



Changes in Intake of Fruits and Vegetables and Weight Change in US Men and Women Followed for up to 24 Years: Analysis from Three Prospective Cohort Studies

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Accessibility

- 1 Changes in Intake of Fruits and Vegetables and Weight Change in US Men and Women Followed for up
- 2 to 24 Years: Analysis from Three Prospective Cohort Studies
- 3 **Short Title:** Fruits, vegetables and weight change
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Abstract

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Background: Current dietary guidelines recommend eating a variety of fruits and vegetables. However, based on nutrient composition, some particular fruits and vegetables may be more or less beneficial for maintaining or achieving a healthy weight. We hypothesized that greater consumption of fruits and vegetables with a higher fiber content or lower glycemic load would be more strongly associated with a healthy weight. Methods and Findings: We examined the association between change in intake of specific fruits and vegetables and change in weight in three large prospective cohorts of 133,468 US men and women. From 1986 to 2010, these associations were examined within multiple 4-year time intervals, adjusting for simultaneous changes in other lifestyle factors including other aspects of diet, smoking status, and physical activity. Results were combined using a random effects meta-analysis. Increased intake of fruits was inversely associated with 4-year weight change: total fruits -0.53 lbs per daily serving (95% CI -0.61, -0.44), berries -1.11 lbs (95% CI -1.45, -0.78), and apples/pears -1.24 lbs (95% CI -1.62, -0.86). Increased intake of several vegetables was also inversely associated with weight change: total vegetables -0.25 lbs per daily serving (95% CI -0.35, -0.14), tofu/soy -2.47 lbs (95% CI, -3.09 to -1.85 lbs) and cauliflower -1.37 lbs (95% CI -2.27, -0.47). On the other hand, increased intake of starchy vegetables, including corn, peas, and potatoes, was associated with weight gain). Vegetables having both higher fiber and lower glycemic load were more strongly inversely associated with weight change compared with lower fiber, higher glycemic load vegetables (p <0.0001). Despite the measurement of key confounders in our analyses, the potential for residual confounding cannot be ruled out and although our food frequency questionnaire specified portion size, the assessment of diet using any method will have measurement error.

- 48 **Conclusions:** Increased consumption of fruits and non-starchy vegetables is inversely associated with
- 49 weight change, with important differences by type suggesting that other characteristics of these foods
- influence the magnitude of their association with weight change.

Introduction

The 2010 Dietary Guidelines for Americans recommends eating a variety of fruits and vegetables to lower risk of chronic disease and to "help adults and children achieve and maintain a healthy weight" [1]. This guidance has a strong evidence base for the prevention of cardiovascular disease, but less so for maintaining a healthy weight. Recently, we reported associations between increased total fruit and total vegetable consumption and weight change in three separate, large prospective studies of 120,877 US men and women age 30-65 years at baseline [2]. However, different fruits and vegetables have individual characteristics that may impact their effects on satiety, glycemic and insulinemic responses, total calorie intake, or energy expenditure. How they are consumed may also influence these factors, for example preparation method, portion size, complements, and substitutes.

Components of fruits and vegetables that may differentiate their impact on weight change include fiber content, glycemic load (GL), and biologically active constituents like polyphenols and sugars. Higher fiber intake increases satiety, which in turn may reduce total energy intake and prevent weight gain [3,4,5,6,7]. Also, lower GL foods produce fewer and smaller postprandial glucose spikes that may decrease subsequent hunger and reduce total energy intake [8]. Furthermore, clinical trial evidence suggests that low GL or low glycemic index (GI) diets may increase resting energy expenditure [9], promoting weight maintenance. In addition, polyphenols, found in meaningful concentrations in many fruits and vegetables, may influence insulin sensitivity [10], the gut microbiome [11], or the anabolic state of adipose tissue, which over a long period of time could promote relative weight stability.

The objective of this study was to examine the relationship between increased fruit and vegetable consumption and weight change over time, including subtypes and individual fruits and vegetables. We limit our analyses to whole fruits, as fruit juice typically includes several grams of added sugars and is associated with an increased risk of diabetes [12] and greater weight gain [2].

Methods

The study protocol was approved by the Institutional Review Board of the Brigham and Women's Hospital and by the Harvard School of Public Health Human Subjects Committee Review Board (ID 2008P000327). All participants provided voluntary responses to mailed questionnaires that served as the participants' informed consent and research aims and use of data were fully explained to each participant.

Study Design and Population

The study population includes three prospective cohorts of men and women. The Nurses' Health Study (NHS) is a cohort of 121,701 female nurses from 11 US states aged 30-55 years at enrollment in 1976 [13]. The Health Professionals Follow-up Study (HPFS) is a parallel cohort of 51,529 male health professionals from 50 states aged 40-75 years at enrollment in 1986 [14]. The Nurses' Health Study II (NHS II) is a cohort of 116,686 younger female nurses aged 25-42 years at enrollment in 1989 from 14 states [15]. Men in the HPFS contributed an average of 3.3 4-year intervals and women in the NHS and NHS II 3.4 4-year intervals. Ninety-nine percent of men in the HPFS are white, 97% of women in the NHS, and 99% of women in the NHS II.

We excluded men and women with a history of chronic disease at baseline including those who had a history of diabetes, cancer, cardiovascular disease, renal disease, pulmonary disease, liver disease, ulcerative colitis, lupus, tuberculosis, multiple sclerosis, amyotrophic lateral sclerosis, or Parkinson's disease at baseline. We censored individuals who developed these conditions during follow-up: at time of diagnosis for cardiovascular disease and 6 years prior for all other diseases. We also excluded individuals who had gastric bypass surgery and newly pregnant or lactating women (one 4-year interval only) and censored individuals at age 65 due to age-related loss of lean muscle mass. Finally, we excluded men and women who had missing baseline lifestyle habits data, who reported implausible

energy intake, or who had blank responses for more than 70 items on the food frequency questionnaire (FFQ). We defined implausible energy intake as < 800 or > 4,200 calories for men and < 600 or > 3,500 calories for women. After exclusions, 35,408 women in the NHS, 17,996 men in the HPFS, and 64,514 women in the NHS II were included in our analysis (details in S18 Table).

Weight Change

Participants in all three cohorts reported height in inches at enrollment and current weight in pounds on biennial questionnaires. Weight change was calculated as the difference in weight between the beginning and end of each 4-year interval where positive differences represent weight gain, and negative differences weight loss. Although these measures are self-reported, they are shown to be valid in these cohorts: among a sample of 123 men in the HPFS and 140 women in the NHS, Pearson correlations coefficients between self-reported weight and technician-measured weight were 0.97 [16].

Dietary Assessment

A validated [17] 131-item semi-quantitative FFQ was administered every 4 years beginning in 1986 in the NHS and HPFS, and in 1991 in the NHS II. We included all fruits and all vegetables on the FFQ in our analyses (S7 Table). Fruits and vegetables with similar nutritional value including fiber and GL were combined, for example apples and pears. We had a total of six 4-year time intervals in the NHS and HPFS (1986-2010, 24 years) and four 4-year time intervals in the NHS II (1991-2007, 16 years). The Harvard University food composition database, derived from the US Department of Agriculture (USDA) data and other outside published sources, was used to calculate nutrients consumed from food items. The USDA defines potatoes as a vegetable, however most Americans do not consider French fries and potato chips a healthy choice, therefore we used unprocessed potatoes for our main analysis (baked,

boiled or mashed white potatoes, sweet potatoes, and yams) and included fried potatoes (French fries and potato chips) as a covariate. This distinction is consistent with previous work [2].

We categorized fruits and vegetables as high or low fiber, defined using the median grams of fiber per serving of those fruits and vegetables included on the FFQ (1.7 grams per serving, S2 and 3 Tables). We categorized fruits and vegetables as high or low GL similarly with cutoffs of 0.7 for vegetables and 6.5 for fruits (S4 and 5 Tables). GL was calculated by multiplying the carbohydrate content of each fruit/vegetable (grams per serving) by the glycemic index of that fruit/vegetable. In addition, we grouped fruits into categories of citrus, melon, and berries and vegetables into categories of cruciferous, green leafy, and legumes based on similar nutritional content (S6 Table). The average Pearson correlation coefficients comparing diet assessment from our FFQ with multiple 7-day food records for 55 foods was 0.48 [18], range 0.24 to 0.76 for individual fruits and 0.13 to 0.53 for individual vegetables (S17 Table) [19].

Covariates

Biennial questionnaires additionally asked participants to report lifestyle habits and any recent physician-diagnosed diseases. We included the following individual-level covariates in all models: baseline age and BMI for that particular time interval, and change in the following lifestyle variables over the same time interval: smoking status, physical activity level [20], hours of sitting or watching TV, hours of sleep, as well as change in intake of the following foods/nutrients: fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, diet beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood. Total energy intake, hypertension, hypercholesterolemia, and related medications were not included as covariates because they are potentially on the causal pathway or are consequences of fruit and

vegetable intake and weight change. The frequency of data collection for physical activity, hours of watching TV, and hours of sleep data varied by cohort (S1 Table).

Statistical Analysis

Multivariable generalized linear regression models were used to examine the independent association between change in weight (lbs) over 4 years and change in intake of fruits and vegetables (servings/day) over the same 4-year time interval, as described in a previous publication [2]. Because each individual contributes multiple time intervals, we used robust variance to account for within-individual repeated measures and results are averaged across all 4-year time intervals. Analyses of total fruits and total vegetables included both variables together in one model. Fiber analyses included all fiber variables in one model: change in intake of high fiber fruits, low fiber fruits, high fiber vegetables, and low fiber vegetables, likewise for GL analyses. Fruit and vegetable subgroup analyses included all six subgroup variables in one model and analyses of individual fruits and vegetables included all specific fruit and vegetable variables in a single model.

Change in weight and change in intake of fruits and vegetables were truncated at the 0.5th and 99.5th percentiles to minimize the influence of outliers. Missing indicators were used for categorical variables and the last observation was carried forward for missing values of continuous variables with the exception of diet (main exposure) and weight (main outcome). Missing values were carried forward only once for diet and weight after which the follow-up was censored. As a sensitivity analysis, we examined change in diet over 4-years and change in weight over the following 4-year interval (for example, change in diet 1986 to 1990 and change in weight 1990 to 1994). Results from the 3 cohorts were pooled using DerSimonian-Laird estimators and the Q statistic to test for heterogeneity. The 3 studies are weighted by the inverse of the sum of the study-specific variance plus the common between-

studies variance (random effects pooling). All analyses used SAS version 9.2 (SAS Institute) and a two-tailed alpha of 0.05.

