**Summary from 20 articles**

**Study cohort size range:**

Before exclusion: 22,476 – 617,119, **mostly around 30,000, For NHANES 9000-20000**

After exclusion: 1,904- 536,969, **mostly around 30,000, For NHANES 9000-20000**

**Exclusion criteria summary:**

(1) Missing dietary variables, missing substantially amount of dietary variables

(2) Bad or inadequate data

(3) Extreme value of total energy intake

(6) Prevalent diseases related to mortality outcomes or prevalent CVD defined as previous coronary bypass, angioplasty/stent, carotid artery surgery, myocardial infarction, stroke, or transient ischemic attack, or angina pectoris or congestive heart failure treated in the past 12 month. Previous malignant neoplasm or cancer before recruitment. Previous diabetes. Previous hemochromatosis.

(7) Uncertain follow-up, loss of follow-up, or those who died before the start of follow-up

(8) Unlikely high daily red meat consumption (>300 g/d) or missing information on red meat consumption.

(9) Women that are pregnant at baseline

(10) Implausible BMI

(11) Subjects with repeated health surveys

**40617** participants initially

(1) Age younger or older than age range considered

**21903** remaining, 18714 exclusions

(2) Missing Alcohol Drinking, Education, marital status, sleep, sedentary lifestyle, smoking

**16251** remaining, 5652 exclusions

(3) Missing history of hypercholesterolemia, history of hypertension, history of diabetes, history of depression, history of cardiovascular disease, history of cancer, history of stroke, family history of diabetes, family history of myocardial infraction

**13131** remaining, 3120 exclusions

(4) Missing family annual income and PIR

**12212 remaining**, 919 exclusions

(5) Missing Occupation category

**11558 remaining,** 654 exclusions

(6) Missing dietary variables: TKCAL, TCARB, TFIBE, TSFAT, TMFAT, TPFAT, TCHOL, TMAGN, F\_FRUIT, V\_TOTAL, PF\_SEAFD, G\_WHOLE, PF\_MPS\_TOTAL, PF\_MEAT, PF\_CUREDMEAT, PF\_POULT, PF\_EGGS, PF\_NUTSDS, PF\_LEGUMES, D\_TOTAL, D\_CHEESE, BEEF\_VEAL, BEEF\_VEAL\_LAMB, BEEF\_VEAL\_PORK BEEF\_VEAL\_PORK\_LAMB. And missing special diet variable, dietary supplement intake.

**11207 remaining**, 351 exclusions

(7) Missing systolic blood pressure

**11047 remaining**, 160 exclusions

(8) Extreme value of total energy intake

**10887 remaining**, 160 exclusions

(8) Missing BMI, Height, Weight, or implausible BMI (<15 or ≥60 kg/m2)

**10797 remaining**, 90 exclusions

(9) Pregnant women

**10715 remaining**, 82 exclusions

(10) Women who are missing Menopausal status, Hormone therapy, Parity, Oral contraceptive use

**10651 remaining,** 64 exclusions

(10) Not available for death linkage

**10639 remaining,** 12 exclusions

**Definition of unprocessed red meat summary:**

(1) Unprocessed red meat intake was reported as two items in the FFQ: “hamburger, ground beef (in casserole, meatballs, etc.)” and “beef or lamb as a main dish (e.g., steak, roast, stew, and pot pies)”.

(2) Beef, pork, veal.

(3) Pork, veal, hamburger, liver, lamb, viscera (offal)

(4) Beef, pork, hamburger, liver, steak, and meats in foods such as chili, lasagna, and stew

(5) Beef or lamb, hamburger

(6) “Beef, pork, or lamb as main dish”, “hamburger,” and “beef, pork, or lamb as a sandwich or mixed dish.”

Summary of definition

(1) BEEF, VEAL, , LAMB

(2) BEEF, VEAL, PORK

(3) BEEF, VEAL, PORK, LAMB

**BEEF+VEAL**

**BEEF+VEAL+PORK**

**BEEF+VEAL+LAMB**

**BEEF+VEAL+PORK+LAMB**

**BEEF+VEAL+PORK+LAMB+GAME MEAT**

**Definition of processed meat summary:**

(1) Processed meat was reported as: “processed beef, lamb (e.g., sausage, salami, and bologna)” and “processed chicken or turkey (e.g., turkey bologna, and turkey ham)”. Pork was classified as processed meat because most of the pork products listed in the single pork question in the FFQ were processed (i.e., “pork (bacon, sausage, ham, chops, ribs, and lunch-meat)”).

