**Article 1: Red and Processed Meat and Mortality in a Low Meat Intake Population**

Author: **Saeed Mastour Alshahrani**

**Study cohort size:** 96000+ (Adventist Health Study-2), after exclusion 72149.

**Exclusion criteria:** (1) missing dietary variables (2) bad or inadequate data (3) missing more than 69 responses in dietary section (4) Canadian resident (5) extreme values of total energy (6) missing age, sex, or race (7) age younger than 25 years at baseline (8) 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.

**Definition of unprocessed red meat:** 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)”.

**Definition of processed meat:** 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)”).

**Assessment of exposure:** The frequency of intake ranged from “never or rarely” to “2+ per day”, and serving sizes consisted of three levels (a half serving, standard serving (3–4 oz.), and one-and-a-half servings). The assigned weights for frequency and serving size in the FFQ used in AHS-2 have been previously described [12]. **The intake in grams per day was calculated using the product-sum method** [[12](https://www.mdpi.com/2072-6643/11/3/622/htm#B12-nutrients-11-00622),[13](https://www.mdpi.com/2072-6643/11/3/622/htm#B13-nutrients-11-00622)].

**Assessment of mortality:** Mortality outcome data were obtained from the National Death Index and were available through December 2015. International Statistical Classification of Diseases, 10th Revision (ICD-10) codes were used to determine the underlying cause of death. Individuals who died due to unnatural causes such as motor vehicle accidents and homicides (ICD-10 letters U, V, W, X, and Y) were censored at their time of death (i.e., they were not considered as cases in the analysis of all-cause mortality). ICD-10 codes for CVD mortality ranged from I00 to I78; cancer mortality ranged from C00 to C97.

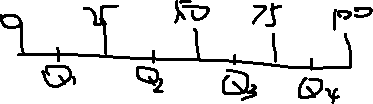
**Variables considered:**

Age, Sex, Race, Marital status, educational level, Multivitamin use, Smoking status, alcohol use, exercise, sleep, current HRT users, Diabetes, Hypertension, Hypercholesterolemia, aspirin use, BMI, Total energy intake, statin use, blood pressure medications, menopausal status (premenopausal, postmenopausal), and hormone therapy, previous screening for colon, prostate, or breast cancers during the last four years, Cruciferous vegetables, fruits, whole grain, legumes, nuts and seeds, total dairy, eggs, unprocessed poultry, processed meat, fish

**Adjusting variables:**

age (attained age as time variable), sex, race, and total energy intake, marital status, educational level, multivitamin use, smoking status, alcohol use, exercise, sleep, body mass index, aspirin use, 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), Cruciferous vegetables, fruits, whole grain, nuts and seeds, total dairy, menopausal status (premenopausal, postmenopausal), and hormone therapy (in postmenopausal women) , fish, and unprocessed poultry. Also, for model 3 in unprocessed red meat, processed meat was adjusted for (0 intake and quartiles of intake) and vice versa, previous screening for colon, prostate, or breast cancers during the last four years.

**Analytical model: Time-dependent Cox-proportional hazards regression with attained age as the time variable and left truncation by age at study entry, controlling for potential confounding covariates, was used to assess the association between the consumption of red and processed meat and all-cause**, CVD, and cancer mortality. We used **multiple imputation**, guided where possible, for missing data [14,15], in which the estimates were calculated from five imputed datasets, and then Rubin’s formula was applied to obtain the average estimates and corrected standard errors. We analyzed intakes of **unprocessed red and processed meats as continuous (log-transformed) variables measured in grams per day (g/day) comparing the 90th percentile of intake with zero-intake.** To assess for possible common associations of unprocessed red and processed meats (which were highly correlated; R = 0.56), **we combined both variables by summing the daily intakes from unprocessed red meat and processed meat together to create one single variable.** **Regression calibration** of the exposures was used, where reported, to minimize the possible bias in the association estimates due to measurement error. Only exposures of interest (red and processed meat) were calibrated, not all dietary covariates. (In this procedure, a shortened version of the main questionnaire (limited to the dietary/FFQ portion), was administered to a 1000-subject (equal allocation for Whites and Blacks) subsample of the AHS-2 cohort. The subsample was approximately representative of the AHS-2 cohort in terms of gender, age, education, and vegetarian status [19]. Six 24-h dietary recalls were also collected from the subsample. From this data, a linear model was produced, regressing the intakes of red and processed meats from dietary recalls on the corresponding intakes from the food frequency questionnaire, controlling for the respective covariates present in each analytic model. The coefficients of the exposures of interest (red and processed meats) from the linear model were used to predict calibrated intake values from the intake values obtained from the FFQ of the original cohort. That is, predicted 24-h recall intake values produced by a linear model regressing intake values from the 24-h recalls against those from the FFQ, adjusted for the analytic covariates, are used in the analytic models to produce calibrated effect estimates. These calibrated intake variables were then used in the analytic models to produce calibrated hazard ratios.) **A 4000-round bootstrap was used to produce bias-corrected and accelerated (BCa) confidence intervals for these hazard ratios.** We also conducted analyses using five categories of intake (i.e., a zero-intake group plus quartiles of consumers). Linear trends across the categories were tested by assigning the medians of intake in each quartile to all participants in that quartile and analyzing them as continuous variables. Also, we assessed the linearity of the relationship between the exposures and mortality outcomes using 4-knot restricted cubic spline regression. Dietary exposures and covariates were energy-adjusted using the residual method [20]. **We tested for interaction of the exposures of interest with age, sex, and race.** Other covariates were also tested for possible interactions with the exposures, and for possible interactions with each other where suspected. **We separately conducted subgroup analyses by sex and race**, in which we used sex- and race-specific ranges and values of intakes for the exposures. Further, we conducted separate analyses on those who reported they never smoked in order to address the effect of residual confounding by smoking in the original models. **The proportional hazards assumption of the model was assessed using log(−log) plots, Schoenfeld residuals, and attained-age interaction terms; there was no violation.** We also calculated population attributable risk comparing the 90th percentile of the combined intake of red and processed meat (~49 g/day) with zero-intake (assuming causality) [21].



