

Supplementary Tables and Figures

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Supplementary Table S1. Long List of Women's Health Initiative Investigators

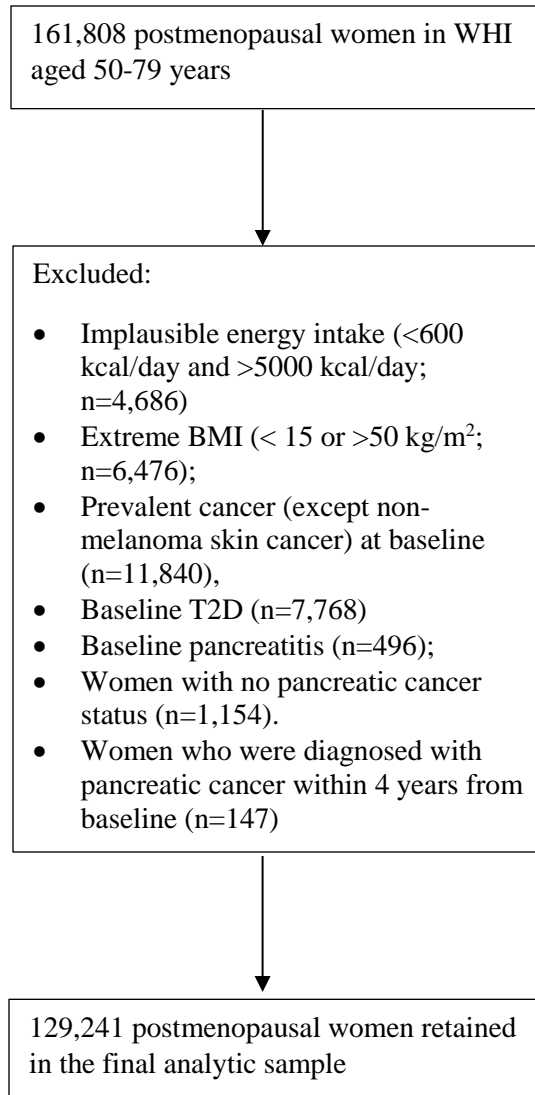
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Supplementary Figure S1. Participant flow chart for the final sample in the Women's Health Initiative