Results

At baseline, men in the HPFS were an average of 47 years old, women in the NHS 49 years old, and women in the NHS II 36 years old (Table 1). After exclusions, the remaining men in the HPFS had an average BMI of 25.1 kg/m², women in the NHS 24.7 kg/m², and women in the NHS II 24.2 kg/m² at baseline. Within each 4-year time interval, men in the HPFS gained an average of 2.1 lbs, women in the NHS 2.8 lbs, and women in the NHS II 5.0 lbs. Men and women in all three cohorts reported a variety of fruit and vegetable intake (S19 Table).

Table 1. Baseline (mean, SD) characteristics and average 4-year lifestyle changes (mean and 1st to 99th percentile range) of men and

women in three prospective cohorts.

| women in three prospective conorts. | | HPFS | NHS | | NHS II | |
|--|--------------------|---------------------|--------------------|----------------------|--------------------|---------------------|
| | n = 19,316 | | n = 40,415 | | n = 73,737 | |
| | Baseline (1986) | 4-Year Change | Baseline (1986) | 4-Year Change | Baseline (1991) | 4-Year Change |
| Age (years) | 47.0 (3.0) | | 48.7 (2.4) | | 36.4 (3.8) | |
| BMI (kg/m²) | 25.1 (1.8) | | 24.7 (2.1) | | 24.2 (4.3) | |
| Weight (Ibs) | 177 (15) | 2.1 (-12.0 to 17.0) | 147 (14) | 2.8 (-13.5 to 21.0) | 145 (27) | 5.0 (-10.5 to 30.0) |
| Physical activity (MET-hr/wk) | 22.9 (19.6) | 5.2 (-28.6 to 78.8) | 14.4 (9.7) | -1.0 (-50.4 to 40.6) | 20.7 (23.8) | 0.4 (-22.3 to 21.6) |
| Alcohol (servings/d) | 0.9 (0.7) | 0.0 (-1.6 to 1.2) | 0.5 (0.4) | 0.0 (-1.0 to 0.6) | 0.3 (0.4) | 0.0 (-0.4 to 0.6) |
| Total fruit without juice (servings/d) | 1.5 (0.7) | 0.1 (-1.5 to 1.8) | 1.5 (0.5) | 0.0 (-1.5 to 1.5) | 1.2 (0.8) | 0.0 (-1.0 to 1.1) |
| Total vegetables (servings/d) | 2.9 (1.0) | 0.2 (-2.2 to 3.2) | 3.2 (0.8) | 0.1 (-2.2 to 2.8) | 3.1 (1.7) | 0.0 (-2.2 to 2.4) |
| Whole-fat dairy (servings/d) | 1.0 (0.6) | -0.1 (-1.9 to 1.1) | 1.2 (0.5) | -0.1 (-1.8 to 1.0) | 0.8 (0.7) | 0.0 (-1.1 to 0.9) |
| Low-fat dairy (servings/d) | 0.9 (0.6) | -0.1 (-1.5 to 1.5) | 0.9 (0.4) | 0.1 (-1.1 to 1.6) | 1.1 (0.9) | 0.0 (-1.1 to 1.3) |
| Seafood (servings/day) | 0.4 (0.2) | 0.0 (-0.5 to 0.4) | 0.3 (0.1) | 0.0 (-0.4 to 0.4) | 0.3 (0.2) | 0.0 (-0.3 to 0.3) |
| Whole grains (servings/d) | 1.5 (0.8) | 0.0 (-1.9 to 2.4) | 0.8 (0.4) | 0.1 (-1.3 to 1.8) | 1.2 (1.0) | 0.0 (-1.2 to 1.1) |
| Refined grains (servings/d) | 1.2 (0.6) | 0.0 (-1.9 to 1.8) | 1.2 (0.5) | 0.0 (-1.4 to 1.4) | 1.3 (0.8) | -0.1 (-1.1 to 1.3) |
| Nuts (servings/d) | 0.3 (0.3) | 0.0 (-0.7 to 0.7) | 0.1 (0.1) | 0.0 (-0.4 to 0.4) | 0.1 (0.1) | 0.1 (-0.1 to 0.6) |
| Sugar-sweetened beverages (servings/d) | 0.3 (0.4) | 0.0 (-0.8 to 0.6) | 0.2 (0.2) | 0.0 (-0.5 to 0.5) | 0.3 (0.6) | 0.0 (-0.7 to 0.6) |
| Juice (servings/d) | 0.8 (0.5) | 0.0 (-1.2 to 1.2) | 0.7 (0.4) | 0.0 (-1.0 to 1.0) | 0.6 (0.7) | -0.1 (-0.9 to 0.7) |
| Sweets (servings/d) | 1.3 (0.8) | 0.0 (-2.0 to 1.9) | 1.2 (0.5) | 0.0 (-1.4 to 1.8) | 1.2 (0.9) | -0.1 (-1.2 to 1.1) |
| Processed meats (servings/d) | 0.4 (0.3) | 0.0 (-0.7 to 0.4) | 0.3 (0.2) | 0.0 (-0.5 to 0.4) | 0.2 (0.2) | 0.0 (-0.3 to 0.4) |
| Trans fat (%) | 1.3 (0.3) | 0.0 (-0.6 to 1.1) | 1.7 (0.3) | -0.2 (-1.0 to 0.7) | 1.6 (0.5) | -0.2 (-0.9 to 0.4) |

An increase in both total fruit intake and total vegetable intake was inversely associated with weight change in all three cohorts (Fig. 1). Pooled across all three cohorts, increased intake of vegetables was associated with a weight change of -0.25 lbs per daily serving over four years (95% CI, -0.35 to -0.14 lbs), and fruits, -0.53 lbs per daily serving (95% CI, -0.61 to -0.44 lbs).

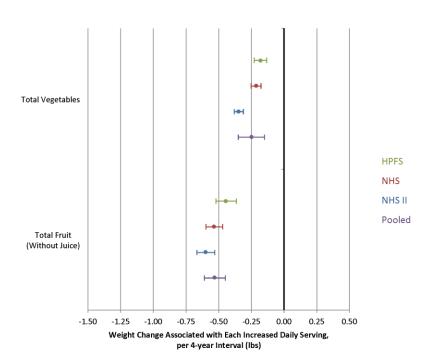


Fig. 1. Relationships between changes in total vegetable and total fruit intake and weight change over 4 years in three cohorts.

Legend:

Total vegetables: string beans, broccoli, cabbage/coleslaw, cauliflower, Brussels sprouts, carrots (raw, cooked, or juice), corn, peas, lima beans, mixed vegetables or vegetable soup, beans, lentils, celery,

squash, eggplant, zucchini, yams, sweet potatoes, baked/boiled/mashed potatoes, spinach, kale, mustard or chard greens, iceberg or head lettuce, romaine or leaf lettuce, peppers, tomatoes, onions, tofu and soy (soy burger, soybeans, miso, or other soy protein)

Total fruit (without juice): raisins, grapes, avocados, bananas, cantaloupe, watermelon, apples, pears, peaches (fresh or canned), apricots (fresh or canned), plums (fresh or canned), strawberries, blueberries, prunes, oranges, grapefruit (fresh or juice)

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

Evaluating specific subgroups of vegetables, increased intakes of cruciferous and green leafy vegetables was inversely associated with weight change: pooled change -0.68 lbs per daily serving of cruciferous vegetables (95% CI, 0.96 to -0.40 lbs) and -0.52 lbs per daily serving of green leafy vegetables (95% CI, -0.83 to -0.22 lbs) (Fig. 2). Among subgroups of fruits, increased intakes of berries and citrus fruits were inversely associated with weight change: pooled change -1.11 lbs (95% CI, -1.45 to -0.78 lbs) for berries and -0.27 lbs (95% CI, -0.37 to -0.17 lbs) for citrus fruits.

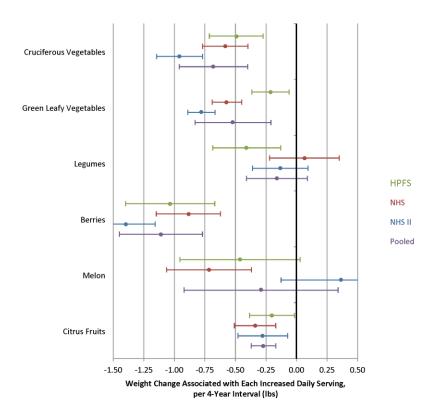


Fig. 2. Relationships between changes in intake of classes of vegetables and fruits and weight change over 4 years in three cohorts.

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Cruciferous vegetables: broccoli, cauliflower, cabbage, Brussels sprouts

Green leafy vegetables: kale, mustard or chard greens, spinach, head or romaine lettuce

Legumes: peas, lima beans, beans, lentils, tofu/soy

Berries: blueberries, strawberries

Melon: cantaloupe, watermelon

Citrus fruits: oranges, grapefruit (fresh or juice)

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

When different fruits were evaluated, increased intakes of several individual fruits were inversely associated with weight change over four years, including blueberries, prunes, apples/pears, strawberries, raisins/grapes, and grapefruit (Fig. 3, S11 and 13 Tables). Increased intakes of many individual vegetables were also inversely associated with weight change, including tofu/soy (-2.47 lbs; 95% CI -3.09 to -1.85 lbs), peppers (-0.76 lbs; 95% CI -1.14 to -0.39 lbs), and carrots (-0.41 lbs; 95% CI -0.51 to -0.42 lbs) (Fig. 4). Not all vegetables were inversely associated with weight change, however, most notably starchy vegetables. For example, additional daily servings of baked, boiled or mashed potatoes (0.74 lbs; 95% CI 0.19 to 1.30 lbs), peas (1.13 lbs; 95% CI 0.37 to 1.89 lbs), or corn (2.04 lbs; 95% CI 0.94 to 3.15 lbs) were each positively associated with weight change (Fig. 5). Changes in intakes of specific fruits and vegetables were not highly correlated (S14-16 Tables).

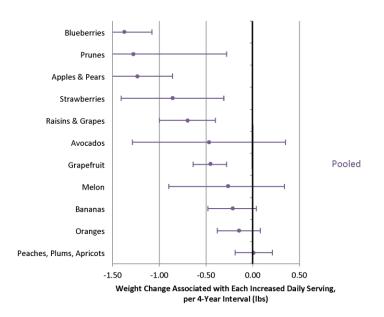


Fig. 3. Relationships between changes in intake of specific fruits and weight change over 4 years in three cohorts.

Legend:

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

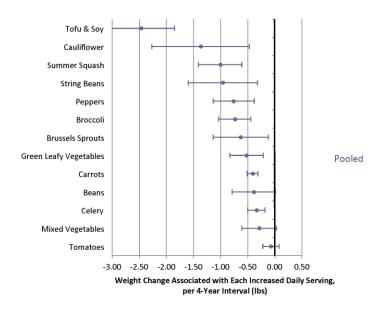


Fig. 4. Relationships between changes in intake of specific vegetables and weight change over 4 years in three cohorts.