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

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).

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.

**Article 2: Mortality in vegetarians and comparable nonvegetarians in the United Kingdom**

**Author: Paul N Appleby**

**Study cohort size:** 60,310 persons pooled mortality data from 2 prospective studies in the United Kingdom, the Oxford Vegetarian Study (OVS) (10) and the EPIC-Oxford cohort

**Definition of meat eaters:** meat eaters (participants who ate meat, irrespective of whether they ate fish, dairy products, or eggs), fish eaters (participants who did not eat meat but did eat fish), vegetarians (participants who did not eat meat or fish, but did eat either or both dairy products and eggs), and vegans (participants who did not eat meat, fish, eggs, or dairy products). **creating 4 diet groups: regular meat eaters (who reported eating meat ≥5 times/wk on average), low meat eaters (who ate meat but did so <5 times/wk), fish eaters, and vegetarians and vegans.**

**Definition of mortality:** The 18 common underlying causes of death for which HRs were calculated were as follows: **malignant cancer** [International Classification of Diseases (ICD)-10 codes C00–97 and equivalent ICD-9 codes], including **colorectal cancer** (ICD-10 C18–20**), pancreatic cancer** (C25), **lung cancer** (C34), **female breast cancer (**C50), **ovarian cancer** (C56), and **cancers of the lymphatic/hematopoietic tissue** (C81–96); **mental and behavioral disorders** (F00–99); **diseases of the nervous system** (G00–99); **circulatory disease** (I00–99), including **ischemic heart disease** (IHD) (I20–25), **cerebrovascular disease** (I60–69), and **other circulatory disease** (I00–15, I26–52, and I70–99); **diseases of the respiratory system** (J00–99); **diseases of the digestive system** (K00–93); **injury, poisoning and external causes** (S00–T98 and V01–Y98); **all other causes** (ICD-10 codes beginning with A, B, D, E, H, and L–R); and **all causes combined**.

**Exclusion criteria:** Participants were excluded from the analysis if they were aged <20 or >89 y at recruitment, or had a previous (registered or self-reported) malignant neoplasm before recruitment; a previous self-reported stroke, heart attack, or angina; uncertain follow-up; or had no information for ≥1 of the factors age, sex, smoking, and diet group at recruitment. EPIC-Oxford participants who did not complete the main questionnaire were also excluded because data on several important factors were thereby unavailable.

**Variable considered:**

Age, Smoking, alcohol consumption, physical activity, marital status, regular use of nutritional supplements, diabetes, blood pressure, receiving long term medical treatment, BMI, Energy, protein, animal protein, plant protein, carbohydrates, total fat, saturated fat, dietary fibers, total meat, red meat, poultry meat, total processed meat, total fish, oily fish, fresh fruit, fresh vegetables

**Adjusting variables:**

Smoking, alcohol consumption, physical activity, marital status, regular use of nutritional supplements, with optional further adjustment for BMI.

**Analytical model: In the main analysis of mortality before age 90 y**,HRs (95% CIs) for 18 common causes of death, including all causes combined, were calculated by **Cox proportional hazards regression with age as the underlying time variable**, with the use of a clustered sandwich variance estimator to allow for intraparticipant correlation among individuals contributing person-years to >1 of the 5 possible phases of follow-up, including OVS recruitment to the earlier of EPIC-Oxford recruitment (if applicable) or death/censoring, EPIC-Oxford recruitment to the earliest of FU1/FU2/FU3 completion (if applicable) or death/censoring, FU1 completion (if applicable) to the earliest of FU2/FU3 completion (if applicable) or death/censoring, FU2 completion (if applicable) to the earlier of FU3 completion (if applicable) or death/censoring, and FU3 completion (if applicable) to death/censoring. For the small number of participants whose diet group was unknown at FU1, FU2, or FU3 completion (∼30 participants at each stage), diet group was deemed to be the same as at EPIC-Oxford recruitment or at the most-recently completed follow-up questionnaire, as appropriate. For the 6 most common causes of death (malignant cancer, circulatory disease, IHD, cerebrovascular disease, diseases of the respiratory system, and all causes combined), **subgroup analyses** were also conducted for men; women; participants with BMI <20 (underweight), BMI 20–24.9 (normal weight), and BMI ≥25 (overweight); never smokers, former smokers and current smokers; **We also conducted the mortality analyses for all 18 causes of death after excluding participants known to have changed diet group at least once during follow-up**. **We also examined mortality before age 75 y.**

**Article 3: High red meat intake and all-cause cardiovascular and cancer mortality: is the risk modified by fruit and vegetable intake?**

**Author:** Andrea Bellavia

**Study cohort size:** 74,645 participants from the Cohort of Swedish Men (COSM) (NCT01127711) and the Swedish Mammography Cohort (SMC)

**Exclusion criteria:** we excluded participants who reported an incorrect national personal identification number or who did not report their personal number (n = 540), those who died before the start of follow-up (n = 97), and those with any history of CVD (n = 6994) or cancer (n = 4390). We further excluded participants with an unlikely extreme value of total energy intake (3 SDs from the log-transformed mean energy intake; n = 709) and those with unlikely high daily red meat consumption (>300 g/d; n = 305) or missing information on red meat consumption (n = 397).