Supplementary Table S1. Long List of Women's Health Initiative Investigators

| | |
|---|---|
| Program Office | National Heart, Lung, and Blood Institute, Bethesda, Maryland) Jacques Rossouw, Shari Ludlam, Joan McGowan, Leslie Ford, Nancy Geller |
| Clinical Coordinating Center | (Fred Hutchinson Cancer Research Center, Seattle, WA) Garnet L. Anderson, Ross Prentice, Charles Kooperberg, Lisa Johnson, Andrea LaCroix, Lesley Tinker, Marian Neuhouser, Susan Heckbert, Alex Reiner, Chongzhi Di, Xiaoling Song, Wayne Rosamond, Shirley Beresford, Chu Chen, Barbara Cochrane |
| Investigators and Academic Centers | (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn E. Manson, Shari Bassuk, Howard Sesso, Lu Wang; (MedStar Health Research Institute, Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, CA) Marcia Stefanick, Mark Hlatky, Marco Perez, Themistocles (Tim) Assimes and Jean Tang; (The Ohio State University, Columbus, OH) Rebecca Jackson, Randall Harris, Electra Paskett, W. Jerry Mysiw, Michael Blumenfeld; (University of Arizona, Tucson/Phoenix, AZ) Cynthia A. Thomson, Tamsen Bassford, Cheryl Ritenbaugh, Zhao Chen, Marcia Ko; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende, Michael LaMonte, Amy Millen, Heather Ochs-Balcom, Christopher Andrews; (University of Florida, Gainesville/Jacksonville, FL) Marian Limacher, Michael Perri, Andrew Kaunitz, R. Stan Williams, Yvonne Brinson; (University of Iowa, Iowa City/Davenport, IA) Jennifer Robinson, Robert Wallace, James Torner, Susan Johnson, Linda Snetselaar; (University of Nevada, Reno, NV) Robert Brunner, Sandra Daugherty1 ; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller, Jane Cauley, N. Carole Milas; (Wake Forest University School of Medicine, WinstonSalem, NC) Sally Shumaker, Stephen Rapp, Claudine Legault, Mark Espeland, Laura Coker, Michelle Naughton |
| Women's Health Initiative Memory Study | (Wake Forest University School of Medicine, Winston-Salem, NC) Mark Espeland, Sally Shumaker, Stephen Rapp, Claudine Legault, Laura Coker, Michelle Naughton |
| Former Principal Investigators and Project Officers | (Albert Einstein College of Medicine, Bronx, NY) Sylvia Wassertheil-Smoller (Baylor College of Medicine, Houston, TX) Haleh Sangi-Haghpeykar, Aleksandar Rajkovic, Jennifer Hays, John Foreyt; (Brown University, Providence, RI) Charles B. Eaton, Annlouise R. Assaf; (Emory University, Atlanta, GA) Lawrence S. Phillips, Nelson Watts, Sally McNagny, Dallas Hall,; (Fred Hutchinson Cancer Research Center, Seattle, WA) Shirley A.A. Beresford, Maureen Henderson; (George Washington University, Washington, DC) Lisa Martin, Judith Hsia, Valery Miller; (HarborUCLA Research and Education Institute, Torrance, CA) Rowan Chlebowski (Kaiser Permanente Center for Health Research, Portland, OR) Erin LeBlanc, Yvonne Michael, Evelyn Whitlock, Cheryl Ritenbaugh, Barbara Valanis; (Kaiser Permanente Division of Research, Oakland, CA) Bette Caan, Robert Hiatt; (National Cancer Institute, Bethesda, MD) Carolyn Clifford1 ; (Medical College of Wisconsin, Milwaukee, WI) Jane |

Morley Kotchen; (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Linda Pottern; (Northwestern University, Chicago/Evanston, IL) Linda Van Horn, Philip Greenland; (Rush University Medical Center, Chicago, IL) Lynda Powell, William Elliott, Henry Black; (State University of New York at Stony Brook, Stony Brook, NY) Dorothy Lane, Iris Granek; (University at Buffalo, Buffalo, NY) Maurizio Trevisan; (University of Alabama at Birmingham, Birmingham, AL) Cora E. Lewis, Albert Oberman; R:\Committees\P&P\Useful Things\Acknow Lists\Long List.doc Last updated 8/17/18 (University of Arizona, Tucson/Phoenix, AZ) Tamsen Bassford, Cheryl Ritenbaugh, Tom Moon; (University of California at Davis, Sacramento, CA) John Robbins; (University of California at Irvine, CA) F. Allan Hubbell, Frank Meyskens, Jr.; (University of California at Los Angeles, CA) Simin Liu, Lauren Nathan, Howard Judd¹; (University of California at San Diego, LaJolla/Chula Vista, CA) Robert D. Langer; (University of Cincinnati, Cincinnati, OH) Michael Thomas, Margery Gass, James Liu; (University of Hawaii, Honolulu, HI) J. David Curb; (University of Massachusetts/Fallon Clinic, Worcester, MA) Judith Ockene; (University of Medicine and Dentistry of New Jersey, Newark, NJ) Norman Lasser; (University of Miami, Miami, FL) Mary Jo O'Sullivan, Marianna Baum; (University of Minnesota, Minneapolis, MN) Karen L. Margolis, Richard Grimm; (University of North Carolina, Chapel Hill, NC) Gerardo Heiss, Barbara Hulka, David Sheps; (University of Tennessee Health Science Center, Memphis, TN) Karen Johnson, William Applegate; (University of Texas Health Science Center, San Antonio, TX) Robert Brzyski, Robert Schenken; (University of Wisconsin, Madison, WI) Gloria E. Sarto, Catherine Allen¹; (Wake Forest University School of Medicine, Winston-Salem, NC) Mara Vitolins, Denise Bonds, Electra Paskett, Greg Burke; (Wayne State University School of Medicine/Karmanos Cancer Institute, Detroit, MI) Michael S. Simon, Susan Hendrix
¹deceased