Legend:

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

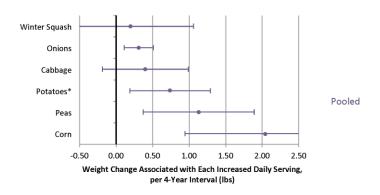


Fig. 5. Relationships between changes in intake of specific vegetables and weight change over 4 years in three cohorts.

Legend:

*Includes baked/boiled/mashed white potatoes, sweet potatoes and yams; excludes french fries and potato chips.

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

Fiber Content and Weight Change

The association between fruit intake and weight change was not modified by the fiber content (pooled p 0.16) or GL (pooled p 0.06) of the individual fruit. Thus, the benefits of greater fruit intake were seen regardless of the fiber content or GL (Fig. 6 and Fig. 7, S2 and 3 Tables). Increased intake of lower fiber vegetables was associated with negative weight change (-0.29 lbs; 95% CI -0.44 to -0.14 lbs) whereas increased intake of higher fiber vegetables was not associated with weight change (0.00 lbs; 95% CI -0.19 to 0.20 lbs). However, when we excluded white potatoes (baked, boiled, or mashed) from the high fiber subgroup, increased intake was associated with negative weight change (-0.19 lbs; 95% CI -0.31 to -0.07 lbs) (S8 Table).



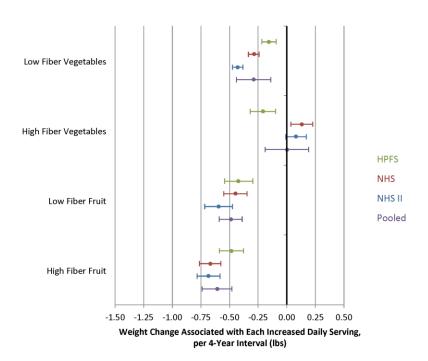


Fig. 6. Relationships between changes in intake of fruits and vegetables classified as either low or high fiber and weight change over 4 years in three cohorts.

Legend:

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.



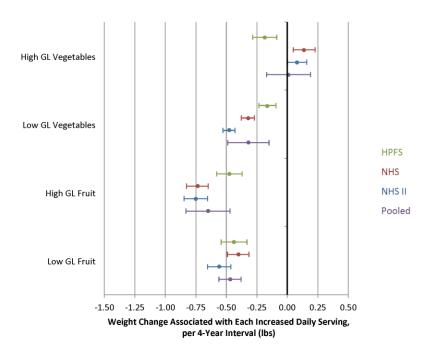


Fig. 7. Relationships between changes in intake of fruits and vegetables classified as either high or low glycemic load (GL) and weight change over 4 years in three cohorts.

Legend:

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

GL and Weight Change

When we categorized vegetables as either lower or higher GL (S4 and 5 Tables), lower GL vegetables were inversely associated with weight change (Fig. 7), a difference that was marginally statistically significant (pooled p 0.05). An increase of one daily serving of a higher GL vegetables was not associated with weight change (–0.01 lbs; 95% CI -0.17 to 0.20 lbs) whereas an increase of one daily serving of a lower GL vegetable was associated with negative weight change (-0.32 lbs; 95% CI -0.49 to -0.15 lbs). Compared to vegetables that were both lower fiber and higher GL, we found greater negative weight change for higher fiber, lower GL vegetables (S1 Figure, pooled p-value <0.0001).

Compared to lower fiber, higher GL fruits, weight change for higher fiber, lower GL fruits was similar: pooled change -0.40 lbs per increased daily serving of higher fiber, lower GL fruits (95% CI -0.58 to -0.21 lbs) vs. -0.57 lbs per increased daily serving of lower fiber, higher GL fruits (95% CI -0.80 to -0.35 lbs). We found no evidence of effect modification by fiber content or GL of fruits.

Sensitivity Analyses

Excluding individuals with missing diet, weight, or covariate information during follow-up and controlling for baseline levels of BMI and total fruit and vegetable intake did not appreciably change our results (S9 and 12 Tables). Additionally adjusting for change in total energy intake to estimate the

association between increased fruit and vegetable intake and weight change independent of changes in total energy produced similar results (Table 2). Increasing the relative proportion of total calories from fruit and vegetables in the diet was also inversely associated with weight change. Finally, using non-isocaloric substitution models, replacing 5% of calories from other foods with 5% of calories from fruits or vegetables was also associated with negative weight change.

Table 2. Energy sensitivity analyses: weight change (lbs) associated with increased consumption of fruits and vegetables over four years.

| Over rour years. | Main analysis | Sensitivity analysis #1 | Sensitivity analysis #2 | Sensitivity analysis #3 |
|---------------------|-------------------------------|--|--|-------------------------|
| | Increase of 1 serving per day | Increase of 1 serving per day, adjusted for change in total energy | Increase of 1 serving per day, energy-adjusted (residual method) | 5 % increase in energy |
| Total fruits | | | | |
| HPFS | -0.44 (-0.52, -0.36) | -0.48 (-0.56 to -0.40) | -0.46 (-0.54 to -0.37) | -0.54 (-0.63 to -0.44) |
| NHS | -0.53 (-0.60, -0.47) | -0.53 (-0.60 to -0.47) | -0.53 (-0.60 to -0.46) | -1.96 (-2.25 to -1.68) |
| NHS II | -0.60 (-0.67, -0.53) | -0.61 (-0.68 to -0.54) | -0.67 (-0.74 to -0.59) | -0.99 (-1.07 to -0.91) |
| Pooled | -0.53 (-0.61, -0.44) | -0.54 (-0.61 to -0.47) | -0.55 (-0.67 to -0.43) | -1.14 (-1.64 to -0.63) |
| Total vegetable | s | | | |
| HPFS | -0.18 (-0.23, -0.13) | -0.20 (-0.25 to -0.15) | -0.20 (-0.25 to -0.15) | -0.61 (-0.73 to -0.49) |
| NHS | -0.21 (-0.25, -0.18) | -0.21 (-0.25 to -0.17) | -0.22 (-0.26 to -0.17) | -1.05 (-1.56 to -0.54) |
| NHS II | -0.35 (-0.38, -0.31) | -0.35 (-0.39 to -0.32) | -0.40 (-0.44 to -0.37) | -1.14 (-1.23 to -1.05) |
| Pooled | -0.25 (-0.35, -0.14) | -0.25 (-0.36 to -0.15) | -0.27 (-0.41 to -0.14) | -0.92 (-1.35 to -0.49) |

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, trans fat, alcohol, and seafood.

When we stratified our analysis by weight at baseline [normal weight (BMI < 25 kg/m^2), overweight (BMI $\geq 25 \text{ and} < 30 \text{ kg/m}^2$), and obese (BMI $\geq 30 \text{ kg/m}^2$] the negative weight change associated with greater intake of fruits and vegetables was stronger among overweight individuals compared to normal weight individuals (S10 Table, p-values for interaction terms between total fruit and BMI 0.03 in HPFS, 0.06 in NHS, and 0.09 in NHS II; p-values for interaction terms between total vegetable intake and BMI 0.03 in all three cohorts). When we stratified our analysis by smoking status (current vs. never or former) associations were similar for nonsmokers compared to current smokers (S10 Table).

Discussion

In our 24-year prospective study with up to seven repeated dietary assessments, increased fruit and vegetable intake was inversely associated with weight change over time. The benefits were greater for fruits compared to vegetables and strongest for berries, apples/pears, tofu/soy, cauliflower, and cruciferous and green leafy vegetables. We found a stronger inverse association between increased intake of higher fiber, lower GL vegetables and weight change, consistent with experimental evidence suggesting an influence of these factors on satiety [8], glucose and insulin responses [21], fat storage [21], and energy expenditure [9].

We found that many vegetables were inversely associated with weight change, but starchy vegetables such as peas, potatoes, and corn had the opposite association where increased intake was associated with weight gain. Although these vegetables have nutritional value (potassium, vitamin C, vitamin B₆, iron, fiber, and protein), they have a higher GL (lower carbohydrate quality) that could explain their positive association with weight change.

Our models were not isocaloric because part of the benefit of fruits and vegetables may be from increased satiety with fewer calories; therefore the main results presented here are non-isocaloric substitutions where individuals could have substituted, for example, one serving per day of apples (74 calories per serving) instead of one serving per day of orange juice (84 calories per serving).

Alternatively, individuals could have added one serving of apples daily without changing other aspects of their diet. However, individuals will often replace one food item with another when they change their diet. Table 2 compares results from the main analyses that do not adjust for energy intake to results from various models that adjust for total energy, some of which estimate the effect of substitution.

In the first sensitivity analysis (Table 2), models are additionally adjusted for change in total energy intake. By controlling for change in total energy, this model estimates the association between increased fruit or vegetable intake and weight change independent of changes in total energy or in other words, through mechanisms other than reduced calorie intake. These results are very similar to models that do not include energy intake, however it is difficult to estimate total calorie intake precisely with FFQs therefore these results should be interpreted with caution. This model allows total energy intake to change among individuals within each 4-year time interval, therefore it is not isocaloric. This is not a substitution model because individuals could have replaced other foods with fruits and vegetables or they could have simply added more fruits and vegetables to their diet.

The second energy sensitivity analysis examines change in energy-adjusted fruit and vegetable intake. Energy adjustment using the residual method looks at the composition of the diet instead of absolute intake, in other words, fruit and vegetable intake relative to other individuals with the same total daily energy intake. These results are similar, suggesting that increasing the relative amount of fruits and vegetables in the diet is also negatively associated with weight change. Again, this is not a substitution model because individuals could have increased the proportion of fruits and vegetables in their diet by replacing other foods with fruits and vegetables or by increasing fruit and vegetable intake

without changing other aspects of their diet. The third sensitivity analysis examines substitutions, however it still allows total energy intake to change over time in individuals and therefore is not isocaloric. These results suggest that replacing 5% of calories from other foods with 5% of calories from fruits or vegetables is inversely associated with weight change.

Previous prospective studies of fruit and vegetable intake have mixed findings [22]. Among 373,803 participants in the European Prospective Investigation into Cancer and Nutrition cohort, there was no association between baseline fruit and vegetable intake and weight change over 5 years [23], but this study used a single baseline measure of diet that did not incorporate change over time. On the other hand, higher intake of fruits and vegetables was inversely associated with weight change over the following 6 years among 4,287 Australian women [24].

To the best of our knowledge, only three studies have used a change-on-change analysis [2,25,26] and one was a more general analysis of the population included in our study. Barone Gibbs et al. found a similar inverse association between increased fruit and vegetable intake (combined) and weight change over 42 months among 481 women enrolled in a lifestyle intervention study [25].

Drapeau et al. found an inverse association between increased consumption of fruits but not vegetables and change in weight over 6 years among 248 individuals in the Quebec Family Study [27]. Previous clinical trials similarly have mixed findings: increased consumption of total fruits and vegetables over 3 months was associated with weight loss among 103 overweight individuals with sleep-related eating disorders [28], but not over 6 months among 690 healthy study participants [29], or over 2 months in 50 healthy men and women [30].