(2) Sausages, hot dogs, salami, ham, processed meat cuts, liver pate, and blood sausage.

(3) Dry cured ham, cooked ham, sausages [salami, mortadella, blood sausage, spicy pork sausage, würstel], bacon, pancetta, paté

(4) Bacon, beef cold cuts, ham, hotdogs, and sausage

(5) Sausage

(6) “Bacon” (2 slices, 13 g), “hot dogs” (one, 45 g), and “sausage, salami, bologna, and other processed red meats”

(7) All meat products, including ham, bacon, sausages; small part of minced meat that has been bought as a ready-to eat product

**Definition of red meat summary:**

(1) Beef, pork, ham, liver and other organ meats

(2) Beef, pork, mutton/lamb, horse, goat

(3) Pork chops; pork ribs; pig’s feet; regular fresh pork; lean fresh pork; mixed fresh pork; pig, cow, and sheep liver; organ meat, including heart, brain, tongue, tripe, and intestine; and beef and lamb

**NHANES We used:**

NHANES 2015-2016: 9971 removed

NHANES 2013-2014: 10175

NHANES 2011-2012: 9756

NHANES 2009-2010: 10537

NHANES 2007-2008: 10149

Total of 50000 initially

To be continued:

**Analytics:**

**Summary of analytics:**

(1) Time-dependent Cox-proportional hazards regression with attained age as the time variable. Or just Cox-proportional hazards model. HR and 95% CI calculated.

(2) Treat meat variable as continuous: log-transform or not, compared 90th percentile of intake with zero-intake to get effect estimates, or 1-additional ounce equivalent increase. Or categorical (a zero-intake group plus quartiles of consumers, or quintile or quartiles used: lowest as reference). Or divide it by total energy intake and categorize it as fifth (lowest as reference) or just continuous (20 g/1000 kcal/day increase).

(3) Treat food variables (such as Vegetables, Fruits, etc.) as quintiles. Or divide it by total energy intake and categorize it as fifth depending whether using density model.

(4) The standard model (or so-called residual model, substitution model) that adjusted for total energy and the interpretation will be average relative causal effect. Perform multivariable analyses to examine the HRs for mortality when replace 100 g of fish, potatoes, poultry, eggs, vegetables, fruits and nuts, and cereals by 100 g of red meat. Can use leave one out analysis.

The standard model (or so-called residual model, substitution model) could also adjusted for overall meat intake instead of total energy. So that increases in the meat variable of interest reflected reductions in other meat types and the total meat intake remained constant.

In conclusion, residual model could adjust for total energy or total meat, and has a variant model called substitution model that can also include other competing dietary variables.

(5) The unadjusted model that do not adjusted for total or remaining energy intake and the interpretation will be total causal effect.

(6) The all-component model that include all individual dietary component but not total or remaining energy intake and the interpretation will be total causal effect. Evaluated processed and non-processed red meat consumption as 2 distinct exposures in a mutually adjusted model. We also tested another series of models in which each meat variable was adjusted for all other forms of meat, so that all meat types in the model added up to total meat (addition model).

(7) The density methods that divided all nutritional variables by the daily calorie intake and categorized the calorie adjusted values into fifths for the entire cohort. The interpretation will be average relative causal effect rescaled as a proportion of total energy. The density method also adjusted for total energy intake. Leave one out analysis used. These models allow estimation of the effect on each outcome of an increase in the percentage of energy from protein intake. By forcing total energy and other intake, such as dietary fats, to be constant and by excluding carbohydrate from the model, an increase in protein intake by definition statistically results in a decrease in carbohydrate intake. Thus, the effect estimates of protein assume a **substitution interpretation.** The percentage of energy from protein that is “substituted” for carbohydrate is the difference in median energy intake of protein between the highest and lowest quintiles**.**

(7) Interaction with age, sex, race, BMI, smoking, alcohol, fruit, vegetable, or fruit and vegetable combined (FV consumption: 3 predefined groups).

(8) Subgroup analysis by age, sex, race, smoking, BMI, exercise, education, alcohol, income, history of hypertension at baseline, history of diabetes at baseline, levels of fruit, levels of vegetables, fruit and vegetable combined (FV consumption: 3 predefined groups), levels of total energy intake, socioeconomic status, exclude history of diabetes + cancer + CVD, exclude history of hypertension and hypercholesterolemia, censoring follow-up time of participants at 6 or 8 years, exclude early death, including only cancer death, including only CV death, excluding the first two years of observation and related death.

