**Supplemental Table 1.** Components of the dietary (DIS) and lifestyle (LIS) inflammation scores, their general descriptions, rationales for inclusion, and assigned weights

|  |  |  |  |
| --- | --- | --- | --- |
| **Components** | **General descriptions** | **Rationales for inclusion** | **Weights**a |
| *DIS components* |   |  |   |
| Added sugars  | Sugar-sweetened soda, punch, lemonade, fruit drinks, chocolate candy bars, other mixed candy bars, candy without chocolate, jams, jellies, preserves, syrup or honey, dried or canned fruit | Sparse in nutrients; induce postprandial hyperglycemia, which act as stressful stimuli through subsequent repeated mild postprandial hypoglycemia (1) and reduce nitric oxide availability (plays role in regulation of inflammatory response (2)); elevate pro-inflammatory free fatty acid levels (3); produce oxidative stress through oxidation of membrane lipids, proteins, lipoproteins, and DNA (4) | 0.56 |
| Apples and berries | Fresh apples, pears, apple juice or cider, strawberries, blueberries, raspberries, cherries | Contain flavonoids (e.g., anthocyanins, quercetin, and phenolic acids) that suppress pro-inflammatory cytokine production and are powerful antioxidants; potentially increase postprandial plasma antioxidant capacity (5–7) | -0.65 |
| Coffee and tea | Coffee (decaffeinated and regular), herbal and non-herbal tea | Tea contains flavonoids and antioxidants (e.g., epicatechin and quercetin) (8); coffee contains phytochemicals and antioxidants, such as javamide; ﻿both coffee and tea contain varying amounts of caffeine which inhibit secretion of IL-1β induced by adenine and N4-acetylcytidine (9,10) | -0.25 |
| Deep yellow or orange vegetables and fruit | Cantaloupe, peaches, carrots, dark yellow or orange squash, figs | Contain pro-vitamin A carotenoids (e.g., β-carotene and α-carotene), which have a conjugated double-bond structure making them strong antioxidants (11) | -0.57 |
| Fish  | Tuna fish, salmon, other light and dark meat fish, breaded fish cakes or fish sticks | Contain Ω-3 fatty acids, which compete with pro-inflammatory Ω-6 fatty acids by synthesizing eicosanoids and suppress the capacity of monocytes to synthesize IL-1β and TNF-$α $(3,12,13) | -0.08 |
| High-fat dairy  | Whole milk, 2% milk, cream, high-fat ice cream, high-fat yogurt, cream cheese, other high-fat cheeses | Contains calcium, which binds bile acids and free fatty acids, decreasing oxidative damage in the gut; dairy fat contains fatty acids with potential inflammation-reducing properties, such as CLA, *cis-* and *trans-*palmitoleic acid, butyric acid, phytanic acid, and alpha-linolenic acid (14–16) | -0.14 |
| Leafy greens and cruciferous vegetables | Kale, spinach, lettuce (iceberg, head, romaine, or leaf), broccoli, Brussels sprouts, cabbage, cauliflower, parsley, watercress | Contain variety of potent antioxidants (e.g., β-carotene, folacin, magnesium, calcium, glucosinolates, isothiocyanates, lutein, and indoles); contain flavonoids and polyphenols, which activate the transcription factor, Nuclear factor-erythroid 2 (NF-E2)-related factor 2 (Nrf2), which plays a key role in cellular protection against oxidative stress and inflammation (17–27) | -0.14 |
| Legumes | String beans, peas, lima beans, lentils, and beans (excluding soybeans) | Contain folacin, iron, isoflavones, protein, vitamin B6, and have a high antioxidant capacity; rich in fiber, which is associated with beneficial alterations to the gut microbiota, reducing immune response in the gut (10,20,28) | -0.04 |
| Low-fat dairy  | Skim milk, 1% milk, low-fat yogurt, low-fat ice cream, low-fat cottage or ricotta cheese, low-fat cheeses | Similar mechanisms to high-fat dairy (see mechanisms above), with lower fat content | -0.12 |
| Nuts  | Peanut butter, peanuts, other nuts | Contain Ω -3 fatty acids (3,12,29,30) (mechanisms similar to those described above in ‘Fish’) and contain *l*-arginine (20), which improves endothelium-dependent dilation (precursor of the endogenous vasodilator nitric oxide) and decreases platelet aggregation and monocyte adhesion (20)  | -0.44 |