Few studies have examined weight change in relation to specific fruits and vegetables; however, two trials examined interventions that included apples, pears, and grapefruit, all of which were beneficial in our population. Both trials found that increased intake resulted in weight loss - women randomized to eat apples or pears 3 times daily for 12 weeks lost an average of 2.6 lbs [31], while men

and women randomized to eat three grapefruit halves daily for 6 weeks lost an average of 1.3 lbs [32]. Besides polyphenol content, fruits could be beneficial for maintaining or achieving a healthy weight if they are replacing less healthy desserts and snacks, which is often how they are consumed [33].

Limitations

Our study has potential limitations. Although the study FFQ specified portion size, the assessment of diet using any method will have measurement error. However, this error is likely to be random and would tend to underestimate the association between intake of fruits and vegetables and weight change. Results could also be underestimated due to potential reverse causality if individuals who gain weight in the beginning of a 4-year time interval eat more fruits and vegetables later in the 4-year time interval in an effort to lose weight. Furthermore, the high correlation between measured and reported weight in our validation study could be overestimated if all individuals underreported weight by equal amounts.

Although we were able to adjust for changes in physical activity, we cannot rule out the possibility of residual confounding due to health consciousness if individuals who are eating healthier also make other healthier lifestyle changes not captured completely by our questionnaires. Although all participants were health professionals with graduate degrees, there remains a possibility of residual confounding due to unmeasured economic differences between participants within this strata of income and education. Furthermore, our study population consists mainly of white, educated adults. Therefore, our results may not be generalizable to all adults; however, it is unlikely that the biologic mechanisms underlying this association are different in other populations.

Study Strengths

Strengths of our study include the repeated measurement of diet using a validated questionnaire over twenty-four years in over 100,000 adults. Due to the large sample size and long follow-up period, we had the unique opportunity to investigate not only change in total fruit and vegetable intake, but also intake of individual fruits and vegetables and fruits and vegetables classified by fiber content and GL. Looking at within-person change allowed us to control for stable personal characteristics such as gender and ethnicity. Furthermore, by restricting to educated participants with a higher SES, and by consistently adjusting for major confounders across all three cohorts, we were able to reduce residual confounding by these factors and increase statistical power. Finally, we found consistent results across three cohorts that represent a wide range of ages and both genders.

In these three large cohorts, increasing consumption of all fruits and most vegetables was not associated with weight gain. Although the magnitude of weight change associated with each increased daily serving was modest, combining an increase of one-to-two servings of vegetables and one-to-two servings of fruits daily would be associated with substantial weight change, especially if projected to the population level. Furthermore, many individuals find it extremely difficult to lose weight and therefore weight maintenance, as compared to weight gain, is an important goal. Simply maintaining weight from adulthood onward could have a substantial impact on population health.

We observed a robust inverse association between fruit and vegetable intake and long-term weight change in three large prospective cohorts of American adults. Unfortunately most Americans have inadequate fruit and vegetable intake [34,35], and trends indicate that intake has remained relatively constant over time and may even be decreasing in some subgroups of the population [35,36,37]. Furthermore, although fruit juice and potato intakes have decreased over time, both still contribute substantially to total fruit and vegetable intake, and therefore public health recommendations and nutritional guidelines ought to emphasize individual or subgroups of specific fruits and vegetables that maximize the potential for weight maintenance and disease prevention [34].

In conclusion, our findings support benefits of increased fruit and vegetable consumption for preventing long-term weight gain and provide further food-specific guidance for the prevention of obesity, a primary risk factor for type 2 diabetes, cardiovascular diseases, cancers, and many other health conditions.

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Author Contributions

Conceived and designed the experiments: WCW, EBR. Performed the experiments: MLB, KJM, LEC, TH, DSL, DM, WCW, FBH, EBR. Analyzed the data: MLB, TH. Wrote the first draft of the manuscript: MLB, EBR. Contributed to the writing of the manuscript: MLB, KJM, LEC, TH, DSL, DM, WCW, FBH, EBR. ICMJE criteria for authorship read and met: MLB, KJM, LEC, TH, DSL, DM, WCW, FBH, EBR. Agree with manuscript results and conclusions: MLB, KJM, LEC, TH, DSL, DM, WCW, FBH, EBR.

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Competing Interests

EBR has funding from the USDA/US Blueberry Highbush Council to conduct observational and experimental studies of blueberries and CVD health outcomes. DM has received ad hoc honoraria and consulting fees from Bunge, Haas Avocado Board, Nutrition Impact, Amarin, Astra Zeneca, Boston Heart Diagnostics, and Life Sciences Research Organization. He is on the scientific advisory board of Unilever North America. DSL has grants from philanthropic organizations and receives royalties from books on obesity. In all cases, these funding sources are unrelated to this project, and the authors perceive no pertinent conflicts. All other authors declare that no competing interests exist.

Data Availability

Health Professionals Follow-up Study, Nurses' Health Study, and Nurses' Health Study II data may be used in collaboration with a principal investigator, please see the study websites for more information: https://www.hsph.harvard.edu/hpfs/hpfs_collaborators.htm and http://www.channing.harvard.edu/nhs/?page_id=52.

Abbreviations

GL – glycemic load

GI – glycemic index

NHS – Nurses' Health Study

HPFS – Health Professionals Follow-up Study

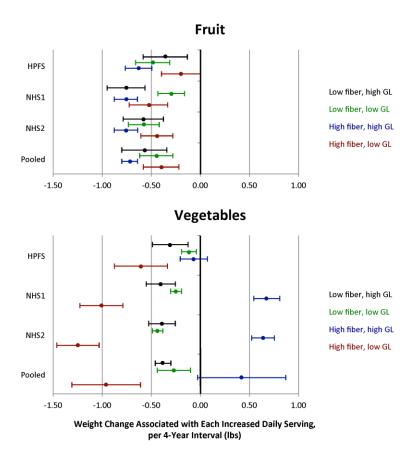
NHS II - Nurses' Health Study II

BMI – body mass index

FFQ – food frequency questionnaire

USDA – United States Department of Agriculture

Supporting Information



S1 Figure. Weight change (lbs) associated with an increase of one serving per day of fruits and vegetables categorized by fiber content and GL per serving.

Legend:

Low fiber, high GL fruits: melon, raisins, grapes

Low fiber, low GL fruits: strawberries, peaches, plums, apricots, grapefruit

High fiber, high GL fruits: prunes, apples, pears, bananas

High fiber, low GL fruits: avocados, blueberries, oranges

Low fiber, high GL vegetables: carrots, cabbage, coleslaw, sauerkraut

Low fiber, low GL vegetables: cauliflower, leafy greens, summer squash, tomatoes, peppers, celery, onions

High fiber, high GL vegetables: beans, lentils, tofu/soy, peas, lima beans, mixed vegetables, winter squash, potatoes, corn

High fiber, low GL vegetables: Brussels sprouts, broccoli, string beans

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

Supplemental Table 1. Frequency of physical activity, hours of watching TV, and hours of sleeping data collection.

| Covariate | HPFS | NHS | NHS II |
|----------------------|---|--|---|
| Physical activity | Data collected biennially. | Data collected biennially. | Data collected in 1991, 1997, 2001, and 2005. |
| | | | Data from 1991 was used to impute values for 1993 and 1995, data from 1997 for 1999, data from 2001 for 2003, and data from 2005 for 2007. |
| Hours of watching TV | Data collected in 1998 and every 2 years thereafter. | Data collected in 1992, 2004, and 2008. | Data collected in 1991, 1997, 2001, and 2005. |
| | Four-year change included as a covariate in each model assuming no change between 1986 and 1998. | Baseline levels rather than change variables were included in each model due to the infrequent timing of collection: data from 1992 was used to impute values for 1986, 1990, 1994, 1998, and 2002. Data from 2004 was used to impute values for 2006. | Baseline levels rather than change variables were included in each model due to the infrequent timing of collection: data from 1991 was used to impute values for 1995, data from 1997 for 1999, and data from 2001 for 2003. |
| Hours of sleep | Data collected in 1987 and in 2000. | Data collected in 1986, 2000, 2002, and 2008. | Data collected in 2001. |
| | Baseline levels rather than change variables were included in each model due to the infrequent timing of collection: data from 1987 was used to impute values for 1986, 1990, 1994, and 1998. Data from 2000 for 2002 and 2006. | Baseline levels rather than change variables were included in each model due to the infrequent timing of collection: carrying forward data for 1990, 1994, 1998, and 2006. | Data from 2001 used as a covariate in all models. |

Supplemental Table 2. Fiber content of fruits included on the study FFQ

| ruits | g Fiber/serving | g Carb/serving | Carb:fiber ratio | Cal/serving |
|------------------------------|-----------------|----------------|------------------|-------------|
| High fiber | | | | |
| Avocados | 6.7 | 8.5 | 1.3 | 161 |
| Prunes | 3.8 | 33.2 | 8.7 | 125 |
| Apples, pears | 3.6 | 20.0 | 5.6 | 75 |
| Oranges | 3.1 | 15.5 | 5.0 | 62 |
| Bananas | 3.0 | 26.0 | 8.7 | 101 |
| Blueberries | 1.8 | 10.6 | 5.9 | 42 |
| Average | 3.7 | 19.0 | 5.9 | 94 |
| Low fiber | | | | |
| Strawberries | 1.5 | 5.8 | 3.9 | 24 |
| Peaches, plums, apricots | 1.4 | 13.1 | 9.4 | 51 |
| Grapefruit, grapefruit juice | 1.3 | 9.7 | 7.5 | 38 |
| Cantaloupe, watermelon | 1.2 | 11.0 | 9.2 | 46 |
| Raisins, grapes | 1.0 | 20.8 | 20.8 | 79 |
| Average | 1.3 | 12.1 | 10.1 | 48 |