(9) The proportional hazards assumption of the model was assessed using log(−log) plots, Schoenfeld residuals, and attained-age interaction terms. The assumption of proportionality of the hazards was tested by calculating Schoenfeld residuals, regressed against survival time, and tested for a nonzero slope.

(10) Linear trends across the categories were tested by assigning the medians of intake in each quartile (or quintiles) to all participants in that quartile and analyzing them as continuous variables, the coefficient for which was evaluated by the Wald test. Also, we assessed the linearity of the relationship between the exposures and mortality outcomes using 4-knot restricted cubic spline regression. Trend tests were calculated using meat consumption as a continuous variable. To test for non-linear trends, quadratic terms of fermented food intake variables were added to the continuous models.

(11) Multivariable-adjusted estimates for restricted cubic splines were used to calculate dose–response association between SFA intake or red meat consumption and total mortality.

(12) Regression calibration, calibration analysis

(13) Multiple imputation, or replacing missing values with median.

**Model used:**

**Standard (residual model)** Average Relative Causal Effect

(1) Model 1 adjusted for age (attained age as time variable), sex (male and female), race (Black and non-Black), and total energy intake (continuous).

(2) Model 2 adjusted for age (attained age as time variable), sex (male and female), race (Black and non-Black), total energy intake (continuous), marital status (married/common-law and single/widowed/divorced/separated), educational level (up to high school graduate, trade school/some college/associate degree, bachelor degree, and graduate degree), multivitamin use (current use), smoking status (current smoker, quit <1 year, quit 1–4 years, quit 5–9 years, quit 10–19 years, quit 20–29 years, quit ≥30 years, and never smoked), alcohol use (none, rarely, monthly, weekly, and daily), exercise (none, ≤20 min/week, 21–60 min/week, 61–150 min/week, and ≥151 min/week), sleep (≤4 h/night, 5–8 h/night, and ≥9 h/night), body mass index (<18.5, 18.5–24.9, 25.0–29.9, and ≥30.0), aspirin use (yes/no: used weekly for at least two years in the last five years), having ever been diagnosed with or received treatment in the last 12 months for diabetes (yes/no), having been diagnosed in the last 5 years with or received treatment in the last 12 months for hypertension or hypercholesterolemia (yes/no), the use of statin for at least 2 years in the last 5 years, the use of blood pressure medications for at least 2 years in the last 5 years (yes/no), and dietary variables (each variable has 5 levels in g/day) as follows. Cruciferous vegetables (Quintiles: <9.6, 9.6–16.7, >16.7–26.1, >26.1–45.2, >45.2), fruits (Quintiles: <130, 130–224.4, >224.4–322, >322–464.2, >464.2), whole grain (Quintiles: <65, 65–109.9, >109.9–170.3, >170.3–252.2, >252.2), legumes (Quintiles: <17, 17–29.7, >29.7–45.9, >45.9–77.1, >77.1), nuts and seeds (Quintiles: <6.4, 6.4–12.8, >12.8–21.6, >21.6–35.1, >35.1), total dairy (0 intake, quartiles of intake: >0–36, >36–108.1, >108.1–240.9, >240.9), eggs (0 intake, quartiles of intake: >0–3.6, >3.6–7.3, >7.3–20.1, >20.1); and in women, the model also adjusted for menopausal status (premenopausal, postmenopausal), and hormone therapy (in postmenopausal women) (not taking hormone therapy, taking hormone therapy).

(3) Model 3: In addition to covariates in model 2, also adjusted for other meat variables such as fish (0 intake, quartiles of intake: >0–7, >7–12.6, >12.6–21.4, >21.4), and unprocessed poultry (0 intake, quartiles of intake: >0–4.8, >4.8–10.4, >10.4–32.5, >32.5). Also, for model 3 in unprocessed red meat, processed meat was adjusted for (0 intake and quartiles of intake) and vice versa. Models in these analyses are correspondents to models 1, 2, and 3, except energy-adjusted log-transformed continuous dietary variables were used instead of five-level adjustment (90th percentile for unprocessed red meat: 46.5 g/day; for processed meat: 11 g/day; and for combined intake of red and processed meats: 49.1 g/day). 5 Also adjusted for previous screening for colon, prostate, or breast cancers during the last four years.