| Other fruits and real fruit juices | Other fresh fruits than those listed above (e.g., pineapples, honeydew, grapes, kiwi, watermelon, lemon, grapefruit, and oranges), orange juice, grapefruit juice, apple juice, grape juice, and other real fruit juice | Contain antioxidants (e.g., flavonoids, such as hesperidin, naringenin, neohesperidin, limonene, vitamin C, β-cryptoxanthin, plant sterols, salicylates, naringin, nobelitin, and narirutin) with similar mechanisms to those described above (21,31–38) | -0.16 |
| Other vegetables | Other vegetables than those listed above (e.g., okra, green peppers, onions, zucchini, and eggplant) | Contain antioxidants and polyphenols with similar mechanisms to those described above | -0.16 |
| Poultry | Chicken or turkey with and without skin | Inversely associated with inflammation markers (39), contain low amounts of saturated fat (40), and contain *l*-arginine (see mechanisms in ‘Nuts’) | -0.45 |
| Processed meats  | Bacon, beef or pork hotdogs, chicken or turkey hot dogs, salami, bologna, other processed meats | Contain heme iron, which increases the bioavailability of iron, which in turn increases oxidative stress; contain higher saturated fat contents, Ω-6 fatty acids (see ‘Fats’), and additives, such as nitrites, with suspected pro-inflammatory properties (39,41) | 0.68 |
| Red and organ meats | Hamburger, beef, pork, lamb, liver, gizzards, other organ meats | Contain heme iron (see above); contain Ω-6 fatty acids and saturated fat (see mechanisms in ‘Fats’ above) | 0.02 |
| Refined grains and starchy vegetables | Cold and cooked breakfast cereal, white or dark bread, bagels, English muffins, rolls, corn bread, white rice, pasta, pancakes, waffles, potatoes (French fried, scalloped, baked, boiled or mashed), sweet potato/yams, potato chips, crackers, tortillas, popcorn, pretzels, cookies, brownies, doughnuts, cake, pie, sweet rolls, coffee cakes, granola bars | Sparse in nutrients; some processed grains contain emulsifiers, which potentially break down mucin in the gut leading to inflammation (42); and induce hyperglycemia (mechanisms described similar to those described above in ‘Added Sugars’) | 0.72 |
|
| Tomatoes | Tomatoes, tomato juice, tomato sauce, salsa | Contain β-carotene, vitamin C, and lycopene, the latter of which is a potent singlet oxygen quencher and one of the most powerful antioxidants among the natural carotenoids (43–46) | -0.78 |
| Other fats  | Mayonnaise, margarine, butter, vegetable oil | Contain Ω-6 fatty acids and saturated fats (see ‘red and organ meats’ above)  | 0.31 |
| Supplement scorec  | Ranked score of supplements, including: vitamins A, B1, B12, B6, C, D, and E; and β-carotene, folate, niacin, riboflavin, calcium, copper, iron, magnesium, selenium, and zinc | Comprises micro-nutrients, minerals, and vitamins solely from supplement intakes, some with similar mechanisms to those described above (e.g., iron as pro-oxidant, vitamins A, C, and E as antioxidants) | -0.80 |
| *LIS components* |   |   |  |
| Overweight BMI  | Overweight BMI vs. normal BMI  | Adipose tissue synthesizes and releases pro-inflammatory adipokines, such as plasminogen activator inhibitor–1 (PA1) and TNF-α (47,48) | 0.89 |
| Obese BMI | Obese BMI vs. normal BMI | Mechanisms similar to those described above | 1.57 |
| Heavy drinker | Heavy (> 7 drinks/wk for women, > 14 drinks/wk drinks for men) vs. non-drinker | Heavy alcohol intake results in oxidative stress via oxidation of ethanol to acetaldehyde (49,50) | 0.30 |
| Moderate drinker | Moderate (1 – 7 drinks/wk for women, 1 – 14 drinks/wk for men) vs. non-drinker | A metabolite of ethanol is acetate, which can ﻿acutely lower pro-inflammatory free fatty acid concentrations; moderate alcohol intake increases serum adiponectin concentrations (an anti-inflammatory inflammation biomarker) (51) and inhibits IL-6 production and activity (52) | -0.66 |
| Moderately physically active | Individuals in the middle tertile of MET-hours per week | Physical activity improves systemic plasma antioxidant capacity (increases adaptive responses to oxidative stress), increases concentrations of anti-inflammatory cytokines, and lowers vascular wall inflammation (48,53) | -0.18 |
| Heavily physically active | Individuals in the highest tertile of MET-hours per week | Mechanisms similar to those described above | -0.41 |
| Current smoker  | Currently smokes tobacco vs. does not currently smoke tobacco  | Toxins injure tissues, upregulating cytokines and acute phase reactants (54) | 0.50 |