**Definition of Nonprocessed red meat**: fresh and minced pork, beef, and veal. The total intake of red meat, **assessed in g/d,** **was calculated by combining information on the amount and frequency of the consumption of different types of red meat.**

**Definition of Processed red meat:** sausages, hot dogs, salami, ham, processed meat cuts, liver pate, and blood sausage. All reported information was combined to derive continuous variables of total, processed, and nonprocessed meat intake.

**Definition of fruit and vegetables:** Information on daily FV intake was obtained with the use of 14 questions on vegetable consumption (carrots, beetroots, lettuce, cabbage, cauliflower, broccoli, tomatoes, peppers, spinach, green peas, onion, garlic, pea soup, other vegetables), 5 on fruit (oranges, apples, bananas, berries, other fruits), and 1 on orange juice. Total FV consumption was summarized into a single variable, expressed as servings/d, that was obtained by converting the questionnaire responses to a mean daily intake of each item and adding the intake of all items together. To assess the association between red meat consumption and mortality across levels of FV consumption, **the main variable of FV consumption was categorized into 3 predefined levels (low FV intake: <2 servings/d; medium FV intake: 2–4 servings/d; and high FV intake: >4 servings/d).**

**Definition of mortality:** deaths

**Variables considered:**

Sex, age, bmi, total physical activity, smoking status, alcohol consumption, education, diabetes, fruit and vegetable consumption, fish consumption, energy intake

**Adjusting variables:**

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

**Analytical model: Total, processed, and nonprocessed red meat intakes were then categorized into quintiles and investigated as categorical covariates.** **Cox proportional hazard regression with attained age at the event as the primary time scale was used** to assess the association between red meat and FV consumption and the risk of total, CVD, and cancer-specific mortality. **The assumption of proportionality of the hazards was tested by calculating Schoenfeld residuals, regressed against survival time, and tested for a nonzero slope**. No evidence of departure from this assumption was observed in all the reported models. **The lowest quintile of either total, processed, and nonprocessed meat was used as reference category.** **We first assessed the association between quintiles of total red meat consumption and overall mortality, estimating HRs of death in the overall population and across amounts of FV consumption.** **The statistical interaction between red meat and FVs was assessed by testing the product terms of the categorical indicators jointly equal to 0. We next replicated the main analysis over levels of fruit consumption and vegetable consumption, investigated as 2 independent covariates.** Both fruit and vegetable consumption were categorized into 3 predefined groups to reflect low, medium, and high intakes. We also evaluated processed and nonprocessed red meat consumption as 2 distinct exposures in a mutually adjusted model. HRs of death were estimated in the overall population and across levels of FV consumption, testing for the presence of an interaction between processed and nonprocessed meat and FVs in predicting mortality.

**Article 4: Higher Diet Quality Is Inversely Associated with Mortality in African-American Women**

**Author:** Deborah A Boggs

**Study cohort size:** 59,000 women Black Women's Health Study (BWHS). After exclusion, 37001 women.

**Exclusion criteria:** The present analysis excluded women who at baseline were <30 y of age (n = 12,812); had a history of cancer (except nonmelanoma skin cancer) (n = 1488), myocardial infarction (n = 620), stroke (n = 439), or diabetes (n = 2378); left >10 items blank on the FFQ (n = 1510); had implausible energy intake values (<400 or >3800 kcal) (n = 1783); were pregnant at baseline (n = 482) or were missing height or weight (n = 442); or had an implausible BMI (<15 or ≥60 kg/m2) (n = 46).

**Definition of Dietary Approaches to Stop Hypertension (DASH) scores:** We evaluated a DASH score created by Fung et al. (14) that ranks participants based on intake of 8 food and nutrient components. Participants were categorized into quintiles for each component. For fruits (including fruit juice), vegetables, nuts and legumes, whole grains, and low-fat dairy, the lowest quintile was assigned 1 point and the highest quintile was assigned 5 points. For sodium, red and processed meats, and sugar-sweetened beverages, scores were reversed such that the lowest quintile was assigned 5 points and the highest quintile was assigned 1 point. DASH scores can range from 8 to 40; in the present study the scores ranged from 8 to 38. We categorized the scores into quintiles (quintiles 1 and 5 represent low and high adherence, respectively).

**Definition of Prudent and Western dietary patterns:** Prudent and Western dietary patterns were derived with the use of factor analysis of 35 individual foods or food groups, as described previously (15). Factor scores for each pattern were calculated by summing intakes of each food group weighted by that food group's factor loading. The prudent dietary pattern is characterized by high intake of vegetables and fruits, whereas the Western dietary pattern is characterized by high intake of red and processed meat and fried foods. Quintiles 1 and 5 represent low and high adherence, respectively, to each dietary pattern.