(4) Adjusted model: Sex, pack-years of smoking, physical activity, educational status, BMI (in kg/m2), alcohol consumption, diabetes, fish consumption, and total energy, grain intake and soft drink and soda consumption

(5) Residual method: Age, total energy intake, education, marital status, vigorous exercise, television watching, smoking, and alcohol intake. health insurance status, visits to a physician. **Optional adjusting for BMI**

**(6)** Age, sex, year of entering the cohort, years of university education, BMI, smoking, alcohol, physical activity, hours per day watching television, history of hypercholesterolemia, hypertension, and/or depression, CV disease, cancer, and/or diabetes, following special diets at baseline, snacking between meals, and total energy intake (continuous). **age examined as interaction term.**

**(7)** age, gender, place of residence, marital status, educational level, ethnicity, cigarette smoking, opium use, BMI, systolic blood pressure, family history of cancer, occupational physical activity, medication, wealth score, alcohol consumption, and total energy intake, **further adjustments for fruit and vegetable or total grain intake, low-fat dairy foods. Interaction terms: gender, age, BMI, smoking, or wealth score, and dietary protein sources**

**(8)** Baseline age (<40, 40–49, 50–59, 60–69, 70–79, and ≥80 y), educational level (less than secondary, secondary, and more than secondary school graduate), alcohol intake (continuous), urban or rural residence, total energy intake (continuous), fruit and vegetable intake (continuous), BMI (in kg/m2; <18.5, 18.5–19.9, 20.0–24.9, 25.0–29.9, and ≥30.0), and tobacco smoking (never smoked, former smoker, current with <20 pack-years of smoking, and current with ≥20 pack-years of smoking) were adjusted for as potential confounding factors in the multivariate analyses. **Interaction with BMI, baseline period, smoking status**

**(9)** age, BMI, sedentary lifestyle, education, current smoking, intake of alcohol, total energy

(10) age, BMI, sedentary lifestyle, education, current smoking, intake of alcohol, total energy, red meat (>median), fatty fish (>median), fat (>median), berries (>median), Boiled coffee (>median), Blood dishes (>median), Liver/kidney (>median), vegetables (<median), bread (<median), fibre (<median)

(11) intakes of total energy, whole grains, fruits, and vegetables (all in quintiles), age; body mass index (calculated as weight in kilograms divided by height in meters squared) (<23.0, 23.0-24.9, 25.0-29.9, 30.0-34.9, or ≥35.0); race (white or nonwhite); smoking status (never, past, or current [1-14, 15-24, or ≥25 cigarettes per day]); alcohol intake (0, 0.1-4.9, 5.0-14.9, or ≥15.0 g/d in women; 0, 0.1-4.9, 5.0-29.9, or ≥30.0 g/d in men); physical activity level (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥27.0 hours of metabolic equivalent tasks per week); multivitamin use (yes or no); aspirin use (yes or no); family history of diabetes mellitus, myocardial infarction, or cancer; and baseline history of diabetes mellitus, hypertension, or hypercholesterolemia. In women, we also adjusted for postmenopausal status and menopausal hormone use. We further adjusted for intakes of other major dietary variables (fish, poultry, nuts, legumes, and dairy products, all in quintiles) or several nutrients or dietary components (glycemic load, cereal fiber, magnesium, and polyunsaturated and trans fatty acids, all in quintiles) instead of foods

**(12)** In model 1, age, sex and total energy intake (model 1).

**(13)** In model 2, additional adjustment was made for physical activity (inactive, moderately inactive, moderately active and active), education level (low, intermediate and high), hypertension at baseline (yes/no), smoking habit (non-smoker, former smoker and current smoker) and BMI.

**(14)** In model 3, further adjustment was made for energy-adjusted intakes of fruit (continuous), vegetables (continuous) and alcohol (six categories).

**(15)** Fully adjusted model: age, sex, total energy intake, smoking habit, BMI, physical activity, education level, hypertension at baseline, intakes of alcohol, energy-adjusted intakes of fruit and vegetables.

