermediate variables.

The primary limitation of this study was the use of an FFQ instrument to estimate diet costs. Deriving diet costs using a national food prices database may not reflect the actual prices for food paid by individual WHI participants. This is similar to the weakness inherent in deriving

nutrient intakes from nutrient composition databases, which do not reflect potential heterogeneity in the nutrient levels of foods actually consumed. Despite limitations in the use of standard prices database, it represents a meaningful source of information on food prices that can be linked to individual data on diets and health. A related concern is that actual consumer behavior and the importance of cost to consumers was not assessed. Therefore these observational results should be interpreted cautiously. While we did observe a robust association between diet cost and risk of treated diabetes, we do not have any data to indicate that price was a key factor for that respondent, though previous work has indicated that food costs are important determinants of food choice (49). The food price database was based on prices from 2001-2002, which may not capture the distribution of current food costs. Beyond the challenges in using a national food price database, an FFQ is an error-prone instrument in assessing diet cost (or any nutrient). Chief among these limitations is that the FFQ relies on a fixed foods list, which may omit important foods for assessing diet costs. Our reliability study, which estimated diet cost from the WHI FFQ and 4DFRs, indicate a modest correlation between the two instruments (r=0.52). Though the estimate from the 4DFR is not an unbiased estimate of diet cost, it does reduce many of the potential sources of error in the FFQ, including reliance on a fixed food lists and error in recalling portion size. Given concerns regarding the measurement error from the FFQ, we employed regression calibration to account for measurement error in the diet cost estimate. As expected, the strength of the association between diet cost and CVD became stronger. The regression calibration approach used here assumes that the two instruments have uncorrelated errors. However, modest correlated errors yield a better estimate of the exposure-disease relationship than relying on the error-prone instrument alone (43). Further, although we considered the 4DFR an “alloyed gold standard,” the amount of variation in energy intake explained by 4DFR self-report compared to biomarkers

of energy intake is quite limited (44). Nonetheless, the 4DFR explained more of the variation in biomarker-derived energy intakes than the FFQ and may be sufficient for epidemiologic studies.

In addition, though we adjusted for a wide range of potential confounders we cannot rule out residual confounding due to poorly measured or unmeasured variables. **Figure 2** evaluates the impact of each hypothesized confounder on the association between diet cost and diabetes, observed that the SES variables, physical activity and BMI are the most important confounders. While BMI was measured and not based on self-report, the use of questionnaire data to evaluate physical activity likely results in residual confounding by physical activity (57). Future studies of diet cost and health outcomes could make use of objectively measured physical activity data to confirm that the association between diet cost and diabetes is not attributable to residual confounding by physical activity.

Furthermore, education and income were also important confounders of the association between diet cost and diabetes. The use of education and family income as the sole measures of SES may introduce residual confounding by SES. While both measures are routinely collected in health studies they fail to capture the complete dimensions of SES (58). For example, educational attainment does not account for the quality of education and captures experiences that for most study participants occurred many decades prior to baseline. As a measure of access to absolute resources, income-based measures fail to capture total wealth, which is the true underlying variable of interest (59). We limited our analysis to working-age women (<65y) and the income measure was family rather than individual income. The role of diet cost should be explored in other studies that collect richer measures of SES, such as accumulated wealth.

Healthcare access may be an important confounder of the diet cost and diabetes association and could also be a possible mediator of the SES and diabetes association. Health care access

may be particularly important given the use of self-reported incident diabetes as the outcome. In adjusted models, the relationship between diet cost and diabetes risk was unchanged after adjusting for having any insurance or length of time since last medical visit. In addition, having insurance and length of time since last medical visit did qualitatively alter the association between family income and education and diabetes risk. The WHI study population was generally well-insured (94% had insurance) and received frequent medical care (88% visiting a medical provider in the prior two years). However, in less well-insured populations, the impact of health care access on the diet cost and diabetes association should be carefully considered.

Methods for mediation analyses for non-linear models are an area of rapid development (60, 61). We evaluated mediation by comparing the difference in the log hazard ratio for income and education for models with and without diet cost. Applying this approach in non-linear models requires a number of generally untestable assumptions to be made, regarding non-collapsibility of the outcome and the potential challenge of confounding by unmeasured variables of the mediator and outcome. Here, the outcome was sufficiently rare (4.6%) that non-collapsibility is unlikely to pose a problem (61). However, we cannot rule out the possibility that an unknown confounder of the mediator and outcome may bias the observed effects. The consistency of the observed mediation effect between adjusted and unadjusted models relaxes some concerns regarding the impact of confounding on quantifying the mediation effect.

This study also had a number of strengths. First, by comparison to other prospective cohorts, the sample was socioeconomically heterogeneous, which permitted evaluating SES disparities. Second, the study collected dietary data in FFQ and 4DFRs, which allowed us to address the impact of measurement error in evaluating the association between diet cost and diabetes.

Conclusions

In summary, we observed that consuming a higher cost diet was associated with a reduced risk of diabetes. Furthermore, we found that differences in diabetes risk by SES could be partially attributed to differences in diet cost. The extent of this mediation was comparable to other lifestyle factors, such as diet quality or physical activity. This study represents the first prospective examination of the association between diet cost and diabetes. Diet cost appears to be a factor worth additional study as it relates to cardiometabolic disease risk. Future study could evaluate the role of diet cost in diabetes management and the potential prevention of diabetes complications. Given the paucity of research on diet costs and diabetes, the results of this study ought to be compared to those from other studies conducted in different populations.

Table 1. Participant characteristics and average energy-adjusted diet costs in the Women's Health Initiative analytic cohort (n=47,683)

				$/2000 kcal	
	new cases	N	% of total	Mean	95% CI
Age group					
49-54	533	13,524	28.4	4.54	4.52, 4.56
55-59	770	17,442	36.6	4.59	4.58, 4.61
60-64	871	16,717	35.1	4.60	4.58, 4.61
P-trend				<0.001	
Race/ethnicity					
American Indian/Alaskan Native	15	172	0.4	4.24	4.11, 4.37
Asian/Pacific Islander	84	1,343	2.8	4.60	4.54, 4.66
Black	395	3,887	8.2	4.10	4.07, 4.13
Hispanic	154	1,909	4.0	4.12	4.08, 4.16
White, not Hispanic	1484	39,775	83.4	4.65	4.64, 4.66
Unknown (incl. other)	42	597	1.3	4.52	4.45, 4.60
P-difference				<0.001	
Family income ($1000)					
< $10	122	1,183	2.5	4.01	3.96, 4.06
$10-19	225	2,972	6.2	4.11	4.08, 4.14
$20-34	473	8,040	16.9	4.32	4.30, 4.34
$35-49	445	9,110	19.1	4.50	4.48, 4.52
$50-74	440	11,032	23.1	4.64	4.62, 4.66
$75-99	200	5,805	12.2	4.81	4.78, 4.83
$100-149	112	4,522	9.5	4.94	4.91, 4.97
> $150	51	2,356	4.9	5.14	5.10, 5.18
P-trend				<0.001	
Missing	106	2,663	5.6	4.53	4.50, 4.57
Educational attainment					
<High school	139	1,487	3.1	3.92	3.88, 3.96
High school/equivalent	419	6,974	14.6	4.28	4.26, 4.30
Some college	923	17,104	35.9	4.52	4.50, 4.53
College graduate	375	11,775	24.7	4.74	4.72, 4.76
≥Master's degree	318	10,343	21.7	4.79	4.77, 4.81
P-trend				<0.001	
HEI-2005					
Q1: 26-58 [lower diet quality]	631	9,537	20.0	4.17	4.14, 4.19
Q2: 59-66	471	9,537	20.0	4.41	4.39, 4.43
Q3: 67-72	428	9,537	20.0	4.62	4.6, 4.64
Q4: 73-77	345	9,537	20.0	4.79	4.77, 4.8
Q5: 78-93 [higher diet quality]	299	9,536	20.0	4.89	4.88, 4.91
P-trend				<0.001	

Table 1, continued

				$/2000 kcal	
	new cases	N	% of total	Mean	95% CI
AHEI-2010					
Q1: 13-35 [lower diet quality]	579	9,537	20.0	4.08	4.06, 4.10
Q2: 36-42	509	9,537	20.0	4.35	4.33, 4.37
Q3: 42-48	415	9,536	20.0	4.57	4.56, 4.59
Q4: 49-55	382	9,537	20.0	4.81	4.79, 4.82
Q5: 56-95 [higher diet quality]	289	9,537	20.0	5.09	5.07, 5.11
P-trend				<0.001	
Alcohol servings per week					
None	1216	18,189	38.2	4.17	4.16, 4.18
0.21-1.92 per week	589	14,745	30.9	4.43	4.42, 4.44
2-6.9 per week	245	8,932	18.7	4.88	4.86, 4.89
7-13.9 per week	80	3,782	7.9	5.43	5.40, 5.45
≥23 per week	44	2,035	4.3	6.45	6.40, 6.50
P-trend				<0.001	
Recreational physical activity (MET-hours/wk)					
Q1: ≤1.67	718	9,561	20.1	4.19	4.17, 4.20
Q2: 1.75-6.75	523	9,912	20.8	4.42	4.40, 4.44
Q3: 6.83-12.83	393	9,173	19.2	4.59	4.58, 4.61
Q4: 12.87-22.9	307	9,524	20.0	4.76	4.74, 4.78
Q5: ≥23	233	9,513	20.0	4.95	4.93, 4.97
P-trend				<0.001	
Body Mass Index category (kg/m^2)					
Underweight/healthy weight: <25	220	18,662	39.1	4.72	4.71, 4.73
Overweight: 25-29.9	557	16,128	33.8	4.59	4.58, 4.61
Class I Obesity: 30-34.9	658	7,895	16.6	4.42	4.40, 4.44
Class II Obesity: 35-39.9	413	3,157	6.6	4.29	4.26, 4.32
Class III Obesity: ≥40	326	1,841	3.9	4.19	4.15, 4.22
P-trend				<0.001	

Table 2. Association between diet cost, income and education and incidence of diabetes in Women's Health Initiative analytic cohort (n=47,683)

	Uncorrected				Corrected	
	Model 1[1]		Model 2[2]		Model 2[2]	
	HR	95% CI	HR	95% CI	HR	95% CI
Diet cost ($/2000 kcal)						
Per 50% increase	0.62	0.57, 0.67	0.86	0.78, 0.94	0.78	0.67, 0.90
P-value	<0.001		<0.001		0.001	
Linear family income ($1000)						
< $10	3.44	2.78, 4.25	1.43	1.15, 1.78	-	-
$10-19	2.88	2.40, 3.46	1.36	1.13, 1.64	-	-
$20-34	2.42	2.08, 2.81	1.29	1.10, 1.51	-	-
$35-49	2.02	1.79, 2.29	1.23	1.08, 1.39	-	-
$50-74	1.70	1.55, 1.86	1.16	1.07, 1.28	-	-
$75-99	1.42	1.34, 1.51	1.11	1.04, 1.18	-	-
$100-149	1.19	1.16, 1.23	1.05	1.02, 1.09	-	-
≥ $150	ref		ref		-	-
P-trend	<0.001		<0.001			
Linear education						
<High school	2.65	2.26, 3.09	1.44	1.23, 1.69	-	-
High school/equivalent	2.07	1.85, 2.33	1.32	1.17, 1.48	-	-
Some college	1.63	1.50, 1.76	1.20	1.11, 1.30	-	-
College graduate	1.28	1.23, 1.33	1.10	1.05, 1.14	-	-
≥Master's degree	ref		ref		-	-
P-trend	<0.001		<0.001		-	-

[1] Adjusted for study arm, age group and race/ethnicity. Income analyses adjusted for having a partner.

[2] Adjusted for factors from Model 1 in addition to hormone use, recreational physical activity, history of cardiovascular disease, family history of diabetes, hypertension, smoking status, BMI, social support scale and depression status. Diet cost models additionally adjusted for income, having a partner and education.

Table 3. Role of diet measures in accounting for the association between diet cost and diabetes in the Women's Health Initiative analytic cohort (n=47,683)

	Not adjusted for diet measure; HR (95% CI)	Adjusted for diet measure; HR (95% CI)	% mediated (95% CI)	p-value
Uncorrected				
Model 1[1]				
HEI-2005	0.62 (0.57, 0.67)	0.68 (0.63, 0.75)	21.2 (14.1, 28.2)	<0.001
AHEI-2010	-	0.68 (0.62, 0.74)	18.6 (10.9, 26.2)	<0.001
Glycemic load	-	0.62 (0.57, 0.68)	2.3 (0.9, 3.6)	<0.001
Glycemic index	-	0.62 (0.56, 0.68)	1.3 (-8.9, 11.4)	0.81
Alcohol intake (5 levels)	-	0.77 (0.70, 0.85)	47.2 (34.7, 59.6)	<0.001
Model 2[2]				
HEI-2005	0.86 (0.78, 0.94)	0.86 (0.78, 0.94)	0 (-18.9, 18.9)	0.99
AHEI-2010	-	0.87 (0.79, 0.96)	9.6 (-10.8, 30.0)	0.36
Glycemic index	-	0.86 (0.78, 0.94)	1.4 (-2.1, 4.9)	0.44
Glycemic load	-	0.83 (0.75, 0.92)	-21.0 (-53.7, 11.6)	0.21
Alcohol intake (5 levels)	-	0.96 (0.86, 1.05)	66.6 (18.7, 115)	0.006
Corrected[3]				
Model 1[1]				
HEI-2005	0.61 (0.56, 0.66)	0.71 (0.63, 0.79)	30.4	-
AHEI-2010	-	0.72 (0.64, 0.81)	31.9	-
Model 2[2]				
HEI-2005	0.85 (0.77, 0.93)	0.85 (0.77, 0.95)	1.4	-
AHEI-2010	-	0.88 (0.78, 0.98)	14.0	-
Model 3[2]				

[1] Adjusted for study arm, age group and race/ethnicity.

[2] Adjusted for factors from Model 1 in addition to hormone use, recreational physical activity, history of cardiovascular disease, family history of diabetes, hypertension, smoking status, BMI, social support and depression status.

[3] Analyses correcting for measurement error in diet cost do not adjust for OS vs. DM-C because all individuals in validation data come from the DM-C trial.

Table 4. Role of diet cost in explaining association between SES and diabetes in the Women's Health Initiative analytic cohort (n=47,683)

	Not adjusted for diet cost; HR (95% CI)	Adjusted for diet cost; HR (95% CI)	% mediated (95% CI)	p-value
Uncorrected				
Model 1[1]				
Income (comparing < $10,000 to ≥ $150,000)	3.44 (2.78, 4.25)	2.81 (2.26, 3.50)	16.3 (11.0, 21.7)	<0.001
Education (comparing < high school to ≥ master's)	2.68 (2.29, 3.14)	2.31 (1.97, 2.71)	16.1 (11.8, 20.4)	<0.001
Model 2[2]				
Income (comparing < $10,000 to ≥ $150,000)	1.43 (1.15, 1.78)	1.34 (1.07, 1.67)	18.8 (0.8, 36.8)	0.04
Education (comparing < high school to ≥ master's)	1.44 (1.23, 1.69)	1.37 (1.17, 1.61)	14.8 (4.7, 24.9)	0.004
Corrected for measurement error[3]				
Model 1[1]				
Income (comparing < $10,000 to ≥ $150,000)	3.38 (2.74, 4.18)	2.47 (1.91, 3.20)	25.7	-
Education (comparing < high school to ≥ master's)	2.64 (2.26, 3.09)	2.03 (1.65, 2.49)	27.1	-
Model 2[2]				
Income (comparing < $10,000 to ≥ $150,000)	1.43 (1.15, 1.77)	1.25 (0.98, 1.59)	34.2	-
Education (comparing < high school to ≥ master's)	1.44 (1.22, 1.68)	1.31 (1.10, 1.56)	25.3	-

[1] Adjusted for age group, race/ethnicity and study arm (OS vs. DM-C) and HT study arm

[2] Adjusted for age group, race/ethnicity, family history of diabetes, physical activity, HT use, smoking status, history of cardiovascular disease, history of hypertension, social support, depression status and study arm (OS vs. DM-C) and HT study arm. Income models adjusted for partner. Income analysis excludes 5.7% of sample with no income data.