Supplementary Table S2. Distribution of baseline characteristics in the final analytic sample and among excluded participants

| Characteristic | Excluded Sample (N= 32567) | Included Sample (N=129241) | P-value ¹ |
|--|-------------------------------|-------------------------------|----------------------|
| Race/ethnicity, % | | | |
| African American | 16.2 | 7.2 | |
| American Indian or Alaskan Native | 0.7 | 0.4 | |
| Hispanic | 6.6 | 3.3 | <.0001 |
| Asian or Pacific Islander | 2.5 | 2.6 | |
| European American | 72.6 | 85.0 | |
| Other race groups | 1.3 | 1.4 | |
| Age, years | 63.9 (63.8, 64.0) | 63.1 (63.0, 63.1) | <.0001 |
| Body mass index (BMI), kg/m ² | 27.4 (27.3, 27.5) | 27.4 (27.3, 27.4) | 0.6816 |
| Underweight (BMI<15), % | 14.0 | 2.1 | |
| Normal weight (15≤BMI < 25), % | 23.9 | 36.2 | |
| Overweight (25≤BMI < 30), % | 27.0 | 34.6 | <.0001 |
| Obese (BMI ≥30), % | 35.0 | 27.2 | |
| Physical activity, MET-hours/week | 11.4 (11.3, 11.6) | 12.8 (12.7, 12.9) | <.0001 |
| Pack-years of smoking | 10.7 (10.4, 10.9) | 9.9 (9.8, 10.0) | <.0001 |
| Current smoking, % | 7.3 | 6.8 | 0.0003 |
| Aspirin/NSAIDs use, % | 12.6 | 13.6 | <.0001 |
| Statin use, % | 2.7 | 2.2 | <.0001 |
| Hypercholesterolemia, % | 18.5 | 13.7 | <.0001 |
| Educational level, % | | | |
| Less than high school | 7.9 | 4.7 | |
| High school/GED/Some college | 57.1 | 54.1 | <.0001 |
| ≥4 years of college | 34.1 | 40.5 | |
| Total alcohol intake, servings/week | 1.8 (1.7, 1.8) | 2.5 (2.5, 2.5) | <.0001 |
| Gallbladder removal | 16.1 | 11.9 | <.0001 |

¹ P values for continuous variables were determined via independent sample t-test and P values for categorical variables were determined via chi-square test.

Supplementary Table S3. Distribution of baseline characteristics in the final analytic sample and among the whole Women’s Health Initiative cohort

| Characteristic | Whole WHI Cohort (N= 161,808) | Final Analytic Sample (N=129,241) |
|--|--|--|
| Race/ethnicity, % | | |
| African American | 9.0 | 7.2 |
| American Indian or Alaskan Native | 0.4 | 0.4 |
| Hispanic | 4.0 | 3.3 |
| Asian or Pacific Islander | 2.6 | 2.6 |
| European American | 82.5 | 85.0 |
| Other race groups | 1.4 | 1.4 |
| Age, years | 63.2±7.2 | 63.1±7.2 |
| Body mass index (BMI), kg/m ² | 27.4±6.5 | 27.4±5.5 |
| Underweight (BMI<15), % | 4.4 | 2.07 |
| Normal weight (15≤BMI < 25), % | 33.8 | 36.2 |
| Overweight (25≤BMI < 30), % | 33.2 | 34.6 |
| Obese (BMI ≥30), % | 28.7 | 27.2 |
| Physical activity, MET- hours/week | 12.5±13.5 | 12.8±13.5 |
| Pack-years of smoking | 10.0±18.3 | 9.9±17.9 |
| Current smoking, % | 6.9 | 6.79 |
| Aspirin/NSAIDs use, % | 13.4 | 13.6 |
| Statin use, % | 2.3 | 2.2 |
| Hypercholesterolemia, % | 14.6 | 13.7 |
| Educational level, % | | |
| Less than high school | 5.3 | 4.7 |
| High school/GED/Some college | 54.7 | 54.1 |
| ≥4 years of college | 39.2 | 40.5 |
| Total alcohol intake, servings/week | 2.4±4.9 | 2.5±4.9 |
| Gallbladder removed, % | 12.8 | 11.9 |