**Definition of death:** Deaths through 31 December 2011 were identified through linkage with the National Death Index for all participants who had not completed the 2011 questionnaire. **The International Classification of Diseases, Tenth Revision, was used to classify underlying cause of death as death from cardiovascular disease (I00–I99), cancer (C00–C97), or all other causes [excluding “external” causes of death, S00–Y98 (e.g., accidents and homicides)].**

**Variables considered:** age, BMI, education, marital status, exercise, television watching, smoking, alcohol use, total energy intake

**Adjusting variables:** 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**

**Analytical model:** **Cox proportional hazards models were used** to estimate HRs and 95% CIs for the association between diet quality and mortality. Participants contributed to the analysis from 1995 until death, loss to follow-up, or the end of follow-up in 2011, whichever occurred first. Time-varying covariates were updated with the use of the Andersen-Gill data structure (26); this structure creates a new record for each follow-up cycle in which a participant is at risk, and assigns the covariate value for that cycle. **missing data for covariates were modeled as indicator variables**. **The primary analyses did not adjust for BMI, which is considered to be an intermediate between dietary pattern and illness/death.** We conducted **subgroup analyses** within strata of BMI, age, smoking, vigorous exercise, and years of education. **Tests for interaction** were performed by using the likelihood ratio test comparing models with and without crossproduct terms between the variable of interest (e.g., **BMI) and the diet quality score.**

**Article 5: Lifestyle Determinants and Mortality in German Vegetarians and Health-Conscious Persons: Results of a 21-Year Follow-up**

**Author:** Jenny Chang-Claude

**Study cohort size:** 1,904 German vegetarian study

**Definition of meat eaters:** The study participants were classified **into vegetarian** (vegan (those who avoid meat, fish, eggs, and dairy products), lacto-ovo vegetarian (those who avoid meat and fish but eat eggs and/or dairy products)), **and nonvegetarian** (those who occasionally or regularly eat meat and/or fish). **Or, Meat consumption (Never ≤Once a month ,>Once a month,≥3 times/wk), meat product consumption (Never ≤Once a month ,>Once a month), fish consumption (Never ≤Once a month ,>Once a month).**

**Definition of death:** The underlying cause of death was coded by a trained nosologist according to the ninth revision of the International Classification of Diseases and Causes of Death. All causes: ICD-9 001-999

**Variables considered:**

Gender, age group, education, bmi, exercise, smoking, alcohol consumption,

**Adjusting variables:**

Age, gender, smoking, exercise, alcohol, dietary group (vegetarian/nonvegetarian), BMI, education

**Analytical models:** **Standardized mortality ratios (SMR)** were calculated by comparison of observed deaths with those expected based on the age- and sex-specific mortality rates of Germany between 1975 and 1999. Within the total cohort, **Poisson regression was used to investigate possible determinants of mortality by comparing death rates among study participants for various factors simultaneously including vegetarian status, age, sex, education, and BMI.** The highest educational level of the parents was used for subjects under the age of 20 years who had not yet finished schooling. Multiplicative models were fitted to appropriately cross-classified data using PROC GENMOD (SAS System version 8.0). The person-years at risk were used as offset. Maximum likelihood estimates of rate ratios (RR) for exposure variables and 95% confidence intervals (95% CI) based on exact Poisson probabilities were calculated.

**Article 6: Should we recommend reductions in saturated fat intake or in red/processed meat consumption? The Sun prospective cohort study**

**Author**: Ligia J.Dominguez

**Study cohort size: 22,476 participants initially**, after exclusion, **18,540 participants of the SUN (Seguimiento Universidad de Navarra)**

**Exclusion criteria:** We recruited participants who had spent enough time in the study as to be able to complete and return at least the 2-year follow-up questionnaire (>2 years and additional 9 months to account for the lag time in returning the questionnaires) and we excluded 798 participants for this reason. Participants were also excluded from the analyses if they reported total energy intake out of pre-defined limits (800–6000 kcal/d for men and 500–5500 kcal/d for women) or if they left 20 or more items in blank from the FFQ (n = 1512) [35] or they were lost to follow up (n = 1626).

**Definition of meat:** In the semi-quantitative FFQ we explicitly included serving sizes (in grams) according to the typical **serving size** of each food in the Spanish population, corresponding to **125 g of red meat, 125 g of white meat, 50 g of processed meat, and 100 g of total meat.** **The meat variables included consumption of white meat (chicken, turkey, and rabbit), red meat (veal, pork, lamb, liver, viscera (offal), hamburger), and processed meat (dry cured ham [Serrano ham type], cooked ham [York ham type], sausages [salami, mortadella, blood sausage, spicy pork sausage, würstel], bacon, pancetta, paté), as well as total meat considering together all types of meat.** **They treat baseline categories of meat consumption (less than 3 servings per week as reference category, 3–6 servings per week, 7 servings per week [once a day], and more than 7 servings per week) as categorical variable and also treat it as continuous variable examine one additional serving for HR. They considered red meat, total meat, processed meat, and red + processed meat consumption.**

**Definition of death:**

We also checked the National Death Index every six months to confirm the vital status of our participants and to request and complete the data regarding mortality, including the cause of death in our cohort.