(16) stratified by age (one-year age groups), sex, study center, adjusted for education (five categories), body weight (continuous), body height (continuous), total energy intake (continuous), alcohol consumption (continuous), physical activity (four categories), smoking status (seven categories), smoking duration (six categories), meat intake mutually adjusted for each other. Additionally adjusting for fruit and vegetables. **Interaction examined sex and smoking status (never, former, current), alcohol consumption (dichotomized by sex-specific median), and fruit and vegetable consumption (dichotomized by sexspecific median).**

**(17)** These included age at baseline (continuous), total caloric intake (continuous), smoking history (pack-years of smoking for men and ever/never smoking for women), income (four categories), occupation (three categories), education (four categories), comorbidity index (three categories based on the number of existing chronic diseases [18]), physical activity (categories based on MET-hours per day), total vegetable intake (quintiles), total fruit intake (quintiles), and regular alcohol consumption for men (three categories), fish intake, red meat or poultry intake where appropriate.

**All component model or unadjusted model** Total Causal Effect

(1) Unadjusted model: Smoking, alcohol consumption, physical activity, marital status, regular use of nutritional supplements, with optional further adjustment for BMI

(2) Model used: Age, gender, smoking, exercise, alcohol, dietary group (vegetarian/nonvegetarian), BMI, education

(3) Adjusted for sex and age (in 10 categories)

(4) Age, sex, smoking, exercise, BMI, hypertension, consumption of bread, nuts, fish, cheese, coffee, legumes, and fruit

(5) age (continuous), race (non-Hispanic white, non-Hispanic black, Mexican-American, other), sex, cigarette smoking (never, former, current (1–19 cigarettes/day; 20–39 cigarettes/day; 40+ cigarettes/day); missing), alcohol consumption (none, 1–4, 5–29, 30+ times/month), physical activity (none, 0 to <2 to <4 to <6, >6 times/week), socioeconomic status (poor, near poor, middle income, higher income; based on the poverty income ratio), body mass index (BMI) (continuous; calculated as weight in kilograms divided by height in meters squared), marital status (married/living together; never married/widowed; divorced/separated; missing), fruit and vegetables intake (quartiles of intake), history of hypertension, diabetes, hypercholesterolemia, use of aspirin and ibuprofen, use of mineral and vitamin supplements and family history of diabetes or hypercholesterolemia. In women, we also adjusted for hormone replacement therapy and oral contraceptive use. Interaction with sex considered.

(6) age, race, sex, poverty status, and education, body mass index (BMI) and current self-reported smoking status.

(7) Age

(8) gender, smoking, age group, alcohol, social class, fruit, vegetables, puddings, meat, fresh or frozen green vegetables or salad, fresh or frozen red meat, fresh fruit or fruit juice, puddings, cakes, biscuits, sweets.

(9) sex, smoking status, age, body mass index, alcohol use, education level, and exercise level. Men and women were categorized into thirds of the distribution of body mass index of all men and all women, respectively. Alcohol users were categorized as regular drinkers or nonregular drinkers, definitions varied between studies, but the guideline was that regular drinkers consumed ≥1 alcoholic drink/wk. Education was classified as high—equivalent to the completion of American high school or above—or low; in the Oxford Vegetarian Study only data on social class were available and social classes I and II (8) were considered to be equivalent to high education. Exercise was classified as high or low on the basis of criteria used to define the level of activity in each study, with the guideline of producing 2 approximately equal-sized groups in each study.

**The multivariable nutrient density model**average relative causal effect rescaled as a proportion of total energy.

(1) sex, age at entry to study, marital status, ethnicity, education, fifths of a composite deprivation index as an indicator of socioeconomic status, perceived health at baseline, self-reported history of heart disease, stroke, diabetes, and cancer at baseline, cigarette smoking, body mass index, vigorous physical activity, usual activity throughout the day, alcohol consumption, fruit and vegetable intakes (both pyramid servings per day), and total energy intake. vitamin supplement use, family history of cancer (for cancer mortality), and the use of hormone replacement therapy (for women).

(2) age, total energy, saturated fat, polyunsaturated fat, monounsaturated fat, and trans-fat (expressed as percentage of energy and categorized into quintiles), carbohydrates, total fiber, dietary cholesterol, dietary methionine (all quintiles are based on energy-adjusted values), alcohol (≤14 g/day vs. >14 g/day), smoking (never, former, current), activity level (active vs. not active), body mass index (<21.0, 21.0–22.9, 23.0–24.9, 25.0–28.9, ≥29.0), history of hypertension, postmenopausal hormone use, multivitamin use, vitamin E supplement use, education (high school education or less vs. post-high school), and family history of cancer.