Supplementary Table S4. Food group components of the empirical dietary index for hyperinsulinemia (EDIH) score¹ and empirical dietary inflammatory pattern (EDIP) score² in the Women's Health Initiative.

| EDIH components | Weight | Food items |
|--|---------------|---|
| <i>Food components positively associated with C-peptide concentrations</i> | | |
| Processed meat | 0.199 | Processed meats (lunch meat other lunch meat), bacon, hot dog |
| Red meat | 0.25 | Beef, pork and lamb as a main dish, ground meat incl hamburgers, Beef, pork, and lamb as a sandwich, stew, pot pie and casseroles with meat, gravies made with meat drippings, Menudo and tortilla soup |
| High-energy sugary beverages | 0.104 | Regular soft drinks (not diet) |
| Margarine | 0.054 | Margarine |
| Butter | 0.094 | Butter |
| French fries | 0.581 | French fries |
| Non-dark fish | 0.172 | Tuna, shrimp, lobster, scallops, seafood other than dark fish |
| Eggs | 0.124 | Egg |
| Low-fat dairy | 0.025 | Low-fat milk, sherbet or ice milk, yogurt, low-fat desserts |
| Cream soup | 0.787 | Chowder or cream soup |
| Tomatoes | 0.095 | Fresh tomato & tomato juice, tomato sauce |
| Poultry | 0.183 | Chicken & turkey, fried chicken, Chicken or turkey with or without skin |
| <i>Food components inversely associated with C-peptide concentrations</i> | | |
| Green leafy vegetables | -0.055 | Spinach& mustard greens& turnip greens& collards, iceberg or head lettuce, romaine or leaf lettuce |
| Wine | -0.165 | Red, white wine |
| Coffee | -0.035 | Coffee (regular or decaffeinated) |
| High-fat diary | -0.046 | Whole milk, cream, sour cream ice cream, cream cheese, other cheese |
| Whole fruit | -0.029 | Raisins, grapes, avocado, banana, cantaloupe, watermelon, orange, apple, pear, grapefruit, strawberries, blueberries, peaches, apricots, plums |
| EDIP components | Weight | Food items |
| <i>Food components positively associated with concentrations of inflammatory markers</i> | | |
| Processed meat | 157.121 | Hot dogs, processed meats (including processed meat sandwich) , bacon |

| | | |
|--|-----------|--|
| Red meat | 135.786 | Hamburger, beef /pork /lamb sandwich, beef /pork/ lamb main dish |
| Organ meat | 45.528 | Livers |
| Other fish | 243.829 | Canned tuna, shrimp, breaded fish, lobster, scallops or other seafood |
| Other vegetables | 136.891 | Corn, mixed vegetables, eggplant, celery, alfalfa sprouts, mushrooms, green/yellow/red peppers, zucchini, cucumbers |
| | 87.025 | White bread, white rice, bagels/English muffins/rolls, muffins or biscuits, pasta, pancakes or waffles, refined cold breakfast cereals |
| High energy beverage | 154.800 | Cola, Hawaiian punch, caffeine-free coke, pepsi, carbonated beverage with caffeine and sugar, other carbonated beverage with sugar |
| Tomato | 160.659 | Fresh tomatoes, tomato juice, tomato sauce |
| <i>Food components inversely associated with concentrations of inflammatory markers</i> | | |
| Beer | -135.240 | Beer, light beer |
| Wine | -248.816 | White wine, red wine |
| Tea | -128.297 | Tea, tea (not herbal) |
| Coffee | -128.297 | Coffee, decaffeinated coffee |
| Dark yellow vegetable | -166.196 | Carrots, sweet potatoes, winter squash |
| Green leafy vegetable | -188.935 | Spinach, iceberg lettuce, romaine lettuce |
| Snack | -43.825 | Potato/corn chips, popcorn, crackers |
| Fruit juice | -60.660 | Apple juice, orange juice, grape juice, prune juice, other juice |
| Pizza | -1169.052 | Pizza |