[3] Analyses correcting for measurement error in diet cost do not adjust for OS vs. DM-C because all individuals in validation data come from the DM-C trial.

Table 5. Association between diet cost and incidence of diabetes using alternative parameterizations of diet cost in the Women's Health Initiative analytic cohort (n=47,683)

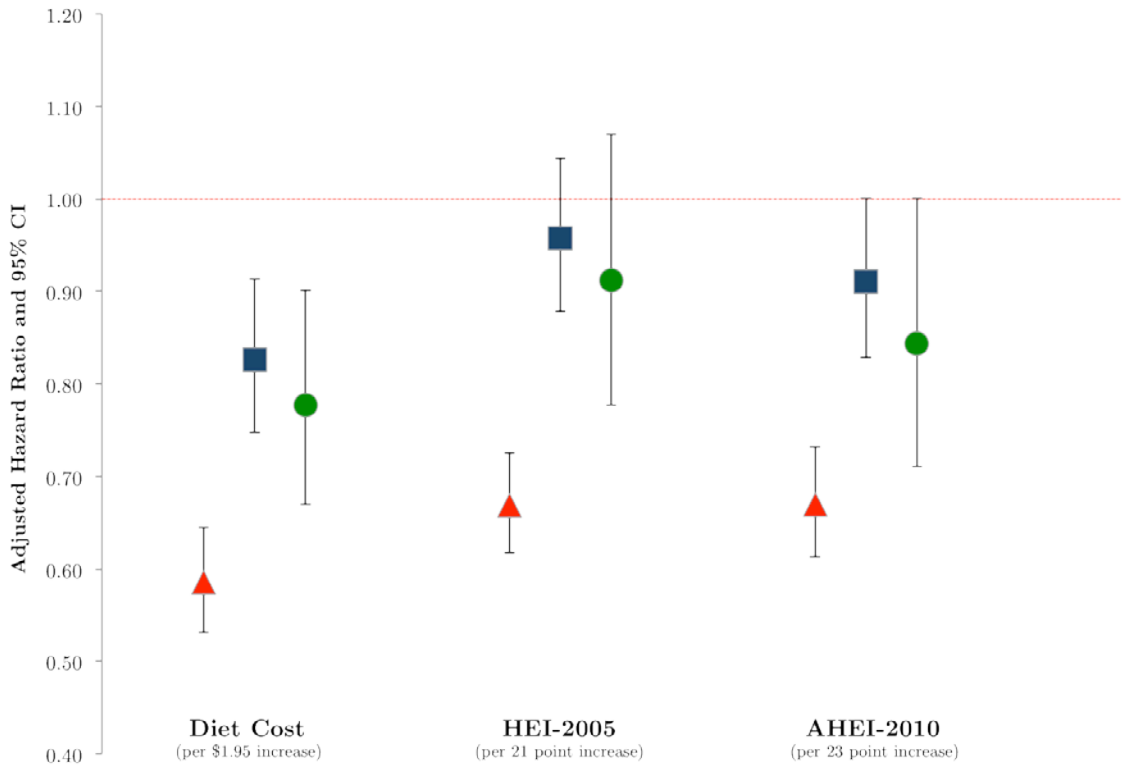
	Uncorrected				Corrected	
	Model 1[1]		Model 2[2]		Model 3[2,4]	
	HR	95% CI	HR	95% CI	HR	95% CI
Diet cost ($/2000 kcal)						
Per $1.95 increase[3]	0.59	0.53, 0.65	0.83	0.75, 0.92	0.78	0.74, 0.88
P-value	<0.001		<0.001		<0.001	
Diet cost categories						
Q1: $1.39-3.67	1.98	1.69, 2.31	1.21	1.03, 1.43	-	-
Q2: $3.68-4.09	1.56	1.33, 1.83	1.07	0.91, 1.25	-	-
Q3: $4.10-4.46	1.44	1.22, 1.70	1.06	0.90, 1.26	-	-
Q4: $4.47-4.86	1.43	1.21, 1.68	1.18	0.99, 1.39	-	-
Q5: $4.87-5.43	0.98	0.82, 1.18	0.91	0.76, 1.09	-	-
Q6: $5.43-12.09	ref		ref		-	-
P-trend	<0.001		0.006			

[1] Adjusted for study arm, age group and race/ethnicity. Income analyses adjusted for having a partner.

[2] Adjusted for factors from Model 1 in addition to income, having a partner, education attainment, hormone use, recreational physical activity, history of cardiovascular disease, family history of diabetes, hypertension, smoking status, BMI, social support scale and depression status.

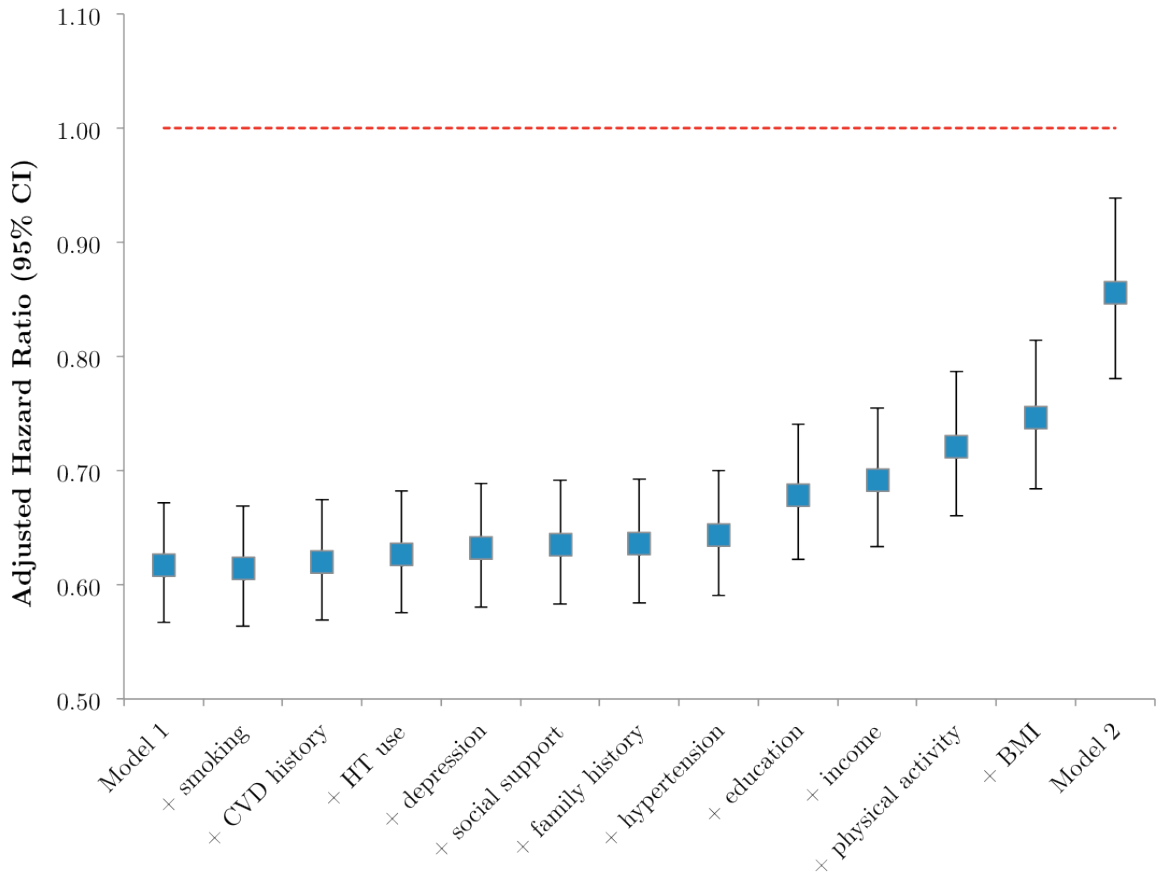
[3] Value corresponds to change per 2*standard deviation increase (SD = $0.975).

Figure 1. Comparison of association between diet cost, HEI-2005, AHEI-2010 and risk of diabetes among Women's Health Initiative analytic cohort (n=47,683)



Hazard ratios correspond to 2-standard deviation increase. Red triangles are from Model 1, adjusted for age group, race/ethnicity and study arm (OS vs. DM-C and HT arm). Blue rectangles are from Model 2, which adjusts for factors from Model 1 in addition to family income, having a partner, education, smoking status, physical activity, social support, depression status, HT use, family history of diabetes, and history of cardiovascular disease and hypertension. Green circles are from regression calibration model from Model 2, but do not include a covariate for OS vs. DM-C, as all participants in the reliability study came from the DM-C.

Figure 2. Comparison of hazard ratios (and 95% CI) upon adjustment for potential confounders of the diet cost and diabetes association in the Women's Health Initiative analytic cohort (n=47,683)



Values represent adjustment for each confounder in addition to Model 1. For example, "+BMI" represents a model adjusting for age group, race/ethnicity, study arm and BMI.

Model 1 adjusts for age group, race/ethnicity and study arm (OS vs. DM-C and HT study arm). Model 2 adjusts for Model 1 in addition to the other variables in the figure.

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Chapter 3: Diet cost and risk of cardiovascular disease: does diet cost mediate the association between socioeconomic status and cardiovascular disease risk?

Abstract

Background: Diet cost has been implicated as an important determinant of diet quality. However, no prospective studies have evaluated whether diet cost is associated with risk of cardiovascular disease (CVD).

Methods: A prospective cohort study among 42,632 women 49-64y using data from the Observational Study and the control arm of the Dietary Modification trial of the Women's Health Initiative was conducted to evaluate the association between diet cost and risk of CVD. This study had two aims: 1) to examine the association between diet cost and CVD and; 2) to determine the extent by which the socioeconomic gradient in CVD was explained by diet cost. To estimate diet costs, a national food price database was linked to the WHI food frequency questionnaire. The outcome was defined as the first occurrence of the following: myocardial infarction, coronary heart disease, carotid artery disease, congestive heart failure, ischemic stroke, receipt of coronary artery bypass graft/percutaneous transluminal coronary angioplasty or death due to CVD. Cox proportional hazards models examined the association between diet cost and CVD risk after adjusting for covariates associated with both diet cost and CVD (e.g., age, smoking and income among others).

Results: Over 8 years of follow-up, 1,208 cardiovascular events were observed. After adjusting for covariates, a 50% increase in energy-adjusted diet costs was associated with a 19% reduced risk of CVD (hazard ratio [HR] 0.81; 95% CI 0.72, 0.92). In regression calibration models that incorporated estimated diet costs from a four-day food record, a 50% increase in energy-adjusted diet costs was associated with a 28% reduced risk of CVD (HR 0.72; 95% CI 0.58, 0.88). In models adjusting for established intermediates of the income and CVD association (e.g., physical activity or smoking), women with incomes of less than $10,000/year

had a 2.2-fold increased risk of CVD (95% CI 1.61, 2.93). Diet cost explained 12-19% of the association between income/education and CVD.

Conclusions: As the first report to observe an association between diet cost and CVD these results need to be compared to other studies. Examining upstream factors in CVD risk, including diet costs, expands our understanding of socioeconomic disparities in health, while also exploring the consequences of the contemporary food environment on health.

Introduction

Disparities in the incidence of cardiovascular disease (CVD) by socioeconomic status (SES) have long been observed, though the exact mechanisms involved are unclear (1-4). Individuals of lower SES have been consistently observed to be at elevated risk of cardiovascular disease, including myocardial infarction, coronary heart disease, congestive heart failure, and mortality from CVD (2-5). Some of the associations between SES and higher CVD risk may be explained by the traditional CVD risk factors, including smoking, inadequate physical activity, poor diet, diabetes, obesity, and hypertension (6, 7), all of which have been associated with lower education and incomes

Depending on the population of study, the socioeconomic measure being used and the outcome under study, proximal lifestyle and psychosocial factors including diet, physical activity, smoking, social support or depression, account for some, but not all of the social gradient in CVD (4, 8). These results are generally consistent regardless of how SES was assessed. While the social gradient in CVD is present for both genders, it appears to be stronger among women (2).

The importance of dietary factors in relation to CVD is well established (9). Among dietary factors associated with lower CVD risk are consumption of fruit and vegetables, nuts, whole

grains, polyunsaturated fatty acids, moderate amounts of alcohol and omega-3 fatty acids primarily from fish (specifically for fatal CVD) (10-15). Among dietary factors associated with higher risk of CVD are elevated consumption of processed and red meats, refined grains, and sweets/desserts, and *trans* fatty acids (16-18).

One upstream factor that has not been previously examined in relation to the incidence of CVD is the role of food prices and diet costs. On a per-calorie basis, numerous components of a cardioprotective diet are more costly, whereas many foods associated with an increased risk of CVD are much less costly. In addition, processed meats and sugar-sweetened beverages are preferentially consumed by individuals of lower SES, who are also at increased risk of CVD (19).

Numerous cross-sectional studies have shown that higher quality diets are associated with higher diet costs (20-25). However, no studies have evaluated whether the consumption of a higher cost diet is associated with lower risk of incident CVD. Using data from the Women's Health Initiative (WHI) Dietary Modification (DM) Trial and Observational Study (OS), a prospective cohort study was conducted to examine the association between diet cost and risk of CVD events. Furthermore, the extent by which differences in diet cost explain the observed socioeconomic gradient in CVD is assessed.

Methods

Data for this study came from the WHI DM trial and the OS. The design and baseline descriptions of the WHI studies have been previously described (26). Briefly, 48,835 and 93,676 generally healthy postmenopausal women aged 49-79y were randomly assigned to the DM trial or enrolled in the OS, respectively, at 40 clinical centers across the United States between 1993 and 1998. The DM trial investigated the effect of a low-fat dietary pattern on the incidence of breast and colorectal cancers and heart disease over an average of 7.7 years of follow-up (27,

28). The recommended dietary pattern emphasized increased intake of fruits, vegetables and grains (26). The OS offered opportunities for investigating a broad range of epidemiologic questions. Many women who were not eligible for the DM trial entered the OS.

This section describes the study population, the assessment and reliability of diet costs estimates, potential confounders and intermediates of the diet cost and CVD association, outcomes and the statistical methods used. In addition, the approach used to evaluate the extent by which diet cost explained socioeconomic disparities in CVD events is described.

Study Population

Given the emphasis of the current research on the relation between socioeconomic status (SES), as measured by family income and education, and CVD, this study was restricted to women 49-64y at study baseline. This population was selected as a working-age population where the family income variable would be more meaningful than it would be for older participants. Women from the intervention arm of the DM trial were not included in the present study, as their diets changed dramatically over time due to the intervention.

An analytic cohort was created by combining data from two study arms (OS and DM-C). This was done to increase the available sample size and make use of measurement error correction techniques, which required the availability of date from four-day food records (4DFRs) for a sub-set of participants. The first step in creating the analytic cohort was to make the two study arms as similar to each other as possible (29, 30). Because eligibility for the DM trial depended on consuming a high-fat diet, year-1 was treated as baseline for DM-C participants in order to avoid the complete truncation of dietary intakes based on data from year-0 (31). For the OS, year-0 was baseline.