**Variables considered:**

Gender, martial status, age, education, BMI, Alcohol, activity, television watching, history of depression, hypertension, hypercholesterolemia, history of cardiovascular disease, history of cancer, history of diabetes, total energy intake, adoption of special diet, between meal snacking, vegetables, fruits, legumes, cereals, whole bread, nuts, olive oil, eggs, fish and other seafood, whole dairy product, low-fat dairy product, coffee, carbohydrates, protein, total fat, MUFAs, SFAs, PUFAs (% of total energy), Vitamin C, Vitamin D, Iron from haem sources, Folate, Dietary fiber

**Adjusting variables:**

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.**

**Analytical model:**

**We calculated HR and 95% CI by means of Cox proportional hazards models using the lowest category of consumption as the reference category (less than 3 servings per week).** **Age was the underlying time variable, and different degrees of adjustment were used: 1) adjusted for sex and age (in 10 categories); 2) additional adjustments for year of entering the cohort (4 categories), BMI (continuous), years of university education (continuous), alcohol use (in 5 categories), smoking (in 3 categories), physical activity (MET-h/week) (continuous), hours per day spent watching television (continuous), 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). We also performed all the analyses using as exposure a 1-serving per day increment (as a continuous variable) in the different types of meat consumption**. Trend tests were calculated using meat consumption as a continuous variable. Multivariable-adjusted estimates for restricted cubic splines were used to calculate dose–response association between SFA intake or red meat consumption and total mortality. **We assessed interactions with age using likelihood ratio tests in fully adjusted Cox models. We introduced a product-term with both age and meat servings/d (or SFA intake) as continuous variable in this term.** We also performed multivariable analyses to examine the HRs for mortality when we did isocaloric replacements of MUFA, PUFA, and carbohydrates by SFA, and replaced 100 g of fish, potatoes, poultry, eggs, vegetables, fruits and nuts, and cereals by 100 g of red meat. These variables were incorporated in the same fully-adjusted model as continuous variables, and the differences in their beta-coefficients, variances and covariance were used to calculate the beta-coefficient ± SE for the substitution effect. Subsequently, we used these parameters to estimate the HRs and 95% CIs. **We performed diverse sensitivity analyses by estimating the fully adjusted HR for a 1-serving increment in red meat consumption and total meat consumption after changing several assumptions: 1) including only men or women; 2) considering different allowed limits for total energy intake; 3) adopting allowed limits for total energy intake from percentile 1 to 99; 4) excluding participants with history of diabetes at baseline; 5) Excluding prevalent cancer, CVD, and diabetes; 6) excluding participants with diagnosis of hypertension and hypercholesterolemia at baseline; 7) censoring the follow-up time of participants at 6 or 8 years; 8) excluding early deaths (within the first 2 years of follow-up); 89) adjusting for the Mediterranean diet score calculated as proposed by Trichopoulou et al. [45], excluding meat and alcohol to avoid redundancy (maximum score = 7 points); 10) including only deaths occurring at 60 years of age and over; 11) including only cancer deaths; 12) including only CV deaths.**

**Article 7: Mortality from different causes associated with meat, heme iron, nitrates, and nitrites in the NIH-AARP Diet and Health Study: population-based cohort study**

**Author: Arash Etemadi**

**Study cohort:** 617 119 originally, after exclusion, **536 969 AARP** members aged 50-71 at baseline

**Exclusion criteria:** We excluded people who moved out of the study areas before returning the baseline questionnaire, requested to be withdrawn, died before study entry, indicated that they were not the intended respondent, did not answer substantial portions of the questionnaire, or had more than 10 recording errors; people whose questionnaire was filled in by someone else on their behalf; those reporting extreme daily total energy intake; people with a prevalent cancer before the study entry; and those who had zero person years of follow-up.

**Definition of meat:** Items included in the red meat intake were unprocessed red meat (beef and pork, hamburger, liver, steak, and meats in foods such as chili, lasagna, and stew) and processed red meat (bacon, beef cold cuts, ham, hotdogs, and sausage). White meat included unprocessed chicken, turkey, and fish, canned tuna, and processed white meat (poultry cold cuts, low fat sausages, and low fat hotdogs made from poultry**). We divided all nutritional variables by the daily calorie intake (the nutritional density method) and categorized the calorie adjusted values into fifths for the entire cohort. Calculate g/1000kcal.**

**Definition of death:** Cancer mortality included ICD-10 (international classification of diseases, 10th revision) codes C00-C44, C45.0, C45.1, C45.7, C45.9, C48-C97, and D12-D48. Cardiovascular disease mortality was subdivided into diseases of the heart (ICD-10 codes I00-I09, I10-I13, I20-I51, and I70-I78), and stroke or cerebrovascular diseases (ICD-10 codes I60-I69). We also studied death from respiratory disease (ICD-10 codes J10-J18 and J40-J47), diabetes mellitus (ICD-10 codes E10-E14), infections (ICD-10 codes A00-B99), Alzheimer’s disease (ICD-10 code G30), kidney disease (ICD-10 codes N00-N07, N17-N19, N25-N27), chronic liver disease (ICD-10 codes K70, K73-K74), and all other causes.

**Variables considered:**

Total death (cancer, heat disease, respiratory disease, stroke, diabetes, infections, alzheimer’s disease, chronic kidney disease, chronic liver disease, other causes), gender, age, previous cancer, heart diease, stoke, diabetes, health status, race, smoking, socioeconomic status, education, physical activity, body mass index, alcohol intake, vegetable intake, fruit intake, heme iron intake, nitrate intake, nitrite intake.

**Adjusting variables:**

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).