¹ The EDIH component foods (servings/d) in the WHI were: Red meat (ground meat including hamburgers, beef, pork and lamb as a main dish, or as a sandwich; stew, pot pie and casseroles with meat; gravies made with meat drippings); high-energy sugary beverages, (all regular - not diet - soft drinks); low-energy sugary beverages (the WHI FFQ did not assess low-energy beverages separately from other sugar-sweetened beverages); cream soup (such as chowders, potato, tomato, cheese, ajiaco); processed meat (hot dogs, chorizo; other sausage, bacon, breakfast sausage, scrapple; lunch meat such as ham, turkey; other lunch meat such as bologna); butter, margarine (butter, margarine or oil, on bread or tortillas; margarine or butter added to cooked cereal or grits; butter, margarine, sour cream, oils, or other fat added to vegetables, beans, rice, and potatoes, after cooking); poultry (poultry); French fries (French fries, fried potatoes, fried rice, fried cassava and fritters); non-dark or non-oily fish (fried fish, shrimp, lobster, crab and oysters, canned tuna, tuna salad, and tuna casserole, white fish such as sole, snapper, cod); tomatoes (fresh tomato, tomato juice, tomato sauce, cooked tomato, salsa and salsa picante); low-fat dairy (part-skim or reduced fat cheeses, such as Mexican-type cheeses or mozzarella. Include cheese added to foods and in cooking; low-fat cottage cheese; low-fat or no-fat frozen desserts, such as frozen yogurt, sherbet, ice milk, and low-fat milkshakes; non-fat yogurt (not frozen); all other yogurt (not frozen); low-fat milk; Milk, cream, or creamer in coffee or tea); eggs (eggs); wine (red wine, white wine); coffee or tea (all types); fruits (all types); high-fat dairy (whole milk, evaporated/condense milk, ice cream, cottage cheese and ricotta cheese, other cheese); green leafy vegetables (cooked greens such as spinach, mustard greens, turnip greens, collards; lettuce and plain lettuce salad; mixed lettuce or spinach salad with vegetables).

² The EDIP component foods (servings/d) in the WHI were: processed meat (hot dogs, chorizo, other sausage, bacon, breakfast sausage, scrapple; lunch meat such as ham, turkey; other lunch meat such as bologna); red meat (ground meat including hamburgers, beef, pork, and lamb as a main dish or as a sandwich; stew, pot pie, and casseroles with meat;

gravies made with meat drippings); organ meat (liver, including chicken liver; other organ meats); fish other than dark-meat fish (fried fish, shrimp, lobster, crab and oysters, canned tuna, tuna salad, and tuna casserole, white fish such as sole, snapper, cod); other vegetables (i.e., vegetables other than green leafy vegetables and dark yellow vegetables: red peppers and red chilies, green peppers, green chilies, jalapenos, and green chili salsa, corn, and hominy); refined grains (total grain variable minus whole grain variable, both WHI-computed food groups); high-energy beverages [all regular (not diet) soft drinks]; low-energy beverages (the WHI FFQ did not assess low-energy beverages); tomatoes (fresh tomato, tomato juice, tomato sauce, cooked tomato, salsa and salsa picante); beer (all types); wine (red wine, white wine); coffee or tea (all types); dark-yellow vegetables (carrots, including mixed dishes with carrots; summer squash, zucchini, nopales, and okra; winter squash, such as acorn, butternut, and pumpkin; sweet potatoes and yams; other potatoes, cassava, and yucca—boiled, baked, or mashed); green leafy vegetables (cooked greens such as spinach, mustard greens, turnip greens, collards; lettuce and plain lettuce salad; mixed lettuce or spinach salad with vegetables); pizza (low-fat pizza; other pizza); fruit juice (orange juice and grapefruit juice; other fruit juices such as apple and grape); snacks (snacks such as potato chips, corn chips, tortilla chips, Ritz and cheese crackers; saltines, Snackwell's, fat-free tortilla chips and fat-free potato chips; popcorn).