In addition to using different baseline periods, the more strict exclusion criteria for the dietary modification trial were applied to participants in the OS. This resulted in the exclusion of women with a history of breast cancer, colorectal cancer in past 10 years, endometrial cancer in past 10 years, other cancer within the past 10 years, with the exception of non-melanoma skin cancer, stroke or acute myocardial infarction (MI) 6 months prior to enrollment, body mass index (BMI)<18, hypertension (>200/>105 mm HG), food frequency questionnaire (FFQ) reported daily energy intake of <600 kcal or >5000 kcal, ≥10 meals out per week, special low-fiber diet, special diet due to malabsorption, unintentional weight loss of >15 lb (6.8 kg) in the 6 months prior to baseline, self-reported diabetes at age ≤ 21 (a proxy measure for history of type 1 diabetes).

For both OS and DM-C participants, those without a diet cost estimate were excluded. Those with a prior history of cardiovascular disease were also excluded. Among these individuals, the analytic cohort was further restricted to those with complete data on the variables of interest. Individuals missing data on physical activity, body mass index, opposed hormone therapy, unopposed hormone therapy, history of diabetes, education, smoking status, family history of premature myocardial infarction (MI), hypertension, treated high cholesterol, low-dose aspirin use, social support and depression status were excluded. The primary sample size included 42,632 women 45-64y (32,130 from the OS and 10,502 from the DM-C). Follow-up time used study time and events were enumerated after at least 1-year of follow-up to avoid including prevalent cases in the enumeration of incident CVD. Women were followed for 8 years.

Assessing diet cost

The exposure of interest was estimated diet cost, which was assessed using the WHI FFQ. Food and beverage prices per 100g edible portion from a national food price database were linked to the underlying foods in the WHI FFQ. The food price database was created by the

Center for Nutrition Policy and Promotion (CNPP) at the USDA and was contemporary with 2001-2002 food prices (32). The CNPP price database provided the prices for 6,680 foods and beverages, excluding alcoholic beverages and bottled water. This price database assumed that all foods/beverages are purchased at a store and prepared at home. The method used for estimating alcohol prices has been previously described (20).

Diet costs were energy-adjusted using the residual method to account for differences in energy intake between individuals (33). This method estimates a residual value of diet cost based on the observed relation between energy intake and diet cost. A constant of 2000 kcal was then added to the estimated residual values to ease interpretation. For primary analyses, the diet cost variable was log-transformed to evaluate the impact of a percentage change in diet costs rather than an absolute difference. This was done because one would not expect a 1-dollar increase in diet costs to have the same impact for individuals consuming low versus high cost diets. For reporting purposes the relative risk of CVD associated with a 50% increase in diet costs was estimated. For reference, a 50% increase in diet cost roughly corresponds to the difference between the 85th and 15th percentile values ($5.49 vs. $3.60/day/2,000 kcal). A 50% increase was selected as it roughly corresponds to the difference between extreme quintiles if participants were grouped into five categories. In addition, a 50% increase is comparable to a two standard deviation increase (+$1.95) from the 25th%ile estimate of diet cost (i.e., from $3.90 to $5.85).

In order to assess the measurement characteristics of the diet cost estimate from the FFQ and to utilize approaches to reduce the impact of measurement error, a reliability sub-study was conducted. In brief, the USDA food price database (described above) and the MyPyramid Equivalents Database Version 2.0 were merged with 560 four-day food records (4DFR) completed by women enrolled in the DM-C, of whom 446 were eligible for inclusion in the CVD

analysis. The MyPyramid Equivalents Database includes information on the number of servings of different foods groups and is needed to evaluate the HEI-2005 (34-36).

The 4DFR were originally collected in order to evaluate adherence to the dietary modification trial and to complement data from the FFQ (26). To better measure long-term intake, avoid measuring correlated eating behaviors and include a weekend day, the 4DFR was completed on alternating days. Non-white women were over-sampled to participate in the 4DFR sub-study to more precisely evaluate dietary habits and adherence to the intervention among minority women. The correlation coefficient was 0.52 for a comparison of log-transformed energy adjusted diet costs and 0.51 for the HEI-2005 between the FFQ and 4DFR, comparable to values for saturated fat (0.56), niacin (0.54), or folate (0.52) for nutrients between the FFQ and 4DFR (37).

Potential Confounders

Key covariates were identified that are associated with either diet cost and/or the risk of cardiovascular disease. Variables and their parameterization are described below. All covariates, with the exception of body mass index, were assessed via questionnaire at baseline (or at year 1 for DM-C participants). Socio-demographic covariates included age group (49-54, 55-59, 60-64), race/ethnicity (American Indian/Alaskan Native, Asian/Pacific Islander, black, Hispanic, non-Hispanic white and unknown [including other]), family income (<10, 10-19, 20-34, 35-49, 50-74, 75-99, 100-149, and ≥150 in $1000 and a missing category), educational attainment (<high school, high school graduate/equivalent, some college, college degree/some post-graduate education and master's degree or higher) and having a partner (yes/no). While a complete case approach was used for primary analyses, a missing indicator was used for income (which was missing for 5.7% of respondents). For analyses where income was the independent variable of interest, women missing income information were excluded.

Additional variables included recreational physical activity (<1.5, 1.67-6.75, 6.83-12.83, 12.87-23, ≥23.04 MET [metabolic equivalents] hours/wk), family history of myocardial infarction (MI) prior to age 65 (yes/no), smoking status (never, former smoker less than 20 years, former smoker more than 20 years, current smoker less than 20 years and current smoker more than 20 years), unopposed estrogen use from pills or patches (former, never or current), estrogen plus progesterone use from pills or patches (former, never or current), prevalent diabetes (yes/no) and hypertension (taken pills, diagnosed but no pills, not previously diagnosed), low-dose aspirin use (yes/no), treated high cholesterol (yes/no), body mass index category (<25 [underweight/healthy weight], 25-29.9 [overweight], 30-34.9 [class I obese], 35-39.9 [class II obese], and ≥40 [class III obese] kg/m^2), Center for Epidemiology Studies Depression scale (<0.009 [no depression], 0.009-0.059 [slight depression], ≥0.06 [moderate/severe depression]) and a scale indicating level of social support. With the exception of social support, each of these was modeled as a categorical variable.

Finally, given the inclusion of participants from both the OS and DM-C we adjusted for study arm (OS vs. DM-C) and arm of the HT as participants in the DM-C could also participate in the HRT trial (38). No adjustment was conducted for participation in the Calcium and Vitamin D (CaD) trial arm, as there was no relation between CaD arm and risk of cardiovascular disease (39).

Potential Intermediates

To de-compose the relation between diet cost and CVD we included a number of variables that are consequences of diet cost, but also associated with CVD risk. Additional variables included alcohol servings per week (none, 0<2, 2-6.9, 7-13.9 and ≥14) and Healthy Eating Index-2005 (HEI-2005) as continuous variables (35, 40). Analyses also evaluated the 2010 Alternative Healthy Eating Index (AHEI-2010) as an alternative diet quality measure. The method for

calculating AHEI-2010 is described elsewhere (16). Dietary covariates were assessed via food frequency questionnaire (FFQ). The measurement characteristics of the WHI FFQ have been previously described (37).

Outcome

Report of cardiovascular disease prior to study participation was documented by self-report. The composite cardiovascular disease outcome was based on time to first event for the following: myocardial infarction (MI), coronary heart disease, carotid artery disease, congestive heart failure, ischemic stroke, receipt of coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA), or death due to cardiovascular disease, These outcomes were adjudicated centrally or locally and were defined as described in previous publications (41).

Statistical methods

Cox proportional hazards regression models were used to estimate the relative risk of incident CVD associated with a 50% increase in diet cost. The first set of models (Model 1) adjusted for study arm, age group, and race/ethnicity. Model 2 additionally adjusted for socio-demographic and behavioral factors associated with risk of CVD and diet cost, including family income, educational attainment, having a partner, family history of premature MI, smoking status, HRT use, recreational physical activity, BMI, prevalent diabetes, hypertension, treated high cholesterol, low-dose aspirin use, and CES-D depression score and a social support scale. Additional analyses added each dietary factors, including HEI-2005, AHEI-2010 and alcohol consumption, which were hypothesized to be intermediates of the diet cost and cardiovascular disease association. Each of these dietary factors was evaluated independently.

Because the estimate of diet cost is an error-prone measure, regression calibration was used to account for measurement error in the estimate of diet cost, treating data from the 4DFR as an alloyed gold standard (42, 43). An “alloyed gold standard” is a reference measure that is not a perfect gold standard, but rather a measure that captures the true exposure of interest better than the primary instrument (i.e., the FFQ). While clearly, the 4DFR is an imperfect measure of diet as shown by studies of doubly labeled water, it has been shown to have better measurement characteristics than an FFQ (44). This approach reduces the bias from measurement error assuming that the errors in the two instruments are uncorrelated, though previous work has shown that even in the presence of modest correlated errors, the estimate from regression calibration should yield a less biased estimate of the observed exposure-disease relationship using the error-prone measure (43). The %blinplus SAS macro was used to implement regression calibration (45).

In additional analyses, the relationship between diet cost and the two diet quality measures (HEI-2005 and AHEI-2010) with risk of CVD was compared. To compare these three measures we scaled these variables to estimate the hazard ratio of CVD based on a two standard deviation increase in diet cost or diet quality score, akin to a standardized coefficient. Regression calibration was also used based on HEI-2005 and AHEI-2010 estimates from the 4DFR.

Mediation Framework

The extent by which the association between socioeconomic status (SES) and CVD is mediated or explained by diet cost was also assessed. This included the same covariates from the previous Model 2, but did not include the other SES variable in the assessment of mediation (i.e., education was not included as a covariate in the assessment of diet cost mediating the relation between income and CVD). To facilitate estimation of a summary measure of mediation

we coded both SES variables as continuous variables (e.g., income <$10,000 = 1; $10-19,999 = 2, etc.). The functional form of each SES variable was assessed to compare continuous coding and categorical coding to determine whether treatment of these variables as continuous appropriately captured the SES-CVD association. Mediation was quantified by calculating the percentage change in the regression coefficients (log hazard ratio) for income and education in two models, one that omits diet cost and a second that includes diet cost (46). The %mediate SAS macro was used to assess the extent to which diet cost mediated the association between the two SES measures and CVD, the confidence interval of the proportion explained and a p-value for mediation (47). The formula used to derive standard errors of the mediated effect was derived from Equation 5 in Lin *et al* (46). Exploratory analyses examined the extent to which the SES-CVD association was mediated after accounting for measurement error in the diet cost estimate using the same approach. Additional mediation analyses evaluated the extent by which the association between diet cost and CVD was explained by different dietary measures, including HEI-2005, AHEI-2010 and alcohol intake.

The proportional hazards assumption was evaluated for all primary analyses by evaluating the Schoenfeld residuals. Analyses were conducted using Stata 13.1 (College Station, TX) and SAS 9.3 for Windows (Cary, NC 2013) for the %mediate and %blinplus macros (45, 47).

Results

Population characteristics

Subject characteristics are described in **Table 1**. Average diet costs by socio-demographic, anthropometric and behavioral characteristics are also provided. The mean age at study baseline was 58.1y (SD=4.1). The cohort was primarily non-Hispanic white, and had a wide range of family incomes. Nine percent of the cohort had family incomes less than $10,000/year, while more than a quarter had family incomes greater than $75,000. A similarly broad

distribution of education was observed, though only a small proportion of women had not graduated from high school. Thirty-nine percent of the cohort was normal weight/underweight (BMI <25 kg/m^2) and 27.7% were obese (BMI ≥30 kg/m^2). The average HEI-2005 score was 68.3 (SD=10.4) (out of 100 possible) and the average number of MET hours from recreation physical activity per week was 13.5 (SD=14.4).

The average energy-adjusted diet cost was $4.58 (SD=$0.98; median=$4.47; 10^{th} percentile=$3.45; 90^{th} percentile=$5.81). Estimated diet costs were related to socio-demographic, anthropometric and behavioral characteristics of the study sample. Higher education and income were positively associated with higher diet costs. The diet costs of women with family incomes greater than $150,000 were 28% higher than women with incomes less than $10,000 (p-trend<0.001). A similar relationship was observed for education (p-trend<0.001).

There was a link between diet quality and diet cost. Women with healthier diets, as measured by both HEI-2005 and AHEI-2010, tended to consume more costly diets (per calorie) than women with poorer quality diets (p-trend<0.001). Women who were more physically active also consumed more costly diets (p-trend<0.001). Those with lower BMIs consumed less costly diets than did heavier participants (p-trend<0.001). Non-Hispanic white women consumed significantly more expensive diets (per calorie) than did non-Hispanic black and Hispanic/Latina women (p-difference<0.001).

Associations between CVD, SES and diet quality (HEI and AHEI)

The average length of follow-up was 7.7 years and 1,208 cardiovascular events were observed. The incidence rate of composite CVD was 369 per 100,000 person-years.

In minimally adjusted models, both income and education were strongly and negatively associated with CVD risk (see Table 2). Compared to individuals with incomes greater than $150,000/year women with incomes less than $10,000 had a 4.3-fold increased risk of CVD (HR 4.34; 95% CI 3.25, 5.81). A similar association was observed for education. Women with less than high school education had a 2.6-fold increased risk of CVD compared to those with a master's degree. After accounting for additional CVD risk factors, compared to high-income women, those with incomes less than $10,000 had a 117% increased risk of CVD (HR 2.17; 95% CI 1.61, 2.93) compared to women with incomes greater than $150,000.

Association between diet cost and CVD

The association between diet cost, income and education as they relate to risk of CVD is provided in **Table 2**. In minimally adjusted models, a 50% increase in diet costs was associated with a 37% reduced risk of CVD (95% CI 29-44%). After adjusting for potential confounders, a 50% increase in diet cost was associated with a 19% reduced risk of CVD (95% CI 8-22%). In analyses accounting for measurement error in the diet cost estimate, a 50% increase in diet cost was associated with a 28% reduced risk of CVD (hazard ratio [HR] 0.72; 95% CI 0.58, 0.88). For reference, a 50% increase in diet cost roughly corresponds to the difference between the 85th and 15th percentile values ($5.49 vs. $3.60/day/2,000 kcal).

To better understand the mechanisms contributing to the observed association between diet cost and CVD secondary analyses evaluated whether the association between diet cost and dietary measures, including HEI-2005, AHEI-2010 and alcohol intake, explained some of the diet cost-CVD association (see **Table 3**). In uncorrected adjusted models, both HEI-2005 and AHEI-2010 explained some of the observed association between diet cost and CVD. In models that accounted for measurement error in the assessment of the diet quality measures, accounting for AHEI-2010 resulted in a non-significant association between diet cost and CVD.

Accounting for HEI-2005 also attenuated the observed association between diet cost and CVD, but to a lesser extent than AHEI-2010.

The extent of the association between CVD and diet cost was also compared to other dietary factors (see **Figure 1**). After adjusting for covariates, a 2-standard deviation increase in diet cost ($1.95) and HEI-2005 (21-points) was associated with a 22% reduced risk of CVD (HR 0.78; 95% CI 0.68, 0.89) and a 16% reduced risk (HR 0.84; 95% CI 0.75, 0.94), respectively. For AHEI-2010 a 23-unit increase was associated with an 18% reduced risk of CVD (HR 0.82; 95% CI 0.72, 0.93).

Diet cost as a mediator of the socioeconomic gradient in CVD

A secondary goal of this analysis was to assess the extent by which differences in diet cost may account for the socioeconomic gradient in CVD. Mediation analyses suggested that diet cost accounted for some of the observed association between income and CVD (14.2% [95% CI 3.9, 24.6%]), after accounting for numerous covariates (see **Table 4**). The mediating effect was similar in adjusted and unadjusted models, but was marginally stronger for education as opposed to income. We conducted secondary analysis examining the extent to which the SES-CVD association was mediated by diet cost after accounting for measurement error in the diet cost estimate. Thirty-eight percent of the association between income and CVD was explained by diet cost after accounting for measurement error in the diet cost estimate.