**Analytical models:** **We estimated hazard ratios and 95% confidence intervals with time since entry into the study as the underlying time metric, by using Cox proportional hazards regression models with the lowest fifth of the calorie adjusted intakes as the reference categories,** after checking the violation of the proportional hazard assumption. **As the differences between the lowest and the highest fifths were different among various types of meat, we also analyzed the effects of a fixed intake increase (20 g/1000 kcal/day) on the outcomes.** As our main hypothesis was to test the change in mortality risk by substituting different meat products without changing the overall meat intake, the main model was a “**substitution model**.” **This model was adjusted for total meat intake, so that increases in the meat variable of interest reflected reductions in other meat types and the total meat intake remained constant.** **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); increase in any individual meat variable resulted in an increase in the person’s total meat intake.** In all the models, we used median values of each fifth to test for linear trends. We also stratified the population by important potential effect modifiers and tested the interaction between these variables and the main variables of exposure. **We did several sensitivity analyses: excluding people who reported a previous diagnosis of heart problem, stroke, diabetes, or cancer at baseline; stratifying by the duration of follow-up; including the 2010 Healthy Eating Index as an independent variable in the model (to adjust for the potentially confounding effect of the overall healthiness of the diet) 21; and using the residual method for calorie adjustment instead of the nutritional density.** We also did a **calibration analysis** to correct the estimates of daily red meat intake in the entire cohort for measurement error, using data from a subset of participants with two non-consecutive 24 hour dietary recalls (n=1877).

**Article 8: Dietary Protein Sources and All-Cause and Cause-Specific Mortality: The Golestan Cohort Study in Iran**

**Author: Maryam S. Farvid PhD**

**Study cohort: 49,112 initially**, after exclusion, **42,403** Golestan Cohort Study in Iran.

**Exclusion criteria:** Participants were excluded owing to loss of follow up ( n =63); extreme total energy intake (<600 or >4,200 kcal/day, n =436); or prior diagnosis of chronic disease, including cancer, diabetes, CHD, or stroke ( n =6,210)

**Definition of meat:** Total red meat items listed on the food frequency questionnaire included unprocessed (beef or lamb, hamburger) and processed (sausage) red meat; poultry included chicken; fish included tuna, stellate sturgeon, carp, smoked fish, salted fish, and other fish; and legumes included soybeans, beans, lentils, peas, and split peas. Participants were asked about the frequency of food item consumption per day, week, month, or year. The standard serving sizes for these food items were 85 g for cooked beef, lamb, hamburger, chicken, and fish; 45 g for sausage; 100 g for cooked beans, lentils, peas, split peas, and soybeans; and 54 g for eggs. **Participants were divided into quintiles according to food group intake. serving/day calculated**

**Definition of death:** All collected documents were reviewed, and the cause of death was coded according to the ICD-10. In this analysis, deaths were classified as due to CVD (ICD-I00–I99); CHD (ICD-I20–I52); stroke (ICD-I60–I69); cancer (ICD-C00–D48); gastrointestinal cancers (ICD-C15–26); and other cancers (ICD-C00–14, ICD-C30–97, and ICD-D00–48).

**Variables considered:**

Age, BMI, gender, ethnicity, martial status, current smokers, opium use, place of residence (rural), physical activity, total red meat intake, poultry intake, fish intake, egg intake, legume intake, total dairy food intake, total grain intake, total fruit intake, total vegetable intake, total energy intake.

**Adjusting variables:**

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**

**Analytical model:** **Cox proportional hazards regression was used to estimate age-adjusted and multivariate-adjusted hazard ratios (HRs) and 95% CIs for all-cause and disease-specific mortality in relation to total red meat, poultry, fish, egg, and legume consumption. Missing covariate data, which included five participants for BMI and eight participants for systolic blood pressure, were replaced with median values.** The effect of substituting one serving/day of poultry, fish, legumes, or eggs for one serving/day of total red meat was estimated by including these food items simultaneously as continuous variables in the multivariate-adjusted model. The HRs and 95% CIs for the **substitution effect** were estimated from the difference between the regression coefficients, variances, and covariance. **In sensitivity analyses, participants who died as a result of external events (i.e., accidents, intoxication, suicide, or other types of injury; n =217) were excluded. Further, the authors evaluated whether the association between protein-rich food intake and all-cause mortality risk was modified by gender, age, BMI, smoking, and wealth score.(interaction)**

**Article 9: Associations between diet and cancer, ischemic heart disease, and all-cause mortality in non-Hispanic white California Seventh-day Adventists**

**Author: Gary E Fraser**

**Study cohort:** 34192 California Seventh-day Adventists

**Definition of meat:** 3 categories of dietary habits were defined. These were vegetarian, those who ate no fish, poultry, or meat (29.5%); semivegetarian, those who ate fish and poultry, but <1 time/wk (21.2%); and nonvegetarian, referring to the remaining subjects (49.2%).

**Definition of death:** In addition, computerized matching with state death tapes and the National Death Index was used to identify fatal cases.

**Variables considered:**

Age, sex, beef, poultry, fish, vegetarian meat substitutes, soft margarine on bread, eggs, doughnuts, coffee, tomatoes, legumes, nuts, green salads, canned fruit, dried fruit, citrus fruit, winter fruit, other fruit, all fruit, whole-grain bread, beer or wine, hard liquor, bmi, diabetes, hypertension, rheumatoid arthritis, rheumatism, colon cancer, breast, lung, prostate, uterine

**Adjusting variables:**

Age, sex, smokig, exercise, BMI, hypertension, consumption of bread, nuts, fish, cheese, coffee, legumes, and fruit

**Analytical models: Not enough information on this paper**

**Odds ratios adjusted for age calculated for vegetarians, semi vegetarians, and nonvegetarians. Incidence and relative risk calculated between vegetarians and non-vegetarians. Regression?**

**Article 10: Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies**

**Author: Jung Eun Lee**

**Study cohort: 296,721** men and women, 8 Asian prospective cohort studies in Bangladesh, China, Japan, Korea, and Taiwan

**Exclusion criteria:** We excluded participants who did not provide food-frequency questionnaires (FFQs) (n = 8177) and those for whom time under study was missing (n = 467).