Supplemental Table 3. Fiber content of vegetables included on the study FFQ

| Vegetables | g Fiber/serving | g Carb/serving | Carb:fiber ratio | Cal/serving |
|--|-----------------|----------------|------------------|-------------|
| High fiber | | | | |
| Beans, lentils | 8.4 | 28.6 | 3.4 | 159 |
| Tofu, soybeans, soy burger, miso, other soy protein | 4.7 | 9.0 | 1.9 | 123 |
| Peas, lima beans | 4.4 | 13.5 | 3.1 | 73 |
| Mixed, stir-fry vegetables | 4.0 | 11.9 | 3.0 | 59 |
| Baked/mashed potatoes, yams, sweet potatoes | 3.5 | 32.9 | 9.4 | 144 |
| Brussels sprouts | 3.2 | 6.5 | 2.0 | 33 |
| Winter squash | 2.9 | 9.1 | 3.1 | 38 |
| Broccoli | 2.6 | 5.6 | 2.2 | 27 |
| String beans | 2.0 | 4.4 | 2.2 | 19 |
| Corn | 2.0 | 15.8 | 7.9 | 66 |
| Average | 3.8 | 13.7 | 3.8 | 74 |
| Low fiber | | | | |
| Carrots | 1.7 | 4.9 | 2.9 | 21 |
| Cabbage, coleslaw, sauerkraut | 1.6 | 8.6 | 5.4 | 85 |
| Cauliflower | 1.4 | 2.5 | 1.8 | 14 |
| Spinach, kale, mustard greens, iceberg/romaine lettuce | 1.4 | 2.6 | 1.9 | 14 |
| Eggplant, zucchini | 1.3 | 3.5 | 2.7 | 14 |
| Tomatoes | 1.1 | 3.5 | 3.2 | 16 |
| Peppers | 0.3 | 0.7 | 2.3 | 3 |
| Celery | 0.3 | 9.1 | 30.3 | 3 |
| Onions | 0.2 | 1.3 | 6.5 | 6 |
| Average | 1.0 | 4.1 | 6.3 | 20 |

Supplemental Table 4. Glycemic load (GL), glycemic index (GI), and calories per serving of fruits included on the study

| Fruits | | GL | GI | Cal/serving |
|--------|------------------------------|------|------|-------------|
| Low | v GL | | | |
| | Avocados | 0.5 | 5.9 | 161 |
| | Strawberries | 2.3 | 30.0 | 24 |
| | Grapefruit, grapefruit juice | 2.4 | 30.2 | 38 |
| | Blueberries | 5.6 | 38.7 | 42 |
| | Peaches, plums, apricots | 5.7 | 50.5 | 51 |
| | Oranges | 6.2 | 52.4 | 62 |
| | Average | 3.8 | 34.6 | 63 |
| Hig | h GL | | | |
| | Cantaloupe, watermelon | 7.6 | 93.8 | 46 |
| | Apples, pears | 7.9 | 55.9 | 75 |
| | Raisins, grapes | 13.0 | 42.2 | 79 |
| | Prunes | 13.9 | 26.1 | 125 |
| | Bananas | 16.1 | 70.7 | 101 |
| | Average | 11.7 | 57.7 | 85 |

Supplemental Table 5. Glycemic load (GL), glycemic index (GI), and calories per serving of vegetables included on the study FFQ

| Vegetables | GL | . GI | Cal/serving |
|---|---------------------|---------|-------------|
| Low GL | | | |
| Peppers | 0.1 | 1.3 | 3 |
| Celery | 0.1 | 1.8 | 3 |
| Cauliflower | 0.2 | 5.6 | 14 |
| Spinach, kale, mustard greens, iceberg/ | romaine lettuce 0.2 | 6.3 | 14 |
| String beans | 0.4 | 6.2 | 19 |
| Eggplant, zucchini | 0.4 | 8.2 | 14 |
| Onions | 0.4 | 4.5 | 6 |
| Tomatoes | 0.4 | 8.3 | 16 |
| Broccoli | 0.5 | 7.1 | 27 |
| Brussels sprouts | 0.6 | 7.1 | 33 |
| Average | 0.3 | 5.6 | 15 |
| High GL | | | |
| Carrots | 1.8 | 21.6 | 21 |
| Cabbage, coleslaw, sauerkraut | 2.1 | 18.3 | 85 |
| Winter squash | 3.7 | 41.3 | 38 |
| Mixed, stir-fry vegetables | 4.4 | 33.7 | 59 |
| Tofu, soybeans, soy burger, miso, other | soy protein 4.8 | 47.6 | 123 |
| Peas, lima beans | 6.0 | 37.0 | 73 |
| Beans, lentils | 9.0 | 41.4 | 159 |
| Corn | 9.7 | 50.0 | 66 |
| Baked/mashed potatoes, yams, sweet p | otatoes 22. | 5 104.3 | 144 |
| Average | 7.1 | 43.9 | 85 |

Supplemental Table 6. Definitions of fruits and vegetables.

| Vegetables | | |
|--|---|--|
| Total vegetables | String beans, broccoli, cabbage/coleslaw, cauliflower, Brussels sprouts, carrots (raw, cooked, or juice), corn, peas, lima beans, mixed vegetables or vegetable soup, beans, lentils, celery, squash, eggplant zucchini, yams, sweet potatoes, baked/boiled/mashed potatoes, spinach, kale, mustard or chard greens, iceberg or head lettuce, romaine or leaf lettuce, peppers, tomatoes, onions, tofu and soy (soy burger, soybeans, miso, or other soy protein) | |
| Legumes | Peas, lima beans, beans, lentils, tofu or soy | |
| Cruciferous vegetables | Broccoli, cauliflower, cabbage, Brussels sprouts | |
| Green leafy vegetables | Kale, mustard or chard greens, spinach, lettuce (head or romaine) | |
| Potatoes | Baked, boiled or mashed potatoes, yams or sweet potatoes | |
| ruit | | |
| Total fruit | Raisins, grapes, avocados, bananas, cantaloupe, watermelon, apples, pears, peaches (fresh or canned), apricots (fresh or canned), plums (fresh or canned), strawberries, blueberries, prunes, oranges, grapefruit (fresh or juice) | |
| Melon | Cantaloupe, watermelon | |
| Citrus fruits Oranges, grapefruit (fresh or juice) | | |
| Berries | Strawberries, blueberries | |

Supplemental Table 7. Food frequency questionnaire fruit and vegetable serving sizes.

| Fruits | | |
|-----------|--|-----------------------------------|
| | Raisins | 1 oz or small pack |
| | Grapes | 1/2 cup |
| | Avocado | 1/2 fruit or 1/2 cup |
| | Banana | 1 |
| | Cantaloupe | 1/4 melon |
| | Watermelon | 1 slice |
| | Apples | 1 |
| | Pears | 1 |
| | Peaches, apricots or plums | 1 fresh, or 1/2 cup canned |
| | Strawberries | 1/2 cup fresh, frozen or canned |
| | Blueberries | 1/2 cup fresh, frozen or canned |
| | Prunes | 6 dried or 1/4 cup canned |
| | Oranges | 1 |
| | Grapefruit | 1/2 |
| | Grapefruit juice | Small glass |
| Vegetable | S | |
| | String beans | 1/2 cup |
| | Broccoli | 1/2 cup |
| | Raw cabbage or coleslaw | 1/2 cup |
| | Cooked cabbage or sauerkraut | 1/2 cup |
| | Cauliflower | 1/2 cup |
| | Brussels sprouts | 1/2 cup |
| | Raw carrots | 1/2 carrot or 2-4 sticks |
| | Cooked carrots | 1/2 cup |
| | Carrot juice | 2-3 oz |
| | Corn | 1 ear or 1/2 cup frozen or canned |
| | Peas or lima beans | 1/2 cup fresh, frozen, canned |
| | Mixed or stir-fry vegetables | 1/2 cup |
| | Vegetable soup | 1 cup |
| | Beans or lentils | 1/2 cup baked or dried |
| | Celery | 2-3 sticks |
| | Dark yellow/orange (winter) squash | 1/2 cup |
| | Eggplant, zucchini, or other summer squash | 1/2 cup |
| | Potatoes | 1 baked or boiled or 1 cup mashed |
| | Yams or sweet potatoes | 1/2 cup |
| | Cooked spinach | 1/2 cup |
| | Raw spinach | 1 cup |
| | Kale, mustard greens or chard | 1/2 cup |
| | Iceberg or head lettuce | 1 serving |
| | Romaine or leaf lettuce | 1 serving |

| Green, yellow or red peppers | 3 slices or 1/4 pepper |
|------------------------------|------------------------|
| Tomatoes | 2 slices |
| Tofu or soybeans | 3-4 oz |
| Fresh onion | 1 slice |
| Cooked onion | 1/2 cup |

Supplemental Table 8. Weight change (lbs) associated with an increase of one serving per day of fruits and vegetables classified as high or low fiber and GL, excluding potatoes, n = 133,468 men and women.

| | Main Analysis | Excluding Potatoes* |
|-----------------------|------------------------|------------------------|
| High fiber fruit | -0.61 (-0.74 to -0.49) | -0.62 (-0.74 to -0.49) |
| Low fiber fruit | -0.49 (-0.59 to -0.38) | -0.48 (-0.58 to -0.38) |
| High fiber vegetables | 0.00 (-0.19 to 0.20) | -0.19 (-0.31 to -0.07) |
| Low fiber vegetables | -0.29 (-0.44 to -0.14) | -0.28 (-0.43 to -0.14) |
| | | |
| Low GL fruit | -0.47 (-0.56 to -0.37) | -0.45 (-0.55 to -0.36) |
| High GL fruit | -0.65 (-0.83 to -0.48) | -0.65 (-0.81 to -0.48) |
| Low GL vegetables | -0.32 (-0.49 to -0.15) | -0.30 (-0.46 to -0.14) |
| High GL vegetables | 0.01 (-0.17 to 0.20) | -0.10 (-0.24 to 0.05) |

^{*} Baked, boiled, or mashed white potatoes, yams, and sweet potatoes.

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

Supplemental Table 9. Weight change (lbs) associated with an increase of one serving per day of total fruits and total vegetables using a complete case analysis, additionally adjusting for baseline fruit and vegetable intake and weight, and using weight change in the future 4-year interval.

| | Main Analysis: | Complete Case: | Additionally adjusted for | Weight change in future |
|--------------|--------------------------|--------------------------|---------------------------|-------------------------|
| | missing diet and weight | individuals with missing | baseline total fruit | 4-year interval |
| | data carried forward one | diet or weight data | intake, total vegetable | |
| | cycle | excluded | intake, and weight | |
| Total n | | | | |
| HPFS | 19,316 | 18,930 | 19,316 | 18,541 |
| NHS | 40,415 | 39,775 | 40,415 | 40,110 |
| NHS II | 73,737 | 65,649 | 73,737 | 71,540 |
| Pooled | 133,468 | 124,354 | 133,468 | 130,191 |
| Total Fruit | | | | |
| HPFS | -0.44 (-0.52, -0.36) | -0.42 (-0.50, -0.34) | -0.52 (-0.60, -0.44) | -0.06 (-0.14, 0.02) |
| NHS | -0.53 (-0.60, -0.47) | -0.54 (-0.61, -0.47) | -0.59 (-0.66, -0.52) | 0.05 (-0.01, 0.12) |
| NHS II | -0.60 (-0.67, -0.53) | -0.74 (-0.82, -0.67) | -0.74 (-0.81, -0.67) | 0.11 (0.03, 0.19) |
| Pooled | -0.53 (-0.61, -0.44) | -0.58 (-0.90, -0.27) | -0.62 (-0.74, -0.49) | 0.03 (-0.05, 0.12) |
| Total Vegeta | ables | | | |
| HPFS | -0.18 (-0.23, -0.13) | -0.18 (-0.23, -0.13) | -0.17 (-0.22, -0.12) | 0.05 (0.00, 0.10) |
| NHS | -0.21 (-0.25, -0.18) | -0.25 (-0.29, -0.21) | -0.20 (-0.24, -0.16) | 0.11 (0.07, 0.15) |
| NHS II | -0.35 (-0.38, -0.31) | -0.47 (-0.51, -0.44) | -0.33 (-0.37, -0.29) | 0.04 (0.00, 0.08) |
| Pooled | -0.25 (-0.35, -0.14) | -0.33 (-0.62, -0.04) | -0.23 (-0.34, -0.13) | 0.07 (0.03, 0.11) |

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, trans fat, alcohol, and seafood.