In primary analyses, there was some evidence that the proportional hazards assumption was violated (Schoenfeld residuals global test $p<0.05$ for analyses treating education and income as the main effects). The variables responsible for the violation of the assumption were identified and subsequent analyses stratified on these variables allowing the baseline hazards to vary. Comparing the results of the simple Cox model to the stratified Cox model revealed that the main effect coefficients of interest were qualitatively unchanged (<1% change in log hazard ratio

of interest). Therefore, violation of the proportional hazards assumption was not considered a major threat to the validity of the estimated hazard ratios of interest.

Discussion

Association between diet cost and CVD

In this prospective cohort study, a 50% increase in diet costs was associated with a significantly reduced risk of CVD. In analyses accounting for measurement error in the estimate of diet cost, a 50% increase in diet cost was associated with a 30% reduced risk of CVD (95% 13-43%).

The association between diet cost and CVD was explained in large part to measures of diet quality (e.g., HEI-2005 and AHEI). HEI-2005 and AHEI-2010 accounted for 17-30% of the association between diet cost and CVD, while alcohol intake explained very little of the association between diet cost and risk of CVD and was a non-significant intermediate variable. In analyses using regression calibration to account for measurement error in the diet quality estimates, 27-44% of the association between diet cost and CVD was accounted for by diet quality measures, though AHEI-2010 appeared to explain more the association (44% after accounting for covariates). While higher scores for both the HEI-2005 and AHEI-2010 were associated with a reduced risk of CVD (see **Figure 1**), AHEI-2010 had a stronger relation to diet cost (r=0.38 for AHEI-2010 and r=0.31 for HEI-2005). The stronger relation between AHEI-2010 and diet cost, as compared to HEI-2005 may be driven by the components of the two diet quality scores. While the components of all foods/beverages consumed make up the HEI-2005 score (e.g., a cracker may have components of total grains, sodium, solid fat and/or saturated fat), the AHEI-2010 includes only foods previously observed to be associated with risk of chronic disease (16). The two scores also treat some similar dietary constituents differently. For example, alcohol is treated as a dietary component to avoid in the HEI-2005 score, while the AHEI-2010 treats moderate alcohol as a dietary component to encourage. Furthermore, AHEI-

2010 treats 100% fruit juice as a food group to avoid, while HEI-2005 includes 100% fruit juice in the total fruit score (a food group to encourage).

Comparing the observed association between diet cost and CVD in context with other dietary factors associated with CVD is informative. Compared to the effect of AHEI-2010 and HEI-2005 on CVD risk, the effect of diet cost was marginally stronger. A 2-standard deviation increase in diet costs was associated with a 22% reduced risk of CVD compared to 18% for AHEI-2010 and 16% for HEI-2005. In models accounting for measurement error in diet cost and the diet quality measures, a 2-standard deviation increase in diet cost was associated with a 31% reduced risk of CVD, compared to 29% for HEI-2005 and 31% for AHEI-2010. This is the first explicit comparison of diet cost with standard diet quality scores on the risk of CVD.

The primary analyses here examined risk of CVD associated with a 50% increase in daily diet cost. The average daily cost observed in this population was $4.58, which would correspond to an increase to $6.87 or a $2.29 increase. This corresponds to $836/year based on 2001-2002 prices or $1100 in 2013 dollars after accounting for inflation. Whether this amount poses an actual barrier is an open question, though there is considerable evidence that individuals are highly sensitive to food costs, particularly individuals of lower SES. After taste, food cost was described as the most important factor in choosing foods (48). In 2007-2010, 40% of US adults reported that food prices were “very important” in choosing foods at the grocery store, while only 11% said it was “not important” or “not too important” (49). As one would expect, lower income adults were 2.8-times as likely to identify food cost as a “very important” consideration compared to higher income adults (49).

Prospective studies evaluating diet cost and health are few. To our knowledge, this is the first prospective study evaluating the association between diet cost and CVD. Prior prospective analyses of WHI data revealed a similar association between increased diet cost and risk of

treated type 2 diabetes. A 50% increase in diet cost was associated with a 14% reduced risk of diabetes (HR 0.86; 95% CI 0.78, 0.94). Diabetes is a well-established risk factor for CVD and the previously observed association between diet cost and diabetes represents one possible mechanism for the results observed here. A previous study conducted in an older Taiwanese population, observed that spending on vegetables was associated with reduced risk of death, while total spending was not associated with risk of death (50). Another prospective study, conducted in Spain, found that lower diet costs were not associated with an increased risk of weight gain, though this study did not evaluate any other health outcomes (51). To date, most research focused on diet costs have been cross-sectional studies describing the relation between cost and diet quality (20-23, 25, 51). It has also been suggested that socioeconomic disparities in diet quality are partially attributed to diet cost (52, 53). In relation to health outcomes, a limited number of cross-sectional studies have observed an inverse association between diet cost and body mass index (25, 54). The present study fills an important gap in the literature and represents the first prospective evaluation of diet cost and CVD. Future research using prospective studies should consider the relationship between diet cost and intermediates, including markers of inflammation or the incidence of hypertension.

Diet cost as a mediator of the SES-CVD association

Given the socioeconomic gradient in CVD and diet cost, we also attempted to quantify the extent by which the socioeconomic gradient in CVD could be attributed to differences in diet cost. Mediation analyses revealed that about 12-19% of the association between SES and CVD could be attributed to diet cost after accounting for covariates.

The socioeconomic gradient in CVD has been attributed to proximal factors, including the traditional CVD risk factors, including high cholesterol, hypertension, tobacco use, diabetes and physical inactivity (4, 8). Additional psychosocial factors, including social support and

depression are thought to play a role in explaining the SES-CVD gradient (4, 55). Whether these factors account for the entirety of the social gradient in CVD is unclear, as the role of intermediate factors varies by study population (e.g., by gender or country), socioeconomic indicator (e.g., income, education or social class) being used and outcome of interest (e.g., death due to CVD or myocardial infarction). Furthermore, the extent by which these risk factors account for the social gradient depends on the strength of their relation to measures of SES. For example, a comparison of data from United Kingdom and France revealed that lifestyle factors accounted for differences in all-cause mortality by SES in the UK, but not France (56). The current study included the standard risk factor intermediates, but includes diet cost as a novel, upstream variable. Here, we observed that a modest amount of the association between income/education and CVD incidence was explained by differences in diet cost (see **Table 4**). The impact of diet cost as a mediator was similar to the impact of prevalent diabetes (13.8%), physical activity (11.3%), BMI (16.1%), but weaker than the collective effect of all behavioral covariates described in the footnote of **Table 2** (64.4%). For dietary factors, the mediating effect of HEI-2005 and AHEI-2010 respectively was 6.5% and 7.7%. When standard mediation approaches were applied to the regression coefficients from measurement-error correction models the extent by which the association between income and education and CVD was explained by diet cost increased from 14.7% and 17.8% to 32.2% and 38.3% respectively. Given the qualitative difference between the corrected and uncorrected estimated mediation effects, future work should formalize how to incorporate methods to correct for measurement error in evaluating mediation. Differences in the extent of measurement error for potential intermediates complicate the ranking of intermediate variables. Despite challenges in interpreting mediation effects, the impact of diet cost was comparable or stronger than two widely used measures of global diet quality.

The primary limitation of this study was the use of an FFQ instrument to estimate diet costs. Deriving diet costs using a national food prices database may not reflect the actual prices for food paid by individual WHI participants as the price database assumes a constant food price and that all foods are consumed at home. The use of a fixed price is similar to the weakness inherent in deriving nutrient intakes from nutrient composition databases, which do not reflect potential heterogeneity in the nutrient levels of foods actually consumed. Despite limitations in the use of standard prices database, it represents a meaningful source of information on food prices that can be linked to individual data on diets and health. A related concern is that actual consumer behavior and the importance of cost to consumers was not assessed. Therefore these observational results should be interpreted cautiously. While a robust association between diet cost and risk of treated CVD was observed, we do not have any data to indicate that price was a key factor for that respondent, though previous work has indicated that food costs are important determinants of food choice (48). The food price database was based on prices from 2001-2002, which may not capture the distribution of current food costs. Beyond the challenges in using a national food price database, an FFQ is an error-prone instrument in assessing diet cost (or any nutrient). Chief among these limitations is that the FFQ relies on a fixed foods list, which may omit important foods for assessing diet costs. Our reliability study, which estimated diet cost from the WHI FFQ and 4DFRs, indicate a modest correlation between the two instruments (r=0.52). Though the estimate from the 4DFR is not an unbiased estimate of diet cost, it does reduce many of the potential sources of error in the FFQ, including reliance on a fixed food lists and error in recalling portion size. Given concerns regarding the measurement error from the FFQ, we employed regression calibration to account for measurement error in the diet cost estimate. As expected, the strength of the association between diet cost and CVD became stronger. The regression calibration approach used here assumes that the two instruments have uncorrelated errors. However, modest correlated errors

yield a better estimate of the exposure-disease relationship than relying on the error-prone instrument alone (43). Further, although we considered the 4DFR an “alloyed gold standard,” the amount of variation in energy intake explained by 4DFR self-report compared to biomarkers of energy intake is quite limited (44). Nonetheless, the 4DFR explained more of the variation in biomarker-derived energy intakes than the FFQ and may be sufficient for epidemiologic studies.

In addition, though we adjusted for a wide range of potential confounders we cannot rule out residual confounding due to poorly measured or unmeasured variables. **Figure 2** evaluates the impact of adjustment for each potential confounder of the association between diet cost and CVD risk. The SES variables, as well as physical activity and BMI resulted in the largest change in the hazard ratio. While BMI was measured and not based on self-report, the use of questionnaire data to evaluate recreational physical activity likely results in residual confounding by physical activity (57). Future studies of diet cost and health outcomes could make use of objectively measured physical activity data to confirm that the association between diet cost and CVD is not attributable to residual confounding by physical activity.

The use of education and family income as the measures of SES is also problematic and could also contribute to residual confounding. While both measures are routinely collected in health studies they fail to capture the complete dimensions of SES (58). For example, educational attainment does not account for the quality of education and captures experiences that for most study participants occurred many decades prior to baseline. As a measure of access to absolute resources, income-based measures fail to capture total wealth, which is the true underlying variable of interest (59). We limited our analysis to working-age women (<65y) and the income measure was family rather than individual income. The role of diet cost should be explored in other studies that collect richer measures of SES, such as accumulated wealth.

Healthcare access may be an important confounder of the diet cost and CVD association and could also be a possible mediator of the SES and CVD association. In adjusted models, the relationship between a 50% increase in diet cost and CVD was unchanged after adjusting for having any insurance or length of time since last medical visit. In addition, having insurance and length of time since last medical visit did qualitatively alter the association between family income and education and CVD risk. The WHI study population was generally well-insured (94% had insurance) and received frequent medical care (88% visiting a medical provider in the prior two years). However, in less well-insured populations, the impact of health care access on the diet cost and CVD association should be carefully considered.

Methods for mediation analyses for non-linear models are an area of rapid development (60, 61). We evaluated mediation by comparing the difference in the log hazard ratio for income and education for models with and without diet cost. Applying this approach in non-linear models requires a number of generally untestable assumptions to be made, regarding non-collapsibility of the outcome and the potential challenge of confounding by unmeasured variables of the mediator and outcome. Here, the outcome was sufficiently rare (2.8%) that non-collapsibility is unlikely to pose a problem (61). However, we cannot rule out the possibility that an unknown confounder of the mediator and outcome may bias the observed effects. The consistency of the observed mediation effect between adjusted and unadjusted models relaxes some concerns regarding the impact of confounding on quantifying the mediation effect.

This study also had a number of strengths. First, by comparison to other prospective cohorts, we had a diverse socioeconomic sample, which allowed us to assess the extent to which SES disparities in CVD could be attributed to differences in diet cost. Second, the study collected dietary data in FFQ and 4DFRs, which allowed us to address the impact of measurement error in evaluating the association between diet cost and CVD.

Conclusions

In summary, higher diet costs were associated with a reduced risk of CVD, which appeared to be mediated by the relation between diet quality and diet cost, specifically the AHEI-2010. Furthermore, we observed the social gradient in CVD risk could partially be attributed to differences in diet cost. The extent of this mediation was comparable to other lifestyle factors, including diet quality and physical activity. This study represents the first prospective examination of the association between diet cost and CVD and results suggest the diet cost play an important role in CVD risk. Future health studies should evaluate incorporating data on dietary expenditures to sidestep the limitations in using a national food price database. The results of this study need to be compared to other studies conducted in different contexts and populations.

Table 1. Participant characteristics and average energy-adjusted diet costs in the Women's Health Initiative analytic cohort (n=42,632)

				$/2000 kcal	
	new cases	N	% of total	Mean	95% CI
Age group					
49-54	157	12,275	28.8	4.54	4.52, 4.56
55-59	425	15,674	36.8	4.59	4.58, 4.61
60-64	626	14,683	34.4	4.59	4.58, 4.61
P-trend				<0.001	
Race/ethnicity					
American Indian/Alaskan Native	7	169	0.4	4.24	4.11, 4.37
Asian/Pacific Islander	21	1,298	3.0	4.62	4.56, 4.68
Black	127	3,653	8.6	4.11	4.08, 4.14
Hispanic	35	1,818	4.3	4.12	4.08, 4.16
White, not Hispanic	1,007	35,158	82.5	4.65	4.64, 4.66
Unknown (incl. other)	11	536	1.3	4.51	4.44, 5.93
P-difference				<0.001	
Family income ($1000)					
< $10	62	1,059	2.5	4.01	3.95, 4.06
$10-19	136	2,662	6.2	4.12	4.09, 4.15
$20-34	281	7,175	16.8	4.32	4.30, 4.34
$35-49	248	8,112	19.0	4.50	4.48, 4.52
$50-74	215	9,907	23.2	4.64	4.62, 4.66
$75-99	105	5,219	12.2	4.80	4.78, 4.83
$100-149	68	4,046	9.5	4.93	4.90, 4.96
> $150	32	2,069	4.9	5.12	5.08, 5.17
P-trend				<0.001	
Missing	61	2,383	5.6	4.56	4.52, 4.60
Educational attainment					
<High school	80	1,345	3.2	3.94	3.89, 3.99
High school/equivalent	255	6,266	14.7	4.29	4.27, 4.31
Some college	456	15,243	35.8	4.51	4.50, 4.53
College graduate	222	10,506	24.6	4.74	4.72, 4.76
≥Master's degree	195	9,272	21.8	4.78	4.76, 4.80
P-trend				<0.001	
HEI-2005					
Q1: 26-58 [lower diet quality]	344	8,527	20.0	4.18	4.15, 4.20
Q2: 59-66	243	8,526	20.0	4.41	4.39, 4.43
Q3: 67-72	238	8,527	20.0	4.62	4.60, 4.64
Q4: 73-77	205	8,526	20.0	4.78	4.76, 4.80
Q5: 78-93 [higher diet quality]	178	8,526	20.0	4.89	4.88, 4.91
P-trend				<0.001	
AHEI-2010					
Q1: 13-35 [lower diet quality]	299	8,527	20.0	4.08	4.06, 4.10
Q2: 36-41	260	8,526	20.0	4.35	4.33, 4.37
Q3: 42-48	260	8,527	20.0	4.57	4.55, 4.59
Q4: 49-55	244	8,526	20.0	4.80	4.78, 4.81
Q5: 56-95 [higher diet quality]	145	8,526	20.0	5.08	5.06, 5.10
P-trend				<0.001	