**Definition of meat:** The number of items for red meat, poultry, and fish varied from 6 to 17 across studies (see Supplemental Table 1 under “Supplemental data” in the online issue). **We quantified food-group intake in grams per day or servings per day using the reported frequency of intake of each relevant food item and study-specific portion sizes.** **g/day calculated.** **Because the number of food items varied across studies, in the main analysis, we obtained HRs and 95% CIs using study- and sex-specific quartiles of grams per day of each food group.**

**Variables considered:**

Age, educational, alcohol intake, urban or rural residence, total energy intake, fruit and vegetable intake, BMI, and tobacco smoking, socioeconomic status, baseline period

**Adjusting variables:**

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**

**Analytical models:** **Using individual-level data, we calculated study-specific HRs and 95% CIs using a Cox proportional hazards model; age was used as the time metric.** Outcomes of interest included all-cause mortality and cancer and CVD mortality. **For males and females separately, cohort-specific HRs were pooled to compute cross-cohort estimates by using a random-effects model.** The random-effects model also produced a trend test for pooled HR estimates. Tertiles rather than quartiles of poultry intake were used to ensure an adequate number of cases in each category. In supplemental analyses, we computed pooled cohort HRs from cohort-specific estimates computed by using uniform cutoffs rather than cohort-specific cutoffs to construct intake quartiles and tertiles. In other supplemental analyses, we included 2 additional cohort studies that offered nonquantitative dietary intake data: 1) the Korean Multi-Center Cancer Cohort Study (19) and 2) the Radiation Effects Research Foundation in Hiroshima and Nagasaki, the Life Span Study cohort (20), which had assessed diet by using nonquantitative FFQs (data on frequency of intake only). We tested for heterogeneity across studies using a likelihood ratio test that compared random- and fixed-effect models for pooled cohort effect estimates. **Because socioeconomic status may be related to meat intake and disease pattern in Asian populations and because meat intake varies over time, we also examined whether the associations varied by educational level**. **Also, we examined whether BMI, smoking status, or baseline period modified the associations.**

**Article 11: Meat consumption and diet quality and mortality in NHANES III**

**Author: R Kappeler**

**Study cohort: 17 611 participants** from Third National Health and Nutrition Examination Survey (NHANES III) (1986–2010)

**Exclusion critieria**: We excluded individuals who had a history of myocardial infarction, stroke, heart failure or cancer (n=2353). We further excluded individuals whose questionnaire had missing answers for meat consumption (n=86). After all exclusions, our analytic cohort consists of 8239 men and 9372 women.

**Definition of meat: Red meat intake was calculated using the frequency of consumption of all types of beef, pork, ham, liver and other organ meats**. White meat included chicken and turkey and processed meat included bacon, sausage and other processed meats. The category fish included only the item fish. ***times/week calculated with 5 groups.***

**Definition of mortality:** Based on the National Death Index, data underlying cause of death were used for case definition according to the ICD-9 through 1998, and the remainder according to ICD-10. Cardiovascular mortality was defined by any of the ICD-9 codes 390–434 and 436–459 and ICD-10 codes I00–I99. Cancer mortality was defined by ICD-9 codes 140–239 and ICD-10 codes C00–C34, C37–C41, C43–C49, C50–C52, C54–C65, C67–C80, C82–C85, C88, C90–C95 and C97. All-cause mortality included all specified causes as well as unknown cause.

**Variables considered:** sex, age, race, hypertension, diabetes, Hypercholesterolemia, dietary supplement use, smoking, physical activity, social economic status, marital status, BMI, waist circumference, vegetables intake (times/month), Fruits—times/month, Processed meat—times/month, White meat—times/month, Fish—times/month

**Adjusting variables:** 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.**

**Analytical models:** For this study, **we included all participants who were 18 years of age or older at the examination and from whom mortality data were available.** **We used time-dependent Cox proportional hazards regression models** to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). **The entire cohort was divided into categories of red meat, processed meat, white meat and fish consumption, and multivariate-adjusted HRs are reported using the lowest category as the referent category.** **The cut-points for the groups were as follows: red meat: 6; 14; 29; 44 times/month;** processed meat: 0; 6; 14; 29 times/month; white meat: 0; 3; 8; 12 times/month; fish: 0; 2; 4; 8; times/month. Trend tests were performed by assigning to each subject the median value for the consumption category1, 2, 3, 4, 5 into which the subject fell and modeling this term as a continuous variable, the coefficient for which was evaluated by the Wald test. **We tested for interaction between sex and meat or fish consumption by including a cross-product term along with the main effect terms in the Cox regression model.** The statistical significance of the cross-product terms was evaluated using the Wald test.

**Article 12: Associations of Dietary Protein with Disease and Mortality in a Prospective Study of Postmenopausal Women**

**Author: Linda E. Kelemen**

**Study cohort:** 41,836 originally, after exclusion, **29,017** women were available for analysis. Iowa Women’s Health Study

**Exclusion criteria:** We excluded women who, at baseline, were premenopausal, who reported a history of cancer other than skin cancer, known heart disease, or known diabetes, and who left 30 or more food items blank or had total energy intake less than 600 kcal/day (2.5 MJ/day) or more than 5,000 kcal/day (20.9 MJ/day).