Supplemental Table 10 Weight change (lbs) associated with an increase of one serving per day of total fruits and total vegetables stratified by BMI and smoking status.

| | Main Analysis: | Normal Weight: | Overweight: | Obese: | Nonsmokers: | Smokers: |
|--------------|----------------------|-----------------------|----------------------------------|---------------------------------|----------------------|----------------------|
| | (no BMI restriction) | BMI < 25 kg/ m^2 at | BMI ≥25 kg/m ² and < | BMI \geq 30 kg/m ² | not a current smoker | current smoker at |
| | | baseline | 30 kg/m ² at baseline | at baseline | at the beginning and | the beginning and |
| | | | | | end of each 4-year | end of each 4-year |
| | | | | | time interval | time interval |
| Total n | | | | | | |
| HPFS | 19,316 | 9,559 | 8,422 | 1,319 | 16,642 | 1,210 |
| NHS | 40,415 | 24,393 | 11,015 | 5,007 | 31,620 | 6,264 |
| NHS II | 73,737 | 49,534 | 14,844 | 9,406 | 63,240 | 6,875 |
| Pooled | 133,468 | 83,486 | 34,281 | 15,732 | 111,502 | 14,349 |
| Total Fruit | | | | | | |
| HPFS | -0.44 (-0.52, -0.36) | -0.31 (-0.39, -0.22) | -0.54 (-0.67, -0.41) | 0.02 (-1.24, 1.29) | -0.46 (-0.54, -0.38) | -0.33 (-0.81, 0.15) |
| NHS | -0.53 (-0.60, -0.47) | -0.34 (-0.40, -0.27) | -0.71 (-0.85, -0.57) | -0.99 (-1.29, -0.69) | -0.55 (-0.62, -0.48) | -0.53 (-0.73, -0.34) |
| NHS II | -0.60 (-0.67, -0.53) | -0.35 (-0.42, -0.29) | -0.84 (-1.02, -0.65) | -1.38 (-1.71, -1.06) | -0.59 (-0.66, -0.52) | -0.57 (-0.87, -0.27) |
| Pooled | -0.53 (-0.61, -0.44) | -0.34 (-0.37, -0.30) | -0.69 (-0.86, -0.52) | 0.79 (-1.52, -0.07) | -0.53 (-0.61, -0.46) | -0.52 (-0.66, -0.38) |
| Total Vegeta | bles | | | | | |
| HPFS | -0.18 (-0.23, -0.13) | -0.11 (-0.16, -0.06) | -0.22 (-0.30, -0.14) | -0.97 (-1.69, -0.25) | -0.20 (-0.25, -0.15) | -0.10 (-0.32, 0.13) |
| NHS | -0.21 (-0.25, -0.18) | -0.05 (-0.08, -0.01) | -0.38 (-0.46, -0.29) | -0.58 (-0.75, -0.42) | -0.25 (-0.29, -0.21) | -0.05 (-0.16, 0.06) |
| NHS II | -0.35 (-0.38, -0.31) | -0.20 (-0.23, -0.17) | -0.59 (-0.68, -0.51) | -0.59 (-0.75, -0.44) | -0.37 (-0.41, -0.33) | -0.16 (-0.28, -0.04) |
| Pooled | -0.25 (-0.35, -0.14) | -0.12 (-0.22, -0.02) | -0.40 (-0.60, -0.19) | -0.70 (-0.92, -0.49) | -0.27 (-0.38, -0.17) | -0.10 (-0.17, -0.03) |

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status (BMI stratified analyses only), physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

Supplemental Table 11. Q-statistic for heterogeneity between the three cohorts.

| Fruit/Vegetable | Q-statistic | Fruit/Vegetable | Q-statistic |
|------------------------|-------------|--------------------------|-------------|
| Total fruits | 0.01 | Peaches, plums, apricots | 0.32 |
| Total vegetables | < 0.0001 | Raisins &grapes | 0.03 |
| | | Avocados | 0.95 |
| Low GL fruits | 0.04 | Bananas | 0.01 |
| High GL fruits | <0.0001 | Melon | 0.001 |
| Low GL vegetables | <0.0001 | Apples & pears | <0.0001 |
| High GI vegetables | <0.0001 | Strawberries | 0.01 |
| | | Blueberries | 0.87 |
| High fiber fruits | 0.01 | Prunes | <0.0001 |
| Low fiber fruits | 0.08 | Oranges | 0.06 |
| High fiber vegetables | <0.0001 | Grapefruit | 0.15 |
| Low fiber vegetables | <0.0001 | String beans | 0.0006 |
| | | Broccoli | 0.11 |
| Melon | 0.001 | Cabbage | 0.02 |
| Citrus fruits | 0.5 | Cauliflower | <0.0001 |
| Berries | 0.01 | Brussels sprouts | 0.76 |
| Legumes | 0.05 | Carrots | 0.32 |
| Cruciferous vegetables | 0.0007 | Corn | <0.0001 |
| Green leafy vegetables | <0.0001 | Peas | 0.0004 |
| | | Mixed vegetables | 0.11 |
| | | Beans | 0.07 |
| | | Celery | 0.47 |
| | | Winter squash | 0.07 |
| | | Summer squash | 0.23 |
| | | Green leafy vegetables | <0.0001 |
| | | Peppers | 0.05 |
| | | Tomatoes | 0.15 |
| | | Tofu/soy | 0.08 |
| | | Onions | 0.02 |
| | | Potatoes | <0.0001 |

Supplemental Table 12. Modeling sensitivity analyses: weight change (lbs) associated with increased consumption of fruits and vegetables over four years with and without dietary covariates & with and without updated covariates.

| | Main analysis | No dietary covariates | No updated covariates |
|------------------|----------------------|------------------------|------------------------|
| Total fruits | | | |
| HPFS | -0.44 (-0.52, -0.36) | -0.53 (-0.60 to -0.45) | -0.46 (-0.54 to -0.37) |
| NHS | -0.53 (-0.60, -0.47) | -0.64 (-0.70 to -0.57) | -0.50 (-0.62 to -0.38) |
| NHS II | -0.60 (-0.67, -0.53) | -0.67 (-0.74 to -0.60) | -0.75 (-0.84 to -0.66) |
| Pooled | -0.53 (-0.61, -0.44) | -0.61 (-0.70 to -0.53) | -0.57 (-0.76 to -0.38) |
| Total vegetables | | | |
| HPFS | -0.18 (-0.23, -0.13) | -0.15 (-0.20 to -0.11) | -0.19 (-0.25 to -0.14) |
| NHS | -0.21 (-0.25, -0.18) | -0.20 (-0.23 to -0.16) | -0.21 (-0.28 to -0.14) |
| NHS II | -0.35 (-0.38, -0.31) | -0.34 (-0.37 to -0.31) | -0.47 (-0.52 to -0.42) |
| Pooled | -0.25 (-0.35, -0.14) | -0.23 (-0.34 to -0.12) | -0.29 (-0.49 to -0.10) |

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, and the following aspects of diet (analyses with dietary covariates only): fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, *trans* fat, alcohol, and seafood.

Supplemental Table 13. Cohort-specific associations for specific fruits and vegetables.

| Supplemental Table 13. Cohort | -specific associations to | r specific fruits and vege | etables. | |
|-------------------------------|---------------------------|----------------------------|----------------------|----------------------|
| Fruits | HPFS | NHS | NHS II | Pooled |
| Blueberries | -1.35 (-1.81, -0.89) | -1.33 (-1.85, -0.82) | 1.53 (-2.15, -0.91) | -1.38 (-1.68, -1.09) |
| Prunes | -2.46 (-3.20, -1.72) | -0.73 (-1.10, -0.36) | -0.73 (-1.45, -0.02) | -1.28 (-2.28, -0.28) |
| Apples & pears | -1.45 (-1.65, -1.25) | -1.43 (-1.62, -1.23) | -0.85 (-1.06, -0.64) | -1.24 (-1.62, -0.86) |
| Strawberries | -1.35 (-1.72, -0.98) | -0.58 (-0.97, -0.19) | -0.60 (-1.21, 0.02) | -0.86 (-1.41, -0.31) |
| Raisins & grapes | -0.92 (-1.19, -0.64) | -0.79 (-1.04, -0.54) | -0.39 (-0.67, -0.11) | -0.70 (-1.00, -0.40) |
| Avocados | -0.49 (-1.93, 0.94) | -0.24 (-1.88, 1.40) | -0.57 (-1.74, 0.61) | -0.47 (-1.29, 0.34) |
| Grapefruit | -0.56 (-0.83, -0.28) | -0.29 (-0.50, -0.09) | -0.56 (-0.81, -0.32) | -0.46 (-0.64, -0.27) |
| Melon | 0.35 (-0.14, 0.84) | -0.70 (1.05, -0.35) | -0.45 (-0.94, 0.05) | -0.28 (-0.90, 0.34) |
| Bananas | -0.04 (-0.25, 0.17) | -0.13 (-0.33, 0.07) | -0.48 (-0.69, -0.27) | -0.22 (-0.48, 0.04) |
| Oranges | -0.07 (-0.35, 0.22) | -0.37 (-0.60, -0.13) | -0.01 (-0.25, 0.23) | -0.15 (-0.38, 0.08) |
| Peaches, plums, apricots | 0.14 (-0.20, 0.49) | 0.06 (-0.24, 0.35) | -0.25 (-0.67, 0.16) | 0.01 (-0.19, 0.22) |
| Vegetables | | | | |
| Tofu & soy | -2.68 (-3.20, -2.17) | -2.92 (-3.80, -2.04) | -1.81 (-2.58, -1.03) | -2.47 (-3.09, -1.85) |
| Cauliflower | -2.14 (-2.66, -1.62) | 1.47 (-1.96, -0.97) | -0.47 (-1.07, 0.14) | -1.37 (-2.27, -0.47) |
| Summer squash | -0.88 (-1.43, -0.32) | -1.37 (-1.91, -0.82) | -0.68 (-1.40, 0.03) | -1.01 (-1.41, -0.61) |
| String beans | -1.29 (-1.68, -0.90) | -1.32 (-1.73, -0.91) | -0.18 (-0.72, 0.36) | -0.96 (-1.60, -0.32) |
| Peppers | -1.05 (-1.35, -0.75) | -0.48 (-0.87, -0.08) | -0.70 (-1.25, -0.14) | -0.76 (-1.14, -0.39) |
| Broccoli | -0.95 (-1.28, -0.61) | -0.47 (-0.81, -0.12) | -0.81 (-1.24, -0.37) | -0.74 (-1.04, -0.44) |
| Brussels sprouts | -0.79 (-1.82, 0.24) | -0.75 (-1.70, 0.20) | -0.36 (-1.34, 0.61) | -0.63 (-1.14, -0.12) |
| Green leafy vegetables | -0.78 (-0.89, -0.67) | -0.57 (-0.69, -0.45) | -0.21 (-0.36, -0.05) | -0.52 (-0.83, -0.21) |
| Carrots | -0.46 (-0.60, -0.32) | -0.43 (-0.60, -0.27) | -0.29 (-0.49, -0.09) | -0.41 (-0.51, -0.32) |
| Beans | -0.30 (-0.67, 0.08) | -0.07 (-0.54, 0.41) | -0.80 (-1.26, -0.34) | -0.39 (-0.79, 0.01) |
| Celery | -0.35 (-0.65, -0.04) | -0.43 (-0.67, -0.18) | -0.18 (-0.52, 0.16) | -0.34 (-0.50, -0.19) |
| Mixed vegetables | -0.56 (-0.90, -0.22) | -0.01 (-0.44, 0.41) | -0.25 (-0.67, 0.18) | -0.29 (-0.61, 0.03) |
| Tomatoes | -0.21 (-0.41, -0.01) | -0.02 (-0.21, 0.18) | 0.04 (-0.18, 0.26) | -0.07 (-0.22, 0.09) |
| Winter squash | -0.50 (-1.50, 0.49) | 0.95 (0.12, 1.78) | 0.06 (-0.93, 1.04) | 0.20 (-0.66, 1.07) |
| Onions | 0.47 (0.31, 0.63) | 0.35 (0.18, 0.52) | 0.08 (-0.16, 0.33) | 0.31 (0.11, 0.52) |
| Cabbage | 0.94 (0.33, 1.55) | 0.42 (-0.11, 0.94) | -0.14 (-0.71, 0.43) | 0.40 (-0.19, 0.99) |
| Potatoes* | 1.16 (0.91, 1.42) | 0.89 (0.66, 1.13) | 0.16 (-0.11, 0.44) | 0.74 (0.19, 1.30) |
| Peas | 1.78 (1.33, 2.23) | 1.16 (0.69, 1.62) | 0.42 (-0.10, 0.94) | 1.13 (0.37, 1.89) |
| Corn | 2.83 (2.45, 3.21) | 2.38 (1.92, 2.84) | 0.88 (0.35, 1.42) | 2.04 (0.94, 3.15) |