				$/2000 kcal	
	new cases	N	% of total	Mean	95% CI
Alcohol servings per week					
None	16,454	599	38.6	4.18	4.17, 4.19
0.21-1.92 per week	13,145	327	30.8	4.43	4.41, 4.44
2-6.9 per week	7,891	168	18.5	4.87	4.86, 4.89
7-13.9 per week	3,352	75	7.9	5.42	5.40, 5.45
≥23 per week	1,790	39	4.2	6.45	6.39, 6.50
P-trend				<0.001	
Recreational physical activity (MET-hours/wk)					
Q1: ≤1.5	354	8,548	20.1	4.19	4.17, 4.21
Q2: 1.67-6.75	290	8,904	20.9	4.41	4.39, 4.43
Q3: 6.83-12.83	211	8.133	19.1	4.59	4.57, 4.61
Q4: 12.87-22.9	202	8,554	20.1	4.75	4.73, 4.77
Q5: ≥23	151	8,493	19.9	4.95	4.93, 4.97
P-trend				<0.001	
Body Mass Index category (kg/m^2)					
Underweight/healthy weight: <25	309	16,443	38.6	4.72	4.71, 4.74
Overweight: 25-29.9	383	14,392	33.8	4.59	4.58, 4.61
Class I Obesity: 30-34.9	261	7,126	16.7	4.41	4.39, 4.43
Class II Obesity: 35-39.9	149	2,936	6.9	4.29	4.26, 4.33
Class III Obesity: ≥40	106	1,735	4.1	4.21	4.17, 4.25
P-trend				<0.001	

Table 2. Association between diet cost, income and education and incidence of CVD in Women's Health Initiative analytic cohort (n=42,632)

	Uncorrected				Corrected	
	Model 1[1]		Model 2[2]		Model 2[2]	
	HR	95% CI	HR	95% CI	HR	95% CI
Diet cost ($/2000 kcal)						
Per 50% increase	0.63	0.56, 0.71	0.81	0.72, 0.92	0.72	0.58, 0.88
P-value	<0.001		<0.001		0.001	
Linear family income ($1000)						
< $10	4.34	3.25, 5.81	2.17	1.61, 2.93	-	-
$10-19	3.52	2.75, 4.51	1.94	1.50, 2.51	-	-
$20-34	2.85	2.32, 3.51	1.74	1.40, 2.15	-	-
$35-49	2.31	1.96, 2.73	1.56	1.31, 1.85	-	-
$50-74	1.88	1.66, 2.12	1.39	1.22, 1.58	-	-
$75-99	1.52	1.40, 1.65	1.25	1.25, 1.36	-	-
$100-149	1.23	1.18, 1.29	1.12	1.07, 1.17	-	-
≥ $150	ref		ref		-	-
P-trend	<0.001		<0.001			
Linear education						
<High school	2.56	2.07, 3.16	1.54	1.24, 1.92	-	-
High school/equivalent	2.02	1.72, 2.37	1.38	1.17, 1.63	-	-
Some college	1.60	1.44, 1.78	1.24	1.11, 1.39	-	-
College graduate	1.26	1.20, 1.33	1.11	1.06, 1.18	-	-
≥Master's degree	ref		ref		-	-
P-trend	<0.001		<0.001		-	-

[1] Adjusted for study arm, age group and race/ethnicity. Income analyses adjusted for having a partner.

[2] Adjusted for factors from Model 1 in addition to opposed hormone use, unopposed hormone use, recreational physical activity, diabetes, family history of premature MI, hypertension, low-dose aspirin use, treated high cholesterol, smoking status, BMI, social support and depression status. Diet cost models additionally adjusted for income, having a partner and education.

Table 3. Role of diet measures in accounting for the association between diet cost and CVD in the Women's Health Initiative analytic cohort (n=42,632)

	Not adjusted for diet measure; HR (95% CI)	Adjusted for diet measure; HR (95% CI)	% mediated (95% CI)	p-value
Uncorrected				
Model 1[1]				
HEI-2005	0.63 (0.56, 0.71)	0.71 (0.62, 0.80)	23.4 (13.5, 33.3)	<0.001
AHEI-2010	-	0.70 (0.62, 0.79)	21.3 (10.4, 32.1)	<0.001
Alcohol intake (5 levels)	-	0.70 (0.61, 0.80)	21.8 (5.7, 37.9)	0.008
Model 2[2]				
HEI-2005	0.81 (0.72, 0.92)	0.85 (0.74, 0.96)	19.3 (0.0, 38.6)	0.051
AHEI-2010	-	0.85 (0.74, 0.96)	20.5 (0.2, 40.9)	0.048
Alcohol intake (5 levels)	-	0.82 (0.72, 0.95)	7.2 (-22.6, 37.1)	0.64
Corrected for measurement error[3]				
Model 1[1]				
HEI-2005	0.63 (0.56, 0.71)	0.73 (0.63, 0.83)	31.3	-
AHEI-2010	-	0.76 (0.65, 0.89)	44.3	-
Model 2[2]				
HEI-2005	0.81 (0.71, 0.91)	0.87 (0.61, 0.97)	26.7	-
AHEI-2010	-	0.89 (0.76, 1.03)	36.1	-

[1] Adjusted for study arm, age group and race/ethnicity. Income analyses adjusted for having a partner.

[2] Adjusted for factors from Model 1 in addition to family income, having a partner, educational attainment, opposed hormone use, unopposed hormone use, recreational physical activity, diabetes, family history of premature MI, hypertension, low-dose aspirin use, treated high cholesterol, smoking status, BMI, social support and depression status.

[3] Analyses correcting for measurement error in diet quality measures does not adjust for OS vs. DM-C because all individuals with 4DFR data come from the DM-C trial.

Table 4. Role of diet cost in explaining association between SES and CVD in the Women's Health Initiative analytic cohort (n=42,632)

	Not adjusted for diet cost; HR (95% CI)	Adjusted for diet cost; HR (95% CI)	% mediated (95% CI)	p-value
Uncorrected				
Model 1[1]				
Income (comparing < $10,000 to ≥ $150,000)	4.34 (3.25, 5.80)	3.62 (2.69, 4.89)	12.3 (6.4, 18.2)	<0.001
Education (comparing < high school to ≥ master's)	2.55 (2.07, 3.16)	2.21 (1.78, 2.75)	15.4 (9.2, 21.6)	<0.001
Model 2[2]				
Income (comparing < $10,000 to ≥ $150,000)	2.17 (1.61, 2.92)	1.94 (1.43, 2.64)	14.2 (3.9, 24.6)	0.007
Education (comparing < high school to ≥ master's)	1.54 (1.24, 1.92)	1.42 (1.14, 1.77)	19.0 (5.3, 32.6)	0.006
Corrected for measurement error[3]				
Model 1[1]				
Income (comparing < $10,000 to ≥ $150,000)	4.29 (3.21, 5.73)	3.10 (2.21, 4.36)	28.6	-
Education (comparing < high school to ≥ master's)	2.55 (2.07, 3.16)	2.04 (1.67, 2.49)	31.7	-
Model 2[2]				
Income (comparing < $10,000 to ≥ $150,000)	2.14 (1.59, 2.89)	1.73 (1.24, 2.42)	38.4	-
Education (comparing < high school to ≥ master's)	1.54 (1.23, 1.91)	1.35 (1.22, 1.50)	43.1	-

[1] Adjusted for study arm, age group and race/ethnicity. Income analyses adjusted for having a partner.

[2] Adjusted for factors from Model 1 in addition to family income, having a partner, educational attainment, opposed hormone use, unopposed hormone use, recreational physical activity, diabetes, family history of premature MI, hypertension, low-dose aspirin use, treated high cholesterol, smoking status, BMI, social support and depression status. Income models adjusted for partner. Income analysis excludes 5.7% of sample with no income data

[3] Analyses correcting for measurement error in diet cost do not adjust for OS vs. DM-C because all individuals in validation data come from the DM-C trial.

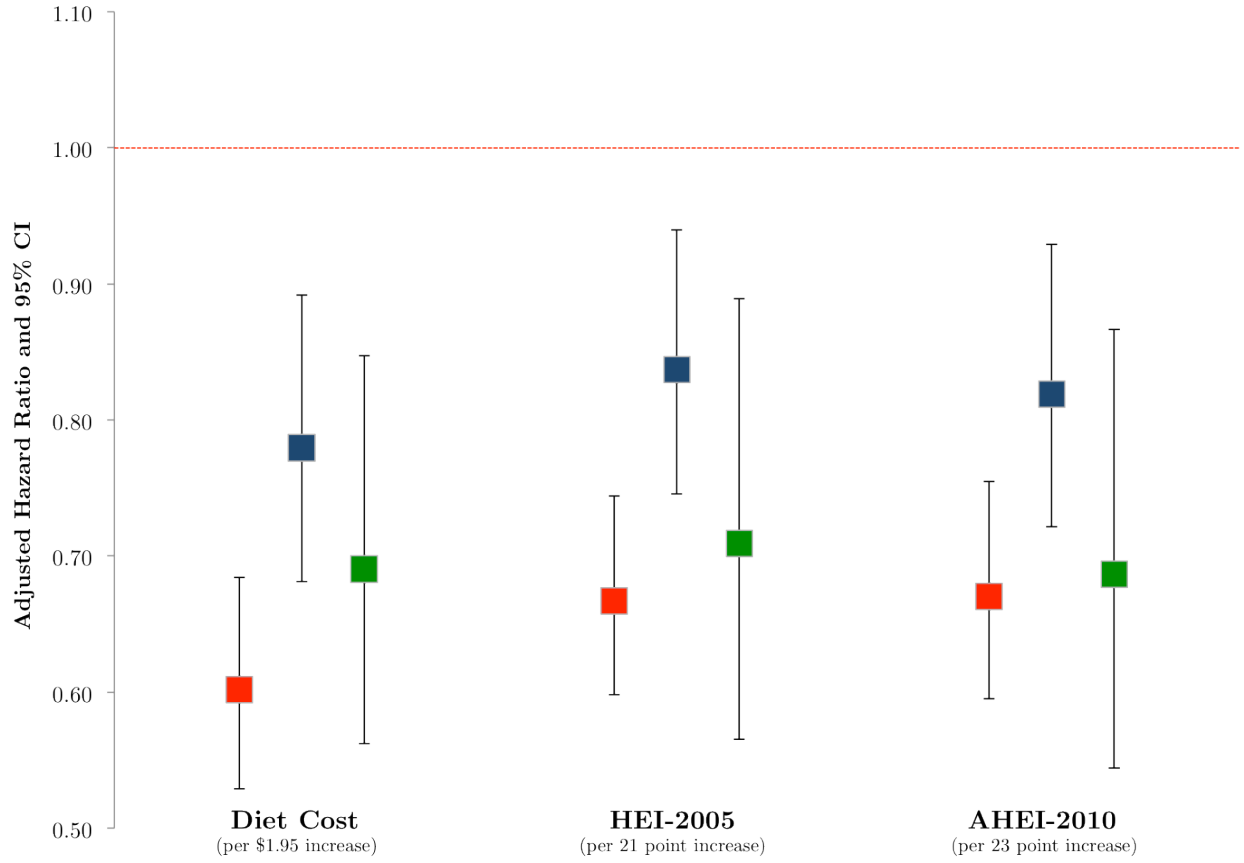
Table 5. Association between diet cost and incidence of CVD using alternative parameterizations of diet cost in the Women's Health Initiative analytic cohort (n=42,632)

	Uncorrected				Corrected	
	Model 1[1]		Model 2[2]		Model 3[2,4]	
	HR	95% CI	HR	95% CI	HR	95% CI
Diet cost ($/2000 kcal)						
Per $1.50 increase	0.68	0.61, 0.74	0.83	0.74, 0.92	0.75	0.64, 0.88
P-value	<0.001		<0.001		<0.001	
Diet cost categories						
Q1: $1.39-3.67	2.05	1.64, 2.56	1.42	1.12, 1.79	-	-
Q2: $3.68-4.09	2.17	1.75, 2.70	1.70	1.36, 2.12	-	-
Q3: $4.10-4.46	1.88	1.50, 2.34	1.56	1.25, 1.96	-	-
Q4: $4.47-4.86	1.58	1.26, 1.98	1.38	1.10, 1.74	-	-
Q5: $4.87-5.43	1.37	1.08, 1.73	1.30	1.03, 1.65	-	-
Q6: $5.43-12.09	ref		ref		-	-
P-trend	<0.001		<0.001			

[1] Adjusted for study arm, age group and race/ethnicity. Income analyses adjusted for having a partner.

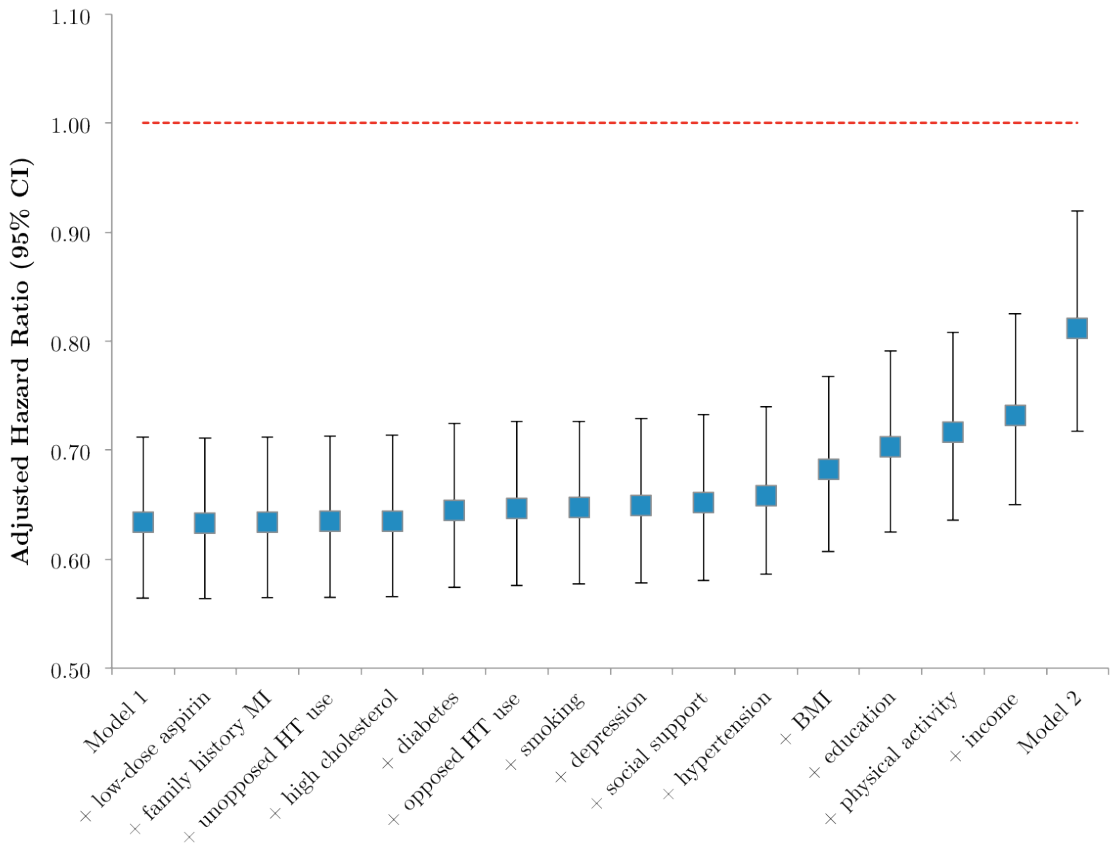
[2] Adjusted for factors from Model 1 in addition to opposed hormone use, unopposed hormone use, recreational physical activity, diabetes, family history of premature MI, hypertension, low-dose aspirin use, treated high cholesterol, smoking status, BMI, social support and depression status. Diet cost models additionally adjusted for income, having a partner and education.