**Definition of meat:** For each food, a common unit or portion size was specified, and participants were asked how often, on average, they had consumed that amount of the item over the past year. The nine responses ranged from “never or less than once per month” to “six or more times per day.” **a percentage of total energy calculated for total protein intake.**

**Definition of death:** Deceased nonrespondents were identified through linkage with the National Death Index.

**Variables considered:** smoking, hypertension, education, postmenopausal hormone use, physical activity, multiple vitamin supplement use, daily alcohol, age, waist/hip ratio, BMI, carbohydrates (% of energy), total fat, saturated fat, polyunsaturated fat, monounsaturated fat, trans-fat, cholesterol, total fiber, methionine, processed and red meat, chicken and poultry, fish and seafood, dairy products, eggs, nuts tofu and legumes, whole grains, refined grains, white bread, rice or pasta, potatoes, sweets and desserts, fruits and vegetables (servings per 1000kcal(4.2MJ))

**Adjusting variables:** 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.

**Analytical models: Substitution model. Macronutrients were expressed as a percentage of total energy,** and other dietary covariates were energy adjusted by the regression method (20). We examined the distribution of potential confounding and risk factors by **quintiles of total protein intake.** **Continuous variables were categorized into quintiles and treated as indicator variables in statistical models following inspection of their relation with each outcome in univariable analysis. We calculated risk ratios and 95 percent confidence intervals using Cox regression, and we modeled survival as a function of age (21), using as the referent the lowest quintile of protein intake. We assessed the relation between dietary protein and each outcome with multivariable-adjusted nutrient density models (22).** 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** (12, 22). 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**. For each endpoint, we first assessed the effect of an isoenergetic substitution of each of total, animal, and vegetable protein for total carbohydrate**. Next, we assessed the effect of an isoenergetic substitution of vegetable protein for animal protein while holding constant the intakes of carbohydrate, total energy, and potential confounding factors. Thus, the difference in the percentage of energy from protein (or protein type) between the lowest and the four remaining quintiles varied according to the comparison under study. While the use of nutrient values was necessary to evaluate our hypotheses of protein for carbohydrate substitutions on various outcomes, realistically most individuals interchange foods when implementing dietary changes. **Therefore, we also evaluated the effect of an isoenergetic substitution of various intakes of high-protein foods, standardized as servings per 1,000 kcal/day (4.2 MJ/day), for carbohydrate-dense foods while holding constant total energy, dietary fats, and other components of protein foods such as cholesterol.** This was done to better isolate the effect on our outcomes of the protein in these foods separate from the effects of other nutrients that have established associations with our outcomes.

**Article 13: The Mortality Risk of Elevated Serum Transferrin Saturation and Consumption of Dietary Iron**

**Author: Arch G. Mainous**

**Study cohort: 9,229** persons aged 35 to 70 years at baseline from NHANES II

**Exclusion criteria:** For the present study we excluded pregnant women, as well as the 2 respondents in the NHANES II who indicated that they had been told by a physician that they have hemochromatosis. These 2 respondents were excluded because they might have received treatment for their hemochromatosis.

**Definition of red meat:** Second, to provide a general estimate of heme iron intake rather than total iron, each participant was asked the weekly frequency of eating various types of meat. Red meat consumption at least 7 times per week was considered high consumption.

**Definition of mortality:** Mortality was measured as all-cause mortality. Mortality status was ascertained solely by computerized matching to national databases and evaluation of the resulting matches.

**Variables considered:**

Age, race, sex, poverty income ratio, education level, body mass index, smoking, health status, charlson comorbidity index

**Adjusting variables:**

**age, race, sex, poverty status, and education, body mass index (BMI) and current self-reported smoking status**. In an effort to control for severity of illness, we included self-reported health status as well as comorbid conditions. A variety of conditions were assessed in the NHANES II. Comorbidities were positive responses in the baseline interview to questions regarding whether a physician ever told the patient that he or she had each of the following conditions: **cirrhosis, diabetes, high blood pressure, heart failure, heart attack, stroke, hardening of the arteries, rheumatic fever, rheumatic heart disease, heart murmur, ulcer (peptic, stomach, duodenal), chronic enteritis, ulcerative colitis, spastic colon or mucous colitis, gallstones, hepatitis, yellow jaundice, pleurisy, low blood pressure, cataracts, glaucoma, thyroid disease, polio or paralysis, goiter, hiatus hernia of the diaphragm, cancer, benign tumor, trouble with blood not clotting properly, loss of blood from stomach or bowels, nervous breakdown, neck injury, back injury, anemia, arthritis, gout, asthma, chronic bronchitis, emphysema, tuberculosis, and kidney problems.** The **Charlson Comorbidity Index** was calculated from the responses to these questions. This index is a validated tool for predicting mortality in longitudinal studies.12

**Analytical models: We classified the population into 4 groups based upon normal and elevated transferrin saturation, and low and high iron intake. The criteria for high iron intake (total iron and red meat consumption) were analyzed separately**. For the analysis of the mortality, we used sampling weights to calculate prevalence estimates for the civilian noninstitutionalized US population. Because of the complex sampling design of the survey, we performed all analyses using the statistical software package SUDAAN, as recommended by the National Center for Health Statistics. Using the population estimates generated by SUDAAN, we computed Kaplan-Meier curves to show graphically the unadjusted relationship between all-cause mortality and elevated serum transferrin saturation and low or high iron ingestion. **We performed Cox proportional hazards analysis with all-cause mortality for serum transferrin saturations of greater than 55% controlling for age, race, sex, poverty status, education, BMI, smoking status, and Charlson Comorbidity Index.**