^{*}Includes baked/boiled/mashed white potatoes, sweet potatoes, and yams; excludes french fries and potato chips.

Adjusted for baseline age and BMI and change in the following lifestyle variables: smoking status, physical activity, hours of sitting or watching TV, hours of sleep, fried potatoes, juice, whole grains, refined grains, fried foods, nuts, whole-fat dairy, low-fat dairy, sugar sweetened beverages, sweets, processed meats, non-processed meats, trans fat, alcohol, and seafood.

Supplemental Table 14. Intercorrelations between changes in food intake 1986-1990: results from the Health Professionals Follow-up Study.

| | Fruit | Vegetables | Juice | Whole-fat dairy | Low-fat dairy | Fried potatoes | Whole grains | Refined grains | Nuts | Sugar sweetened beverages | Diet beverages | • . | Processed meats | Non-processed meats | Frequency fried food | % trans fat | Seafood | Alcohol |
|--------------------|-------|------------|-------|-----------------|---------------|----------------|--------------|----------------|------|------------------------------|----------------|------|-----------------|------------------------|----------------------|-------------|---------|---------|
| Fruit | | 0.24 | 0.10 | 0.02 | 0.06 | -0.04 | 0.09 | 0.01 | 0.04 | -0.02 | 0.00 | 0.00 | -0.01 | 0.00 | -0.04 | -0.17 | 0.10 | -0.02 |
| Vegetables | | | 0.10 | 0.03 | 0.03 | 0.03 | 0.09 | 0.09 | 0.04 | 0.00 | 0.02 | 0.05 | 0.04 | 0.09 | -0.01 | -0.11 | 0.17 | 0.02 |
| Juice | | | | 0.06 | 0.01 | 0.02 | 0.03 | 0.03 | 0.03 | 0.00 | 0.00 | 0.02 | 0.04 | 0.01 | -0.01 | -0.09 | 0.04 | 0.01 |
| Whole-fat dairy | | | | | -0.09 | 0.06 | 0.00 | 0.05 | 0.02 | 0.03 | 0.01 | 0.06 | 0.11 | 0.07 | 0.06 | 0.08 | -0.02 | 0.02 |
| Low-fat dairy | | | | | | -0.02 | 0.07 | 0.01 | 0.00 | -0.02 | 0.01 | 0.01 | -0.02 | 0.00 | -0.03 | -0.09 | 0.03 | -0.01 |
| Fried potatoes | | | | | | | 0.01 | 0.08 | 0.03 | 0.08 | 0.02 | 0.11 | 0.14 | 0.17 | 0.18 | 0.22 | 0.00 | 0.03 |
| Whole grains | | | | | | | | -0.01 | 0.01 | 0.00 | 0.02 | 0.01 | 0.01 | 0.00 | -0.03 | -0.07 | 0.07 | 0.01 |
| Refined grains | | | | | | | | | 0.02 | 0.06 | 0.01 | 0.08 | 0.09 | 0.07 | 0.05 | -0.03 | 0.04 | 0.01 |
| Nuts | | | | | | | | | | 0.02 | 0.03 | 0.05 | 0.02 | 0.02 | 0.02 | -0.06 | 0.04 | 0.03 |
| Sugar sweetened k | ever | ages | | | | | | | | | -0.13 | 0.07 | 0.07 | 0.06 | 0.06 | -0.05 | 0.00 | 0.00 |
| Diet beverages | | | | | | | | | | | | 0.03 | 0.00 | 0.02 | 0.02 | 0.04 | 0.04 | -0.03 |
| Sweets | | | | | | | | | | | | | 0.09 | 0.11 | 0.06 | 0.31 | 0.01 | -0.01 |
| Processed meat | | | | | | | | | | | | | | 0.18 | 0.11 | 0.13 | -0.02 | 0.04 |
| Non-processed me | eat | | | | | | | | | | | | | | 0.13 | 0.15 | 0.00 | 0.03 |
| Frequency fried fo | od | | | | | | | | | | | | | | | 0.24 | -0.02 | 0.02 |
| % trans fat | | | | | | | | | | | | | | | | | -0.11 | -0.09 |
| Seafood | | | | | | | | | | | | | | | | | | 0.03 |
| Alcohol | | | | | | | | | | | | | | | | | | |

Correlations ≥ |0.10| (what we considered biologically relevant) are shown in bold. All values shown in bold had a p-value < 0.0001.

Supplemental Table 15. Intercorrelations between changes in food intake 1986-1990: results from the Nurses' Health Study I.

| | Fruit | Vegetables | Juice | Whole-fat dairy | Low-fat dairy | Fried potatoes | Whole grains | Refined grains | | Sugar sweetened beverages | Diet beverages | Sweets | Processed meats | Non-processed meats | Frequency fried food | % <i>trans</i> fat | Seafood | Alcohol |
|--------------------|-------|------------|-------|-----------------|---------------|----------------|--------------|----------------|------|------------------------------|----------------|--------|-----------------|------------------------|----------------------|--------------------|---------|---------|
| Fruit | | 0.24 | 0.09 | 0.05 | 0.07 | -0.03 | 0.08 | 0.00 | 0.05 | -0.02 | 0.02 | -0.01 | 0.00 | 0.02 | -0.02 | -0.17 | 0.12 | -0.01 |
| Vegetables | | | 0.08 | 0.04 | 0.06 | 0.00 | 0.10 | 0.06 | 0.04 | -0.01 | 0.04 | 0.01 | 0.03 | 0.09 | -0.02 | -0.11 | 0.20 | 0.02 |
| Juice | | | | 0.05 | 0.01 | 0.02 | 0.03 | 0.04 | 0.03 | 0.02 | -0.02 | 0.02 | 0.03 | 0.03 | 0.01 | -0.08 | 0.03 | 0.02 |
| Whole-fat dairy | | | | | -0.10 | 0.06 | 0.01 | 0.08 | 0.02 | 0.03 | 0.02 | 0.06 | 0.08 | 0.06 | 0.04 | 0.02 | -0.01 | 0.04 |
| Low-fat dairy | | | | | | -0.04 | 0.05 | -0.01 | 0.00 | -0.03 | 0.01 | -0.03 | -0.03 | 0.00 | -0.03 | -0.11 | 0.05 | -0.02 |
| Fried potatoes | | | | | | | 0.01 | 0.10 | 0.04 | 0.07 | 0.01 | 0.11 | 0.14 | 0.10 | 0.11 | 0.17 | -0.02 | 0.03 |
| Whole grains | | | | | | | | -0.07 | 0.03 | 0.00 | 0.02 | 0.01 | 0.01 | 0.01 | -0.02 | -0.04 | 0.08 | 0.01 |
| Refined grains | | | | | | | | | 0.01 | 0.04 | 0.01 | 0.09 | 0.12 | 0.10 | 0.04 | 0.00 | 0.02 | 0.01 |
| Nuts | | | | | | | | | | 0.00 | 0.01 | 0.06 | 0.02 | 0.02 | 0.02 | -0.04 | 0.03 | 0.01 |
| Sugar sweetened b | ever | ages | | | | | | | | | -0.14 | 0.04 | 0.05 | 0.05 | 0.04 | -0.04 | -0.01 | 0.01 |
| Diet beverages | | | | | | | | | | | | 0.02 | 0.00 | 0.02 | 0.00 | 0.03 | 0.03 | 0.00 |
| Sweets | | | | | | | | | | | | | 0.08 | 0.09 | 0.06 | 0.30 | -0.02 | -0.02 |
| Processed meat | | | | | | | | | | | | | | 0.18 | 0.09 | 0.10 | -0.02 | 0.02 |
| Non-processed me | eat | | | | | | | | | | | | | | 0.09 | 0.13 | -0.01 | 0.03 |
| Frequency fried fo | od | | | | | | | | | | | | | | | 0.22 | -0.02 | 0.01 |
| % trans fat | | | | | | | | | | | | | | | | | -0.13 | -0.07 |
| Seafood | | | | | | | | | | | | | | | | | | 0.01 |
| Alcohol | | | | | | | | | | | | | | | | | | |

Correlations ≥ |0.10| (what we considered biologically relevant) are shown in bold. All values shown in bold had a p-value < 0.0001.