Figure 1. Relation between measures of diet quality and diet cost and risk of cardiovascular disease in Women's Health Initiative analytic cohort (n=42,632)



Red values (Model 1) are adjusted for age group, race/ethnicity and study arm. Blue values (Model 2) are adjusted for factors from Model 1 in addition to family income, having a partner, educational attainment, opposed hormone use, unopposed hormone use, recreational physical activity, diabetes, family history of premature MI, hypertension, low-dose aspirin use, treated high cholesterol, smoking status, BMI, social support and depression status. Green values (Model 2) are from regression calibration, which corrects for measurement error in the exposure. Scale of each variable is based on 2 x standard deviation (e.g., standard deviation for HEI-2005 was 10.5 points, so association between HEI-2005 and CVD was assessed per a 21 point increase.

Figure 2. Comparison of hazard ratios (and 95% CI) upon adjustment for potential confounders of the diet cost and CVD association in the Women's Health Initiative analytic cohort (n=42,632)



Values represent adjustment for each confounder in addition to Model 1. For example, "+BMI" represents a model adjusting for age group, race/ethnicity, study arm and BMI.

Model 1 adjusts for age group, race/ethnicity and study arm (OS vs. DM-C and HT study arm). Model 2 adjusts for Model 1 in addition to the other variables in the figure.

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Chapter 4: Diet cost and mortality among post-menopausal women age 49-64y in the Women's Health Initiative

Abstract

Background: Diet cost has been implicated as an important determinant of diet quality. No studies have evaluated whether diet cost is associated with risk of all-cause mortality.

Methods: A prospective cohort study among 49,336 post-menopausal women 49-64 years using data from the Observational Study and the control arm of the Dietary Modification trial of the Women's Health Initiative was conducted to evaluate the association between diet cost and mortality risk. To estimate diet costs, a national food price database was linked to a food frequency questionnaire. Energy-adjusted diet costs were log-transformed to evaluate the impact of a relative increase in diet costs. Cox proportional hazards models examined the association between diet cost and mortality after adjusting for covariates associated with diet cost and/or mortality.

Results: Over 12 years of follow-up, 2,055 deaths were observed. Diet cost was not significantly associated with mortality (HR for 50% increase diet cost: 0.95; 95% CI 0.87, 1.04). When restricting the analysis to healthy never smokers (n=20,323 and n=553 deaths), a 50% increase in diet costs was associated with a non-significant 15% reduced risk of death (HR 0.85; 95% CI 0.70, 1.03).

Conclusions: This study represents the first prospective examination of the association between diet cost and mortality in the United States. Despite the absence of a strong diet cost and mortality association, evaluations of diet cost as they relate to other health outcomes remain a promising area of future research.

Introduction

Numerous studies have linked dietary factors, including nutrients, food groups, diet quality scores and dietary patterns to all-cause mortality (1-8). Diet cost has been implicated as an important determinant of diet quality and has been linked to many of the dietary patterns and scores related to mortality, including the Alternative Healthy Eating Index, Healthy Eating Index-2005 and a Mediterranean dietary pattern (9-13). Following taste, food cost has been described as the most important factor in choosing foods (14). Recently, 40% of US adults reported that food prices were “very important” in choosing foods at the grocery store, while only 11% said it was “not important” or “not too important” (15). As one would expect, lower income adults were 2.8-times as likely to identify food cost as a “very important” consideration compared to higher income adults (15). Given that lower SES individuals consume lower-cost and poorer quality diets (10), diet costs may also play a role in contributing to SES-differences in mortality (16-18).

Despite the consistent observation that higher cost diets are associated with healthier diets, the impact of diet cost as an upstream determinant of health outcomes has received little direct attention. Until recently, analyses of diet cost as it relates to health outcomes have been hampered by lack of appropriate data. Traditionally, evaluations of food expenditures have focused on families or households, while evaluations of dietary intakes and health outcomes necessarily occur at the individual-level. The development of a national food price database for more than 6,000 foods and beverages can now facilitate analyses of diet cost and health outcomes by linking nationally representative food prices to standard dietary assessment tools available in large-scale health studies.

Using this national food price database, this study prospectively examines the relationship between diet cost and all-cause mortality in a large cohort of 49,336 women. This study represents the first evaluation of diet cost as it relates to mortality in the United States.

Methods

Data for this study came from the WHI Dietary Modification (DM) trial and the Observational Study (OS). The design and baseline descriptions of the WHI studies have been previously described (19). Briefly, 48,835 and 93,676 generally healthy postmenopausal women aged 49-79y at 40 clinical centers across the United States from 1993 and 1998 were randomly assigned to the DM, Calcium and Vitamin D (CaD), or Hormone Therapy (HT) trial, depending on eligibility, or enrolled in the OS. The DM trial investigated the effect of a low-fat dietary pattern on the incidence of heart disease, and breast and colorectal cancers over an average of 7.7 years of follow-up (20, 21). The low-fat dietary pattern emphasized increased intake of fruits, vegetables and grains (19). The OS offered opportunities for investigating a broad range of epidemiologic questions. Many women who were not eligible for the DM trial entered the OS.

This section describes the study population, the assessment and reliability of diet costs estimates, potential confounders and intermediates of the diet cost and mortality association, the study outcome and the statistical methods utilized.

Study Population

Given the emphasis of the current research on the relation between socioeconomic status (SES), as measured by income and education, and mortality, this study was restricted to women 49-64y at study baseline. This population was selected as a working-age population where the family income variable would be more meaningful than it would be for older participants. Women from the intervention arm of the DM trial were not included in the present study, as their diets changed dramatically over time due to the intervention.

We created an analytic cohort by combining data from the OS and the control arm of the DM-trial (DM-C). This was done to increase the available sample size and make use of

measurement error correction techniques, which required the availability of data from four-day food records (4DFRs) for a sub-set of participants (described further below). The first step in creating the analytic cohort was to make the two study arms as similar to each other as possible (22, 23). Because eligibility for the DM trial depended on consuming a high-fat diet, we treated year-1 as baseline for DM-C participants to avoid the complete truncation of dietary intakes (i.e., dietary fat) that would occur if data from year-0 were used (24). For the OS, year-0 was considered baseline in the current study as there was no truncation of dietary intakes.

To further increase the comparability between the OS and the DM-C, the exclusion criteria for the DM trial were applied to participants from the OS. This resulted in the exclusion of women with a history of breast cancer, colorectal cancer in past 10 years, endometrial cancer in past 10 years, other cancer within the past 10 years, with the exception of non-melanoma skin cancer, stroke or acute myocardial infarction (MI) 6 months prior to enrollment, body mass index (BMI)<18, hypertension (>200/>105 mm HG), reported daily energy intake of <600 kcal or >5000 kcal from the food frequency questionnaire (FFQ), ≥10 meals out per week, special low-fiber diet, special diet due to malabsorption, unintentional weight loss of >15 lb (6.8 kg) in the 6 months prior to baseline, self-reported diabetes at age ≤ 21 (a proxy measure for history of type 1 diabetes).

Women missing data on any variables of interest were excluded from analysis: diet cost, education, physical activity, body mass index, hormone use, smoking status, hypertension, high cholesterol, aspirin use, social support, depression status and history of diabetes, cancer or cardiovascular disease. The primary sample size included 49,336 women 49-64y (37,285 from the OS and 12,051 from the DM-C). Because of concerns regarding reverse causality and residual confounding of any potential relation with mortality a secondary cohort was constructed that was restricted to women who never smoked and who had no prior history of cancer or cardiovascular disease. The restricted cohort consisted of 20,232 women (5,033 from the DM-C

and 15,199 from the OS). Follow-up time and events were assessed after at least 2-year of follow-up to further avoid problems of prevalent disease impacting the estimation of the diet cost and mortality relation. Women were followed for up-to 12 years.

Assessing diet cost

The exposure of interest was estimated diet cost assessed using the WHI FFQ. Food and beverage prices per 100g edible portion from a national food price database were linked to the underlying foods in the WHI FFQ. The food price database was created by the Center for Nutrition Policy and Promotion (CNPP) at the USDA and was contemporary with 2001-2002 food prices (25). The CNPP price database provided the prices for 6,680 foods and beverages, excluding alcoholic beverages and bottled water. This price database assumed that all foods/beverages are purchased at a store and prepared at home. The method we used for estimating alcohol prices has been described previously (10).

Diet costs were energy-adjusted using the residual method to account for differences in energy intake between individuals (26). This method estimates a residual value of diet cost based on the observed relation between energy intake and diet cost. A constant of 2000 kcal was then added to the estimated residual values to ease interpretation. For primary analyses, the diet cost variable was log-transformed to evaluate the impact of a percentage change in diet costs rather than an absolute difference. This was done because one would not expect a 1-dollar increase in diet costs to have the same impact for individuals consuming low vs. high cost diets. For most analyses we present the relative risk of mortality associated with a 50% increase in diet costs. For reference, a 50% increase in diet cost roughly corresponds to the difference between the 85^{th} and 15^{th} percentile values ($5.50 vs. $3.62/day). A 50% increase was selected as it roughly corresponds to the difference between extreme quintiles if participants were

grouped into five categories. In addition, a 50% increase is comparable to a two standard deviation increase (+$1.95) from the 25th%ile estimate of diet cost (i.e., from $3.90 to $5.85).

In order to assess the measurement characteristics of the diet cost estimate from the FFQ and to utilize approaches to reduce the impact of measurement error, a reliability sub-study was conducted. In brief, we linked the USDA food price database (described above) and the MyPyramid Equivalents Database to 560 four-day food records (4DFR) completed by women enrolled in the DM-C, of whom 490 were eligible for inclusion in the mortality analysis. The MyPyramid Equivalents Database includes information on the number of servings of different foods groups and is needed to evaluate the Healthy Eating Index – 2005 (HEI-2005) (27, 28).

The 4DFRs were originally collected in order to evaluate adherence to the dietary modification trial and to complement data from the FFQ (19). To better measure long-term intake, avoid measuring correlated eating behaviors and include one weekend day, the 4DFR was completed on alternating days. Non-white women were over-sampled to participate in the 4DFR sub-study to more precisely evaluate dietary habits and adherence to the intervention among minority women. The correlation coefficient was 0.52 for a comparison of log-transformed energy adjusted diet costs and 0.51 for the HEI-2005 between the FFQ and 4DFR, comparable to values for saturated fat (0.56), niacin (0.54), or folate (0.52) for nutrients from the FFQ and 4DFR (29).

Socioeconomic status

Measures of SES represent potential confounders of the diet cost and mortality association. In addition to evaluating the diet cost and mortality association, an additional aim was to determine whether some of the socioeconomic gradient in mortality could be attributed to diet cost. Two SES variables were used in the current analysis: family income and educational attainment. These were assessed at WHI baseline via questionnaire. To capture the broadest association

between SES and mortality, the full range of income values were used (<10, 10-19, 20-34, 35-49, 50-74, 75-99, 100-149, and ≥150 in $1000 and a missing category). Education was coded in 5 groups (<high school, high school graduate/equivalent, some college, college degree/some post-graduate education and master's degree or higher). In all analyses income and education were coded as categorical variables. All analyses including family income adjusted for whether the participant had a partner.

Potential Confounders

Key covariates were identified that are either associated with both diet cost and the risk of mortality. These variables and their parameterization are described below. All covariates, with the exception of body mass index, were assessed via questionnaire at baseline (or at year 1 for DM-C participants). Socio-demographic covariates included age group (49-54, 55-59, 60-64), race/ethnicity (American Indian/Alaskan Native, Asian/Pacific Islander, black, Hispanic, non-Hispanic white and unknown [including other]), family income, education and having a partner (yes/no). Additional variables included recreational physical activity (<1.5, 1.67-6.38, 6.42-12.5, 12.58-22.5, ≥22.58 metabolic equivalents [MET] hours/wk, smoking status (never, former smoker less than 20 years, former smoker more than 20 years, current smoker less than 20 years and current smoker more than 20 years), unopposed estrogen use as pills or patches (former, never or current), estrogen plus progesterone use as pills or patches (former, never or current), hypertension (taking pills, diagnosed but no pills, not previously diagnosed), aspirin use (yes/no), treated high cholesterol (yes/no), measured body mass index category (<25 [underweight/healthy weight], 25-29.9 [overweight], 30-34.9 [class I obese], 35-39.9 [class II obese], and ≥40 [class III obese] kg/m^2), Center for Epidemiology Studies Depression scale (<0.009 [no depression], 0.009-0.059 [slight depression], ≥0.06 [moderate/severe depression]) and a scale indicating level of social support. In addition, dichotomous variables indicating history of diabetes, cardiovascular disease and cancer were included. Each of these was

modeled as a categorical variable, with the exception of the social support scale, which was treated as a continuous variable.

Finally, given the inclusion of participants from both the OS and DM-C, we adjusted for study arm (OS vs. DM-C) and arm of the HT and CaD trial, as participants in the DM-C could also participate in the other trials and there was some evidence that participation in these trials was associated with mortality (30, 31).

Potential Intermediates

To de-compose the relation between diet cost and mortality we evaluated two diet quality variables that are conceptualized to be consequences of diet cost, and also likely associated with mortality. The Healthy Eating Index-2005 (HEI-2005) (28, 32) and the 2010 Alternative Healthy Eating Index (AHEI-2010) (2) were the summary measures used. The HEI-2005 is based on adherence to the 2005 Dietary Guidelines for Americans and the AHEI-2010 is based on observed associations between food/beverage intake and disease risk in the literature. Both of these measures were derived from the WHI FFQ and also from the 4DFR data. The measurement characteristics of the WHI FFQ have been previously described (29).

Outcome and statistical methods

The outcome in the current investigation is all-cause mortality assessed over 12-years of follow-up. After receiving notice of a death, WHI study staff made an effort to obtain information on contributing factors. To ascertain survival and cause of death for all participants, data linkage with the National Death Index was regularly performed. WHI participants who were lost to follow-up or who were known to have died were matched to the National Death Index to search for unreported deaths and identify causes of death (33). Due to limitations in the number of

observed deaths, cause-specific mortality was not evaluated here (e.g., only 213 definite or probably coronary heart disease deaths were observed).

Cox proportional hazards regression was used to estimate the relative risk of mortality. The first set of models (Model 1) adjusted for study arm, age group, and race/ethnicity. Model 2 adjusted for additional socio-demographic and behavioral factors associated with risk of mortality and diet cost, including family income, educational attainment, having a partner, smoking status, HT use, recreational physical activity, BMI, hypertension, high cholesterol, aspirin use, CES-D depression score, social support, and history of diabetes, cardiovascular disease or cancer, in addition to factors from Model 1. Analyses treating income and education as the independent variables did not adjust for the other SES variable. Additional analyses added dietary factors, including HEI-2005 and AHEI-2010 in separate models, which were hypothesized to be intermediates of the diet cost and cardiovascular disease association.

Because the estimate of diet cost is an error-prone measure, we used regression calibration to account for measurement error using the estimate of diet cost from the 4DFR as an “alloyed gold standard” (34, 35). An “alloyed gold standard” is a reference measure that is not a perfect gold standard, but rather a measure that captures the true exposure of interest better than the primary instrument (i.e., the FFQ). While clearly, the 4DFR is an imperfect measure of diet as shown by studies of doubly labeled water, it has been shown to have better measurement characteristics than an FFQ (36). The regression calibration approach reduces the bias from measurement error assuming that the errors in the two instruments are uncorrelated, though previous work has shown that even in the presence of modest correlated errors, the estimate from regression calibration should yield a less biased estimate of the observed exposure-disease relationship using the error-prone measure (35). The %blinplus SAS macro was used to implement regression calibration (37).

Additional analyses evaluated the mechanisms (e.g., diet quality) by which diet cost may influence mortality. Treating diet cost as the primary independent variable of interest the %mediate SAS macro was used to evaluate the extent by which any observed association between diet cost and mortality was explained by diet quality (38).