Supplementary Table S5. Description of covariates used in the current study

| Covariates | Variable Description |
|--|--|
| Total energy intake | Dietary energy intake (kcal/day) |
| Education | <p>1 = Didn't go to school</p> <p>2 = Grade school (1-4 years)</p> <p>3 = Grade school (5-8 years)</p> <p>4 = Some high school (9-11 years)/High school diploma or GED</p> <p>5 = Vocational or training school/Some college or Associate Degree</p> <p>6 = Some post-graduate or professional/College graduate or Baccalaureate Degree</p> <p>7 = Master's Degree/Doctoral Degree (Ph.D, M.D.,J.D.,etc.)</p> <p>Missing values of education were imputed based on income levels</p> |
| Race/Ethnicity | <p>1 = European American</p> <p>2 = African American</p> <p>3 = Hispanic/Latina</p> <p>4 = Other race groups</p> |
| Pack-years of smoking | Continuous variable. A computed variable taking into account years of smoking and number of cigarettes smoked per day on average. |
| Comorbidity Score | A sum of the following chronic diseases/conditions (0=no/1=yes): High cholesterol requiring pills ever, Stroke ever, high blood pressure ever (Does not include gestational high blood pressure), heart disease ever, stroke ever, and rheumatoid/other arthritis ever. |
| Hormone Replacement Therapy (HT) study arm | <p>HT study arm to which the participant was randomized:</p> <p>0 = Not randomized to HT</p> <p>1 = Estrogen-alone intervention</p> <p>2 = Estrogen-alone control</p> <p>3 = Estrogen + Progestin intervention</p> <p>4 = Estrogen + Progestin control</p> |
| NSAID | Baseline nonsteroidal anti-inflammatory agents use: no=0, yes=1 |

| | |
|----------------------------|---|
| Supplement | Number of supplements taken. The variable was created from a sum of the following 23 nutrient and mineral supplements variables (yes=1/no=0): vitamin A, alpha-tocopherol, vitamin B1, vitamin B12, vitamin B2, vitamin B6, beta-carotene, biotin, vitamin C, calcium, chromium, copper, vitamin D, folic acid, iron, magnesium, manganese, molybdenum, niacin, pantothenic acid, retinol, selenium, and zinc |
| Age, years | Age at screening |
| Family history of diabetes | Family history of diabetes: no=0, yes=1 |
| Hormone use | Number of hormones used. The variable was created from a sum of the following 8 WHI variables: Oral contraceptive use ever, diethylstilbestrol use ever, depo-provera use ever, unopposed estrogen use ever, Estrogen + progesterone use ever, Testosterone or other male hormone use, Estratest use, oral daily use of a glucocorticosteroid |
| Physical activity | Total energy expended from recreational physical activity (MET-hours/week) |
| Body mass index (BMI) | Continuous, kg/m ² |
| BMI (categorical) | Three level categorical variable (kg/m ²): 1 = underweight to normal (15 to <18.5) 2 = normal weight (18.5 to <25) 3 = overweight (25 to <30) 4 = obese (30 to 50) |

Supplementary Table S6. Spearman correlation coefficients between the dietary indices (N= 129,241)

| | Correlations using the energy-adjusted dietary indices | Correlations using the dietary indices unadjusted for total energy intake |
|-----------|---|---|
| EDIH-EDIP | 0.59 | 0.58 |
| EDIH-GI | 0.27 | 0.29 |
| EDIH-GL | -0.27 | 0.37 |
| EDIP-GI | 0.28 | 0.29 |
| EDIP-GL | 0.08 | 0.14 |
| GI-GL | 0.33 | 0.29 |

EDIH, empirical dietary index for hyperinsulinemia. EDIP, empirical dietary inflammatory pattern score. GI, glycemic index. GL, glycemic load.