Supplemental Table 16. Intercorrelations between changes in food intake 1986-1990: results from the Nurses' Health Study II.

| | Fruit | Vegetables | | Whole-fat dairy | Low-fat dairy | Fried potatoes | Whole grains | | Nuts | Sugar sweetened beverages | | • , | Processed meats | Non-processed meats | Frequency fried food | % <i>trans</i> fat | Seafood | Alcohol |
|--------------------|--------|------------|------|-----------------|---------------|----------------|--------------|------|-------|------------------------------|-------|------|-----------------|------------------------|----------------------|--------------------|---------|---------|
| Fruit | | 0.29 | 0.13 | 0.03 | 0.12 | -0.03 | 0.13 | 0.06 | 0.05 | -0.02 | -0.01 | 0.01 | 0.01 | 0.01 | -0.03 | -0.18 | 0.11 | -0.02 |
| Vegetables | | | 0.10 | 0.04 | 0.08 | 0.01 | 0.14 | 0.12 | 0.06 | -0.01 | 0.03 | 0.02 | 0.04 | 0.09 | -0.03 | -0.16 | 0.19 | 0.03 |
| Juice | | | | 0.06 | 0.05 | 0.02 | 0.07 | 0.06 | 0.02 | 0.02 | -0.03 | 0.04 | 0.04 | 0.04 | 0.00 | -0.09 | 0.04 | 0.00 |
| Whole-fat dairy | | | | | -0.12 | 0.09 | 0.02 | 0.04 | 0.05 | 0.03 | 0.01 | 0.07 | 0.10 | 0.09 | -0.01 | 0.07 | 0.04 | 0.02 |
| Low-fat dairy | | | | | | -0.05 | 0.11 | 0.04 | -0.01 | -0.01 | -0.02 | 0.00 | -0.01 | 0.00 | -0.01 | -0.14 | 0.03 | -0.03 |
| Fried potatoes | | | | | | | 0.01 | 0.09 | 0.06 | 0.08 | 0.05 | 0.16 | 0.16 | 0.18 | 0.10 | 0.27 | 0.02 | 0.04 |
| Whole grains | | | | | | | | 0.05 | 0.03 | 0.00 | 0.01 | 0.03 | 0.03 | 0.02 | -0.03 | -0.08 | 0.08 | -0.02 |
| Refined grains | | | | | | | | | 0.01 | 0.03 | 0.03 | 0.09 | 0.08 | 0.11 | 0.05 | -0.08 | 0.05 | 0.03 |
| Nuts | | | | | | | | | | 0.02 | 0.02 | 0.07 | 0.04 | 0.04 | 0.01 | 0.00 | 0.04 | 0.02 |
| Sugar sweetened b | oevera | ges | | | | | | | | | -0.16 | 0.06 | 0.05 | 0.06 | 0.03 | -0.07 | 0.00 | 0.00 |
| Diet beverages | | | | | | | | | | | | 0.04 | 0.02 | 0.03 | 0.00 | 0.06 | 0.03 | 0.01 |
| Sweets | | | | | | | | | | | | | 0.10 | 0.11 | 0.06 | 0.28 | 0.02 | 0.00 |
| Processed meat | | | | | | | | | | | | | | 0.20 | 0.05 | 0.13 | 0.03 | 0.03 |
| Non-processed me | eat | | | | | | | | | | | | | | 0.08 | 0.12 | 0.07 | 0.03 |
| Frequency fried fo | od | | | | | | | | | | | | | | | 0.20 | -0.04 | 0.03 |
| % trans fat | | | | | | | | | | | | | | | | | -0.08 | -0.04 |
| Seafood | | | | | | | | | | | | | | | | | | 0.04 |
| Alcohol | | | | | | | | | | | | | | | | | | |

Correlations ≥ |0.10| (what we considered biologically relevant) are shown in bold. All values shown in bold had a p-value < 0.0001.

Supplemental Table 17. Pearson correlation coefficients (r) between mean consumption of fruits and vegetables estimated by dietary record (DR) and food frequency questionnaire (FFQ) among men in the Health Professionals Follow-up Study [19].

| | r |
|---|------|
| Apples, pears | 0.53 |
| Avocados | 0.52 |
| Bananas | 0.76 |
| Blueberries | 0.30 |
| Cantaloupe | 0.40 |
| Watermelon | 0.28 |
| Grapefruit | 0.50 |
| Grapefruit juice | 0.53 |
| Oranges | 0.43 |
| Peaches, plums, apricots | 0.45 |
| Raisins, grapes | 0.42 |
| Strawberries | 0.24 |
| Yams, sweet potatoes | 0.24 |
| Beans, lentils | 0.19 |
| Broccoli | 0.29 |
| Brussels sprouts | 0.31 |
| Sauerkraut | 0.23 |
| Cabbage, coleslaw | 0.21 |
| Cooked cabbage | 0.32 |
| Carrots | 0.34 |
| Cauliflower | 0.20 |
| Celery | 0.19 |
| Corn | 0.32 |
| Eggplant, zucchini | 0.20 |
| Mixed, stir-fry vegetables | 0.13 |
| Peas, lima beans | 0.31 |
| Peppers | 0.38 |
| Spinach | 0.18 |
| Kale, mustard greens | 0.17 |
| Iceberg/romaine lettuce | 0.53 |
| String beans | 0.21 |
| Tofu, soybeans, soy burger, miso, other soy protein | 0.44 |
| Tomatoes | 0.40 |
| Winter squash | 0.28 |

Supplemental Table 18. Exclusions (sequential) at baseline.

| | HPFS | NHS | NHS II |
|------------------------------------|-------------|-------------|-------------|
| Baseline | 1986 - 1990 | 1986 - 1990 | 1991 - 1995 |
| Multiple records | 0 | 0 | 253 |
| Died before data collection | 1 | 37 | 253 |
| 70+ blank responses on FFQ | 298 | 0 | 21 |
| Implausible reported energy intake | 954 | 7,658 | 18,027 |
| Cancer | 3,488 | 10,556 | 2,524 |
| Diabetes | 2,197 | 4,509 | 1,746 |
| Ulcerative colitis | 611 | 1,181 | 1,467 |
| Pulmonary embolism | 278 | 439 | 2,636 |
| Coronary artery bypass graft | 2,224 | 422 | 23 |
| Myocardial infarction | 1,322 | 1,951 | 521 |
| Angina | 1,107 | 3,621 | 496 |
| Stroke | 324 | 511 | 402 |
| Lupus | 0 | 405 | 339 |
| Irritable bowel | 27 | 100 | 112 |
| Over age 65 years | 4,794 | 4,710 | 0 |
| Pregnant | NA | 0 | 8,994 |
| Missing data | | | |
| Physical activity | 180 | 29,674 | 77 |
| Diet | 10,530 | 11,813 | 2,119 |
| ВМІ | 522 | 911 | 422 |
| Weight | 112 | 157 | 1,708 |

Supplemental Table 19. Baseline (mean, SD) fruit and vegetable intake (servings/day) of men and women in three prospective cohorts.

| women in three prospective conorts. | HPFS | NHS | NHS II |
|-------------------------------------|--------------------|--------------------|--------------------|
| | n = 19,316 1986 | n = 40,415 1986 | n = 73,737 1991 |
| Melon | 0.13 (0.11) | 0.17 (0.11) | 0.08 (0.09) |
| Citrus Fruits | 0.35 (0.28) | 0.32 (0.19) | 0.19 (0.23) |
| Berries | 0.11 (0.11) | 0.16 (0.11) | 0.16 (0.20) |
| Legumes | 0.31 (0.19) | 0.20 (0.09) | 0.22 (0.22) |
| Cruciferous Vegetables | 0.44 (0.22) | 0.47 (0.18) | 0.41 (0.34) |
| Green Leafy Vegetables | 0.74 (0.37) | 0.83 (0.31) | 0.67 (0.53) |
| Peaches, Plums, Apricots | 0.10 (0.11) | 0.17 (0.11) | 0.12 (0.17) |
| Raisins & Grapes | 0.13 (0.16) | 0.10 (0.10) | 0.10 (0.18) |
| Avocados | 0.03 (0.04) | 0.02 (0.03) | 0.02 (0.05) |
| Bananas | 0.27 (0.21) | 0.24 (0.14) | 0.23 (0.24) |
| Apples & Pears | 0.34 (0.26) | 0.32 (0.18) | 0.29 (0.30) |
| Strawberries | 0.07 (0.07) | 0.11 (0.08) | 0.12 (0.15) |
| Blueberries | 0.04 (0.05) | 0.05 (0.05) | 0.04 (0.08) |
| Prunes | NA | 0.03 (0.08) | 0.02 (0.10) |
| Oranges | 0.23 (0.21) | 0.19 (0.13) | 0.12 (0.16) |
| Grapefruit | 0.19 (0.22) | 0.21 (0.18) | 0.11 (0.22) |
| String Beans | 0.15 (0.09) | 0.18 (0.08) | 0.15 (0.15) |
| Broccoli | 0.17 (0.10) | 0.21 (0.09) | 0.21 (0.18) |
| Cabbage | 0.11 (0.09) | 0.10 (0.06) | 0.08 (0.10) |
| Cauliflower | 0.10 (0.08) | 0.11 (0.07) | 0.10 (0.13) |
| Brussels Sprouts | 0.04 (0.05) | 0.03 (0.04) | 0.03 (0.06) |
| Carrots | 0.22 (0.19) | 0.33 (0.18) | 0.35 (0.38) |
| Corn | 0.15 (0.09) | 0.13 (0.06) | 0.16 (0.14) |
| Peas | 0.15 (0.09) | 0.13 (0.06) | 0.12 (0.12) |
| Mixed Vegetables | 0.12 (0.10) | 0.07 (0.06) | 0.09 (0.13) |
| Beans | 0.10 (0.09) | 0.07 (0.05) | 0.09 (0.12) |
| Celery | 0.15 (0.15) | 0.20 (0.14) | 0.16 (0.22) |
| Winter Squash | 0.05 (0.05) | 0.06 (0.04) | 0.03 (0.06) |
| Summer Squash | 0.07 (0.07) | 0.09 (0.06) | 0.07 (0.11) |
| Peppers | 0.13 (0.13) | 0.17 (0.12) | 0.14 (0.19) |
| Tomatoes | 0.36 (0.21) | 0.38 (0.17) | 0.26 (0.25) |
| Tofu & Soy | 0.02 (0.05) | 0.01 (0.03) | 0.01 (0.08) |
| Onions | NA | NA | 0.34 (0.38) |
| Potatoes* | 0.34 (0.17) | 0.35 (0.13) | 0.29 (0.20) |

^{*}Baked, boiled, or mashed white potatoes, sweet potatoes and yams; excludes french fries and potato chips.

NA = not on baseline FFQ.