All analyses were conducted among the entire analytic cohort and among the restricted cohort of women who never smoked and had no prior history of cancer of cardiovascular disease. The proportional hazards assumption was evaluated for all primary analyses by evaluating the Schoenfeld residuals. Stata 13.1 (College Station, TX) and SAS 9.3 for Windows (Cary, NC 2013) for the %blinplus and %mediate macros (37, 38) were used for all analyses.

Results

Population characteristics

Subject characteristics are described in **Table 1** as are average diet costs by socio-demographic, anthropometric and behavioral characteristics are also provided. The mean age at study baseline was 58.2y (SD=4.1). The cohort was primarily white, but had a range of family incomes. Nine percent of the cohort had family incomes less than $20,000/year, while more than a quarter had family incomes greater than $75,000. A similarly broad distribution of education was observed, though only a small proportion of women had not graduated from high school. Thirty-eight percent of the cohort was healthy weight/underweight and 28.7% was obese. The average HEI-2005 score was 68.3 (SD=10.5) (out of 100 possible) and the average number of MET hours from recreation physical activity per week was 13.3 (SD=14.3).

The average energy-adjusted diet cost was $4.57 (SD=$0.97; median=$4.46; 10^{th} percentile=$3.44; 90^{th} percentile=$5.81). Diet costs were related to socio-demographic, anthropometric and behavioral characteristics. White women consumed the most expensive

diets, while Hispanic and black women consumed the least costly diets (p-difference < 0.001). A graded relation between income and education and diet cost was observed. The diet costs of women with family incomes greater than $150,000 were 28% higher than women with incomes less than $10,000 (p-trend < 0.001). There was a significant association between diet quality and diet cost. Women with healthier diets, as measured by HEI-2005, tended to consume more costly diets (per calorie) (p-trend < 0.001), as did women who were more physically active (p-trend < 0.001). AHEI-2010 was also associated with diet cost in a similar manner (p-trend < 0.001). Women with lower BMIs consumed more costly energy-adjusted diets than did participants with higher BMIs (p-trend < 0.001).

Overall, the average length of follow-up was 11.8 years and 2,055 deaths were observed. The mortality rate was 353 per 100,000 person-years. Among the restricted cohort (excluding ever smokers and those with a history of cancer and CVD), 553 deaths were observed with an average length of follow-up of 11.9 years (mortality rate of 230.3 per 100,000 person-years).

Social gradient in mortality

In minimally adjusted models, both income and education were strongly and negatively associated with mortality in the complete cohort (see **Table 2**). Compared to individuals with incomes greater than $150,000/year women with incomes less than $10,000 had a 3.1-fold increased mortality risk (HR 3.08; 95% CI 2.48, 3.84). A similar association was observed for education. Women with less than high school education had a 1.8-fold increased risk of mortality compared to those with a master's degree (95% CI 1.52, 2.09). In the restricted sample the association between SES and mortality was weaker, with a modest gradient by income and no association with education. After adjusting for additional confounders in the restricted sample there was no longer a relation between income and mortality. In the complete sample, adjustment for probable intermediates (e.g., tobacco use, physical activity and BMI)

reduced the strength of the income and mortality relation, though it remained significant. However, for education, the association was no longer present after adjustment for intermediates.

Diet cost and mortality

In minimally adjusted models, in both the complete and restricted cohort, a 50% increase in diet cost was associated with a reduced mortality risk (HR 0.76; 95% CI 0.70, 0.83 in the complete cohort and HR 0.74; 95% CI 0.62, 0.89 in the restricted cohort). For reference, a 50% increase in diet costs corresponds to an increase from the 15th percentile ($3.62) to the 85th percentile ($5.43). After adjusting for important confounders in the complete cohort, the association between diet cost and mortality was no longer observed. However, in the restricted cohort there was some suggestion of an association between increased diet cost and reduced mortality risk (HR 0.85; 95% CI 0.70, 1.03; p = 0.09). In regression calibration models a 50% increase in diet costs was associated with an 18% reduced risk of mortality (HR 0.82; 95% CI 0.58, 1.16; p = 0.26).

Given an absence of an association between SES measures and mortality in adjusted models and the relatively weak relation between diet cost and mortality, additional analyses did not examine whether the association between SES and mortality could be attributed to diet cost.

Comparison of diet cost with other diet quality measures

A comparison of the effect of diet cost, HEI-2005 and AHEI-2010 on total mortality is provided in **Figure 1**. As shown above, diet cost was only associated with mortality in minimally adjusted models. Higher HEI-2005 and AHEI-2010 scores were related to reduced mortality risk in both the complete and restricted cohort, and the effect of HEI-2005 was marginally stronger than for AHEI-2010.

Exploring mechanisms of the diet cost and mortality association

While the association between diet cost and mortality was not particularly strong, additional analyses evaluated the extent by which the two diet quality measures may account for the observed association (see **Table 3**). In the complete cohort in minimally adjusted models the two diet quality measures significantly attenuated the effect of diet cost on mortality. In the restricted cohort there is also some suggestion that the pathway between diet cost and mortality is accounted for by diet quality. However, in fully adjusted models there were no longer any significant mediation effects given the lack of an association between diet cost and mortality. In models that account for error in estimating the diet quality measures the mediation effects were strengthened. For example, in Model 1 for HEI-2005, 63% and 65% of the association between diet cost and mortality could be attributed to differences in diet cost in the complete and restricted cohort, respectively. There was no evidence that the proportional hazards assumption was violated for any of the primary analyses (Schoenfeld residuals global test $p>0.10$ for all models.

Discussion

In this prospective cohort study of 49,332 women form the Women's Health Initiative diet cost was not systematically associated with risk of all-cause mortality. When analyses were restricted to never smokers and those who had no history of CVD or cancer, there was some suggestion of an association between higher diet costs and reduced mortality risk. In this group, a 50% increase in diet cost was associated with a 15% reduced mortality risk (95% CI -3, 30% reduced risk). An additional aim sought to examine whether diet cost may account for the association between SES and mortality. However, contrary to expectations, there was no residual association between SES and mortality after accounting for established intermediates

of the SES-mortality relation (e.g., physical activity, smoking or body mass index), so diet cost was not explored as an additional intermediate.

The current study represents the first evaluation of diet cost as it relates to mortality in a prospective cohort study in the United States. Previous research, using data from the same population, observed that consuming a higher cost diet was associated with a significant decreased risk of type 2 diabetes (HR associated with 50% increase in diet cost 0.86; 95% CI 0.79, 0.96) and a composite cardiovascular disease outcome (HR 0.81; 95% CI 0.72, 0.92). To date, these are the only prospective studies evaluating diet cost, overall, in the primary prevention of chronic disease and ill health. A previous study conducted in Taiwan and using a similar approach to evaluate diet costs as used here, observed that expenditures on vegetables and fruit was associated with a decreased mortality risk, while overall spending was not associated with mortality (39). However, these findings are not surprising given that spending on fruits/vegetables is likely collinear with their consumption, which has long been linked to a reduced risk of mortality and chronic disease (40, 41).

Beyond the previously observed association between diet cost and chronic disease risk, the motivation to evaluate diet cost as it relates to mortality is driven by the long-observed link between various dietary measures, including dietary patterns (e.g., Mediterranean or prudent), diet quality scores (e.g., AHEI or HEI-2005), individual foods/food groups (e.g., nuts or vegetables), and nutrients (e.g., fiber or potassium), and mortality risk (1, 3-7). Here, we hypothesized that a higher cost diet cost diet would be associated with a reduced risk of mortality given the previously observed associations between diet cost and diet quality. In fact, many of the dietary patterns, diet quality scores, individual foods/food groups and nutrients listed above that are associated with mortality have been related to diet or food costs (9-11, 13, 42, 43). In the current study the association between diet cost and mortality, in minimally adjusted models was significantly mediated by global measures of diet quality (i.e., HEI-2005

and AHEI-2010). Further, in analyses that account for measurement error in the diet quality scores, there is no longer a significant association between diet cost and mortality after their adjustment.

Despite the hypothesis of an association between higher diet cost and reduced risk of all-cause mortality, the current study observed an equivocal association. The lack of an observed association may be due in part to the limited sample size available after restricting the sample to never smokers and those with no prior history of cancer or cardiovascular disease. This reduced the sample size by nearly 60% and reduced the mortality rate by one-third. While all epidemiologic analyses are subject to reverse causation and residual confounding, analyses using mortality as an outcome are particularly vulnerable, as demonstrated by the long-running debate regarding the association between BMI and mortality (44-46). We sought to reduce the likelihood of residual confounding and reverse causation by delaying follow-up for two years following baseline and applying these restrictions. After applying these restrictions the association between diet cost and mortality, in fully adjusted models, became more apparent. Evaluating restriction of each of these variables separately revealed that the observed results of diet cost and mortality are most sensitive to the exclusion of ever smokers, suggesting that the strong effect of smoking on mortality may overwhelm any potential association of diet cost and mortality. In addition, the choice to include women 49-64y may influence the results. The impact of diet cost on mortality may be more readily apparent among older adults, where coronary heart disease and related outcomes account for a greater proportion of deaths. However, evaluating the association between diet cost and mortality in the current population provides useful information about the overall health impact of diet cost, which can be viewed in parallel with the association between diet cost and other outcomes.

The limitations of this study are worth noting. The primary limitation of the current study, and most observational studies, is the likelihood of residual confounding due to poorly measured or

unmeasured variables. While we made every effort to include potential confounders of the diet cost and mortality association some variables that were included may not be measured adequately. Chief among these potential confounders is recreational physical activity and socioeconomic status, which both have a well-established association with mortality (16, 47). As measured here, higher income, education and physical activity are all associated with higher estimated diet costs. The limitations of income and education as measures of SES are well established (48, 49), as are the challenge in assessing physical activity via questionnaire (50). Here, following adjustment for age group and study arm, adjusting for income and partner increased the hazard ratio for diet cost and mortality from 0.75 to 0.88. Similarly, including physical activity increased the hazard ratio from 0.75 to 0.84. To address concerns regarding measurement error in dietary variables, data were incorporated from an alternative instrument (4DFR) to reduce the impact of measurement. Similar approaches may prove useful for assessing physical activity, particularly when physical activity is a strong confounder of the exposure-disease relationship. For measurement of SES, few measures beyond income and education are included in most health studies; but inclusion of area-based measures or additional questions to assess SES would reduce concerns regarding residual confounding by SES.

Beyond residual confounding, measurement error in assessing diet cost, along with other dietary constituents, is an additional challenge. Deriving diet costs using a national food prices database may not reflect the actual prices for food paid by individual WHI participants. This is similar to the weakness inherent in deriving nutrient intakes from nutrient composition databases, which do not reflect potential heterogeneity in the nutrient levels of foods actually consumed. Despite limitations in the use of standard prices database, it represents a meaningful source of information on food prices that can be linked to individual data on diets and health. Additional challenges in linking the price database to the FFQ include the use of a

fixed food list in the FFQ, which may not adequately represent the foods/beverages consumed by participants. In addition, the food prices assume that all foods are prepared at home and does not account for restaurant purchases. This study was restricted to women who consumed fewer than 10 meals away from home, which alleviates some concerns regarding food away from home. Lastly, the food price database was from 2001-2002 and the study baseline was from 1994-1998. While individual food prices may have changed between these two time periods, the costs of total diets would not be expected to change dramatically. Given concerns regarding measurement of diet costs we compared the FFQ estimate of diet cost with one derived from a 4DFR and found them to be modestly correlated (r=0.51). This value is comparable to findings from other reliability studies examining diet cost (51). Regression calibration approaches were used to account for measurement error in diet cost, HEI-2005 and AHEI-2010 that treated the 4DFR as an “alloyed gold-standard” (i.e., an error-prone instrument that has less error than the original instrument, the FFQ) (35). Further, although the 4DFR was considered an “alloyed gold standard,” the amount of variation in energy intake explained by 4DFRs compared to biomarkers may be limited, and there is evidence that women with higher BMIs are more likely to under-report energy-intakes (36, 52). Nonetheless, the 4DFR explained more of the variation in energy when compared to the FFQ and may be sufficient for epidemiologic studies. Here, the impact of accounting for measurement error in the diet cost estimate was of marginal consequence given the weak relationship with mortality. However, inclusion of data from the 4DFR with HEI-2005 and AHEI-2010 resulted in much stronger effects than from analyses that ignored their error. Future studies of diet cost and health should make use of methods to account for measurement error, otherwise only the strongest associations will be observed.

This study also had a number of strengths. First, this study included rich dietary data, which allowed us to address the limitations of exposure measurement error. Second, despite concerns

over the small number of deaths in the restricted cohort, this study had a large enough sample size to detect a meaningful association between diet cost and mortality. Few studies in this age group of women are adequately powered to examine mortality. Third, in terms of SES, this sample included a wide range of women with 11% living on less than $10,000/year and 12% on more than $100,000/year.

Conclusions

This study represents the first prospective examination of the association between diet cost and mortality in the United States. In summary, we did not observe a strong association between diet cost and mortality. Despite the absence of a strong diet cost and mortality association, evaluations of diet cost as they relate to other health outcomes remain a promising area of future research. Given the paucity of research on diet cost and health outcomes, the results of this study need to be compared to studies conducted in different populations and food environments.

Table 1. Participant characteristics and mean energy-adjusted diet costs in the Women's Health Initiative analytic cohort (n=49,336)

				$/2000 kcal	
	deaths	N	% of total	Mean	95% CI
Age group					
49-54	365	13,809	28.0	4.53	4.52, 4.55
55-59	664	18,042	36.6	4.59	4.57, 4.6
60-64	1,026	17,485	35.4	4.59	4.57, 4.6
P-trend				<0.001	
Race/ethnicity					
American Indian/Alaskan Native	18	193	0.4	4.21	4.08, 4.33
Asian/Pacific Islander	31	1,424	2.9	4.61	4.56, 4.67
Black	237	4,347	8.8	4.11	4.08, 4.14
Hispanic	65	2,003	4.1	4.12	4.07, 4.16
White, not Hispanic	1,676	40,751	82.6	4.64	4.63, 4.65
Unknown (incl. other)	28	618	1.3	4.52	4.40, 4.59
P-difference				<0.001	
Family income ($1000)					
< $10	123	1,355	2.8	4.01	3.96, 4.06
$10-19	223	3,187	6.5	4.11	4.08, 4.15
$20-34	456	8,444	17.1	4.32	4.30, 4.34
$35-49	394	9,439	19.1	4.50	4.48, 4.52
$50-74	409	11,312	22.9	4.64	4.62, 4.65
$75-99	179	5,900	12	4.80	4.78, 4.83
$100-149	112	4,580	9.3	4.93	4.9, 4.96
> $150	55	2,351	4.8	5.13	5.09, 5.18
P-trend				<0.001	
Missing	104	2,768	5.6	4.56	4.52, 4.59
Educational attainment					
<High school	102	1,611	3.3	3.93	3.88, 3.97
High school/equivalent	375	7,307	14.8	4.28	4.26, 4.30
Some college	811	17,862	36.2	4.51	4.50, 4.53
College graduate	423	12,027	24.4	4.74	4.72, 4.75
≥Master’s degree	344	10,529	21.3	4.78	4.76, 4.80
P-trend				<0.001	
HEI-2005					
Q1: 26-58 [lower diet quality]	542	9,868	20.0	4.16	4.14, 4.18
Q2: 59-66	437	9,867	20.0	4.40	4.39, 4.42
Q3: 67-72	409	9,867	20.0	4.62	4.60, 4.63
Q4: 73-77	348	9,867	20.0	4.78	4.76, 4.80
Q5: 78-93 [higher diet quality]	319	9,867	20.0	4.89	4.88, 4.91
P-trend				<0.001	

Table 1, continued.

				$/2000 kcal	
	deaths	N	% of total	Mean	95% CI
AHEI-2010					
Q1: 13-35[lower diet quality]	521	9,869	20.0	4.08	4.06, 4.09
Q2: 36-42	429	9,866	20.0	4.34	4.32, 4.36
Q3: 42-48	388	9,867	20.0	4.57	4.55, 4.58
Q4: 48-55	368	9,867	20.0	4.80	4.78, 4.81
Q5: 56-93 [higher diet quality]	349	9,867	20.0	5.08	5.06, 5.10
P-trend				<0.001	
Recreational physical activity (MET-hours/wk)					
Q1: ≤1.5	585	10,129	20.5	4.18	4.16, 4.2
Q2: 1.67-6.38	441	9.656	19.6	4.41	4.39, 4.43
Q3: 6.42-12.5	391	9.840	19.9	4.58	4.56, 4.6
Q4: 12.58-22.5	332	9,903	20.1	4.75	4.73, 4.77
Q5: ≥22.58	306	9,808	19.9	4.94	4.92, 4.96
P-trend				<0.001	
Body Mass Index category (kg/m^2)					
Underweight/healthy weight: <25	627	18,680	37.9	4.72	4.70, 4.73
Overweight: 25-29.9	613	16,498	33.4	4.59	4.58, 4.61
Class I Obesity: 30-34.9	403	8,413	17.1	4.42	4.40, 4.44
Class II Obesity: 35-39.9	235	3,565	7.2	4.29	4.26, 4.32
Class III Obesity: ≥40	177	2,180	4.4	4.21	4.17, 4.24
P-trend				<0.001	

Table 2. Association between diet cost, income and education and mortality in Women's Health Initiative analytic cohort

	Complete cohort (n=49,336)				Healthy never smokers cohort[1] (n=20,232)			
	Model 1[2]		Model 2[3]		Model 1[2]		Model 2[3]	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Diet cost ($/2000 kcal)								
Per 50% increase	0.76	0.70, 0.83	0.95	0.87, 1.04	0.74	0.62, 0.89	0.85	0.70, 1.03
P-value	<0.001		0.31		<0.001		0.09	
Family income ($1000)[4]								
< $10	3.11	2.23, 4.33	1.70	1.21, 2.38	2.44	1.12, 5.34	1.72	0.78, 3.80
$10-19	2.29	1.69, 3.10	1.56	1.14, 2.12	2.69	1.38, 5.24	2.02	1.03, 3.96
$20-34	1.83	1.38, 2.44	1.39	1.04, 1.85	2.24	1.19, 4.19	1.79	0.95, 3.37
$35-49	1.50	1.13, 1.99	1.21	0.91, 1.61	1.97	1.05, 3.68	1.66	0.88, 3.10
$50-74	1.39	1.05, 1.85	1.21	0.91, 1.60	1.92	1.04, 3.57	1.71	0.92, 3.18
$75-99	1.24	0.92, 1.68	1.16	0.85, 1.56	2.08	1.10, 3.93	1.92	1.01, 3.63
$100-149	1.04	0.75, 1.44	1.03	0.75, 1.43	1.61	0.83, 3.15	1.54	0.79, 3.01
≥ $150	ref		ref		ref		ref	
Missing	1.39	1.00, 1.92	1.15	0.83, 1.60	1.27	0.61, 2.64	1.10	0.53, 2.30
P-trend	<0.001		<0.001		0.004		0.184	
Education								
<High school	1.79	1.43, 2.25	1.10	0.87, 1.39	1.36	0.85, 2.18	0.98	0.61, 1.58
High school/equiv.	1.45	1.25, 1.68	1.07	0.92, 1.24	1.01	0.76, 1.33	0.84	0.63, 1.12
Some college	1.34	1.18, 1.52	1.03	0.90, 1.17	1.12	0.89, 1.41	0.99	0.78, 1.24
College graduate	1.07	0.92, 1.23	0.99	0.86, 1.14	0.98	0.76, 1.26	0.95	0.74, 1.22
≥Master's degree	ref		ref		ref		ref	
P-trend	<0.001		0.25		0.32		0.43	

[1] Restricted to women who are never smokers and have no history of cancer or cardiovascular disease.

[2] Adjusted for study arm (OS vs. DM-C, CaD arm and HT arm), age group and race/ethnicity. Income analyses adjusted for having a partner.

[3] Adjusted for factors from Model 1 in addition to opposed hormone use, unopposed hormone use, recreational physical activity, history of diabetes, hypertension status, aspirin use, treated high cholesterol, smoking status, BMI, social support and depression status. Diet cost models additionally adjusted for income, having a partner and education.

[4] Income analyses based on sample size of 46,568 for complete cohort and 19,055 for restricted cohort. Values from regression calibration analysis corresponding to a 50% increase in diet costs for the complete cohort was a HR 0.95 (95% CI 0.82, 1.09). From the restricted cohort, the HR was 0.82 (95% CI 0.58, 1.16).

Table 3. Role of diet measures in accounting for the association between diet cost and mortality in the Women's Health Initiative analytic cohort

	Complete cohort (n=49,336)				Healthy never smokers cohort[1] (n=20,232)			
	Not adjusted for diet measure; HR (95% CI)	Adjusted for diet measure; HR (95% CI)	% mediated (95% CI)	p-value	Not adjusted for diet measure; HR (95% CI)	Adjusted for diet measure; HR (95% CI)	% mediated (95% CI)	p-value
Uncorrected								
Healthy Eating Index – 2005								
Model 1[2]	0.76 (0.70, 0.83)	0.86 (0.79, 0.95)	46.5 (28.9, 64.7)	<0.001	0.74 (0.62, 0.89)	0.83 (0.69, 1.01)	38.8 (7.5, 70.1)	0.015
Model 2[3]	0.95 (0.87, 1.04)	0.99 (0.90, 1.09)	86.8 (-93.3, 267)	0.35	0.85 (0.70, 1.03)	0.90 (0.74, 1.09)	38.6 (-18.3, 95.4)	0.18
Alternative Healthy Eating Index – 2010								
Model 1[2]	0.76 (0.70, 0.83)	0.83 (0.76, 0.91)	31.9 (-3.6, 67.4)	0.08	0.74 (0.62, 0.89)	0.81 (0.67, 0.98)	27.7 (-3.1, 58.5)	0.08
Model 2[3]	0.95 (0.87, 1.04)	0.99 (0.90, 1.09)	76.7 (-228, 381)	0.62	0.85 (0.70, 1.03)	0.89 (0.73, 1.09)	38.2 (-17.5, 93.8)	0.18
Corrected for measurement error (DQ)[4]								
Healthy Eating Index – 2005								
Model 1[2]	0.76 (0.70, 0.83)	0.90 (0.81, 1.02)	63.0	-	0.74 (0.62, 0.89)	0.90 (0.71, 1.14)	65.7	-
Model 2[3]	0.95 (0.87, 1.05)	1.01 (0.91, 1.12)	124	-	0.85 (0.70, 1.03)	0.93 (0.75, 1.14)	53.6	-
Alternative Healthy Eating Index – 2010								
Model 1[2]	0.76 (0.70, 0.83)	0.89 (0.79, 1.00)	58.2	-	0.74 (0.62, 0.89)	0.84 (0.68, 1.04)	42.6	-
Model 2[3]	0.95 (0.87, 1.05)	1.06 (0.95, 1.19)	228	-	0.85 (0.70, 1.03)	0.93 (0.74, 1.17)	57.8	-
Model 2[3]								

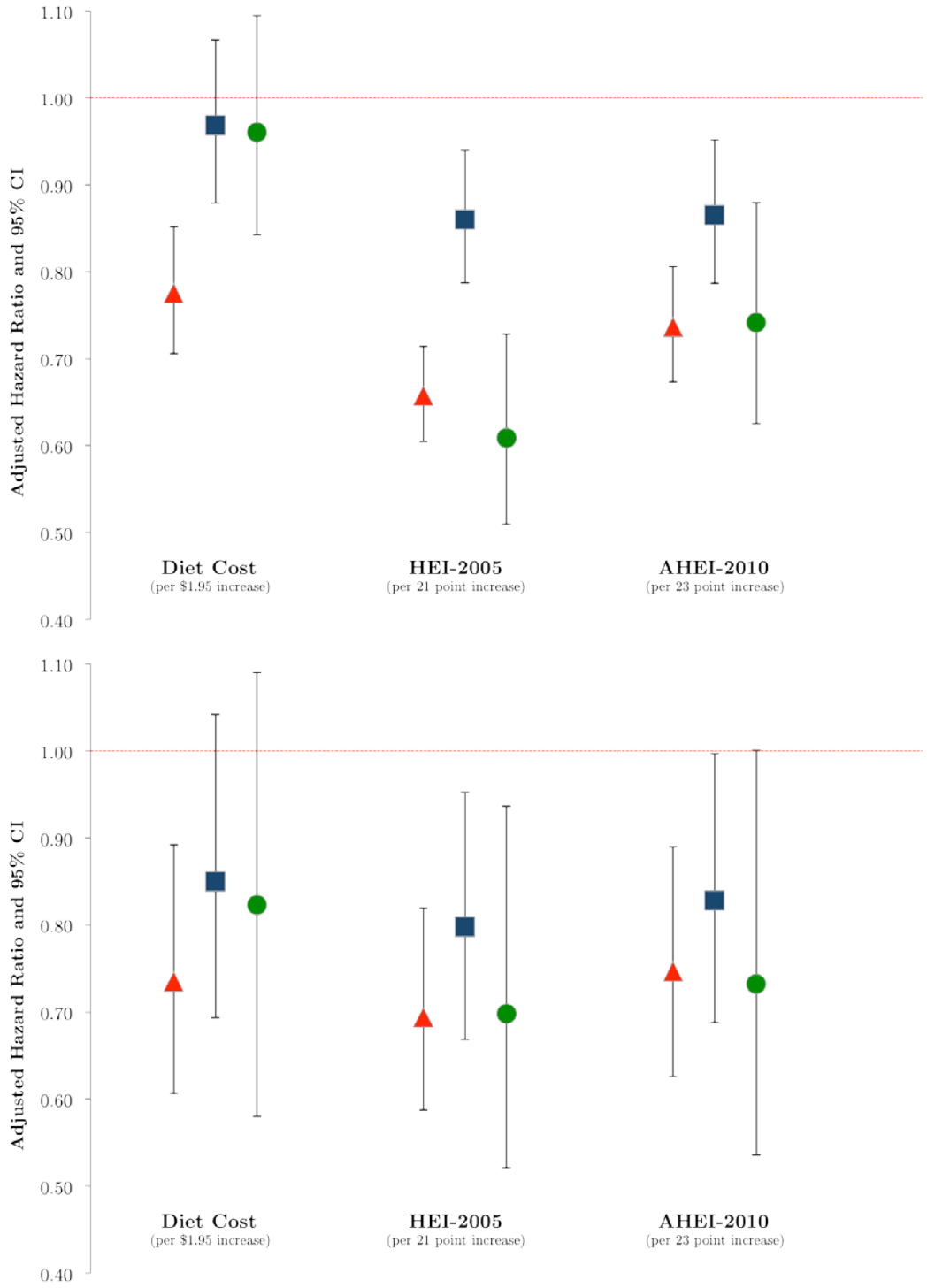
[1] Restricted to women who are never smokers and have no history of cancer or cardiovascular disease.

[2] Adjusted for study arm (OS vs. DM-C, CaD arm and HT arm), age group and race/ethnicity. Income analyses adjusted for having a partner.

[3] Adjusted for factors from Model 1 in addition to opposed hormone use, unopposed hormone use, recreational physical activity, history of diabetes, hypertension status, aspirin use, treated high cholesterol, smoking status, BMI, social support, depression status, income, partner and education.

[4] This analysis corrects for measurement error in the diet quality score using regression calibration. Analyses from regression calibration models do not adjust for participation in the OS.

Figure 1. Comparison of diet cost, HEI-2005 and AHEI-2010 and their relation with all-cause mortality. Entire cohort on top panel and healthy never smokers cohort[1] on bottom panel[2,3,4]



[1] Restricted to women who are never smokers and have no history of cancer or cardiovascular disease.

[2] Red triangle corresponds to Model 1: Adjusted for study arm (OS vs. DM-C, CaD arm and HT arm), age group and race/ethnicity.

[3] Blue rectangle corresponds to Model 2: Adjusted for factors from Model 1 in addition to opposed hormone use, unopposed hormone use, recreational physical activity, history of diabetes, hypertension status, aspirin use, treated high cholesterol, smoking status, BMI, social support, depression status, income, partner and education.

[4] Green circle corresponds to Model 2 from regression calibration model. Analyses from regression calibration models do not adjust for participation in the OS since only women in the DM-C completed a 4DFR (participation in the HT and CaD trial is still accounted for).

Values for each dietary variable correspond to 2*standard deviation (e.g., diet cost SD = $0.975).

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Conclusion

In this dissertation project, we aimed to evaluate the association between diet cost and weight change, type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD) and all-cause mortality. In addition, we evaluated the extent by which the social gradient in these outcomes could be explained by differences in diet cost by income/education. Data from the Women's Health Initiative Dietary Modification trial control arm (DM-C) and Observational Study (OS) was used to evaluate the association between diet cost and health, while also exploring the role of diet cost in explaining the social gradient in these outcomes.

The direction of the association between diet cost and weight change was unexpected. Contrary to expectations that women consuming higher-cost diets would gain less weight than women consuming lower-cost diets, we observed that higher diet costs were associated with excess weight gain. This association was limited to women who had lost weight prior to baseline. Among women who were weight stable or gained weight prior to baseline, there was no association between diet cost and weight change. Studies of behavioral factors and weight change are challenged by the difficulty in accounting for weight trajectories and changes in behaviors driven by prior weight changes or efforts to lose or maintain weight. This is the second study to observe an unexpected association between higher diet costs and increased weight gain (1). Studies linking dietary factors to weight change typically evaluate change in exposure (e.g., change in yogurt or soda intake) (2, 3). Future studies of diet cost and weight should consider evaluating change in diet cost.

While results for weight change were unexpected, consuming a higher cost diet was associated with a decreased risk of T2DM and CVD. A 50% increase in diet cost was associated with a 14% and 18% reduced risk of T2DM and CVD, respectively. A strong social gradient was observed for both outcomes. Established intermediates of the social gradient in these

outcomes, including physical activity, smoking and body mass index, did not explain the entirety of the gradient. Given the significant association between diet cost and T2DM and CVD, the impact of diet cost as a potential factor explaining the social gradient was evaluated. Diet cost explained 15-19% of the association between income/education and T2DM and 12-19% of the association between income/education and CVD. The potential mediating role of diet cost was comparable or stronger to effects of known intermediates, including physical activity and smoking status.

Given the significant association between higher diet costs and reduced risk of T2DM and CVD, one would expect diet costs to be associated with a reduced risk of mortality. For the entire population, we did not observe a significant association between higher diet costs and mortality. Among healthy women who were never smokers, there was some suggestion of an association between diet cost and mortality, though the association was not significant.

This study represents the first prospective examination of the association between diet cost and T2DM and CVD, and the first examination of weight change and mortality in the United States. Given the paucity of research on diet cost and health outcomes, the results of these studies ought to be compared to studies conducted in different populations and food environments. Summarizing population-level approaches to improve diets, the American Heart Association concluded that subsidy strategies to lower prices of more healthful foods/beverages is an effective and useful intervention strategy to improve the diet of the population that ought to be implemented more widely (4). Given the evidence of an association between diet costs and T2DM and CVD observed here, and an emerging consensus that diet costs are important determinants of diet quality, additional research examining the implementation and efficacy of economic incentives that support healthy eating is essential. Reducing health disparities, including those attributed to socioeconomic status is a public health priority (5). Reducing the cost of a healthy diet may have the potential to reduce the social gradient in health.

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