Abbreviations: BMI, body mass index; DIS, dietary inflammation score; LIS, lifestyle inflammation score; MET, metabolic equivalents of task

a Weights are β coefficients from multivariable linear regression models, conducted in a sample (N = 639) of participants in the Reasons for Geographic and Racial Differences in Stroke prospective cohort study (REGARDS), representing the average change in a summary inflammation biomarker z-score (sum of z-scores for high sensitivity C-reactive protein, interleukin-6, interleukin-8, interleukin-10 [the latter with a negative sign]) per one standard deviation increase in a dietary component or the presence of lifestyle component. Covariates in the final model included: age, sex, race (Black or White), education (high school graduate or less vs. some college or more), region (stroke belt, stroke buckle, or other region in the US), a comorbidity score (comprises a history of cancer, heart disease, diabetes mellitus, or chronic kidney disease), hormone replacement therapy (among women), total energy intake (kcal/day), season of baseline interview (Spring, Summer, Fall, or Winter) and regular use of aspirin, other non-steroidal anti-inflammatory drugs, or lipid-lowering medications (≥ twice/wk); and all the dietary/lifestyle components in the DIS and LIS; In the case-control studies, all dietary components were standardized based on the distribution among the controls, by sex, to a mean of zero and standard deviation of 1, and all lifestyle components were dummy variables

b All vitamin and mineral supplement intakes measured (from multivitamin/mineral and individual supplements) were ranked into quantiles of intake and assigned a value of 0 (low or no intake), 1, or 2 (highest intake) for hypothesized anti-inflammatory supplements (e.g., vitamin E), and 0 (low or no intake), -1, or -2 (highest intake) for hypothesized pro-inflammatory supplements (e.g., iron)

**Supplemental Table 2.** Multivariable-adjusted associations of the dietary (DIS) and lifestyle (LIS) inflammation scores with incident, sporadic colorectal adenomas in three pooled case-control studies (CPRU Study, 1991 – 1994; MAP I Study, 1994 – 1997; and MAP II Study, 2002), according to selected adenoma characteristics

|  |  |
| --- | --- |
|   | **Inflammation score**a |
|   | **DIS**b |   | **LIS**c |
| **Adenoma characteristics and inflammation score quintiles** | **N cases** | **Adjusted OR (95% CI)** |   | **N cases** | **Adjusted OR (95% CI)** |
| Adenoma subtype |   |   |   |  |   |
| *Tubular* |   |   |   |  |  |
| 1 | 87 | 1.00 (ref) |   | 72 | 1.00 (ref) |
| 2 | 115 | 1.22 (0.87-1.70) |   | 83 | 1.12 (0.78-1.61) |
| 3 | 103 | 1.11 (0.79-1.56) |   | 120 | 1.51 (1.08-2.12) |
| 4 | 109 | 1.24 (0.88-1.74) |   | 120 | 1.53 (1.09-2.15) |
| 5 | 113 | 1.25 (0.89-1.75) |   | 132 | 1.92 (1.37-2.70) |
| *Ptrend* |  | *0.19* |  |  | *<0.0001* |
| *Pheterogeneity* |  | *ref* |  |  | *ref* |
| *Tubulovillous or villous*  |   |   |   |   |   |
| 1 | 39 | 1.00 (ref) |   | 29 | 1.00 (ref) |
| 2 | 37 | 0.92 (0.56-1.50) |   | 33 | 1.16 (0.68-1.99) |
| 3 | 39 | 0.94 (0.58-1.53) |   | 43 | 1.27 (0.77-2.12) |
| 4 | 45 | 1.06 (0.66-1.72) |   | 58 | 1.71 (1.07-2.80) |
| 5 | 62 | 1.47 (0.94-2.32) |   | 59 | 2.05 (1.27-3.36) |
| *Ptrend* |  | *0.08* |  |  | *0.001* |
| *Pheterogeneity* |  | *0.50* |  |  | *0.93* |
| No. of adenomas |   |   |   |   |   |
| *1 adenoma* |  |  |  |  |  |
| 1 | 91 | 1.00 (ref) |   | 72 | 1.00 (ref) |
| 2 | 93 | 0.99 (0.71-1.39) |   | 71 | 0.99 (0.69-1.44) |
| 3 | 99 | 1.03 (0.74-1.44) |   | 117 | 1.52 (1.09-2.13) |
| 4 | 98 | 1.04 (0.74-1.45) |   | 130 | 1.68 (1.21-2.35) |
| 5 | 122 | 1.28 (0.93-1.78) |   | 113 | 1.68 (1.20-2.37) |
| *Ptrend* |  | *0.12* |  |  | *<0.0001* |
| *Pheterogeneity* |  | *ref* |  |  | *ref* |
| *≥ 2 adenomas* |  |  |  |  |  |
| 1 | 35 | 1.00 (ref) |   | 29 | 1.00 (ref) |
| 2 | 60 | 1.57 (0.98-2.55) |   | 45 | 1.47 (0.88-2.47) |
| 3 | 44 | 1.17 (0.71-1.93) |   | 47 | 1.33 (0.81-2.23) |
| 4 | 56 | 1.55 (0.96-2.54) |   | 49 | 1.42 (0.86-2.36) |
| 5 | 53 | 1.42 (0.88-2.33) |   | 78 | 2.71 (1.70-4.40) |
| *Ptrend* |  | *0.23* |  |  | *<0.0001* |
| *Pheterogeneity* |  | *0.82* |  |  | *0.06* |
| Adenoma size |   |   |   |   |   |
| *< 1 cm* |   |   |   |   |   |
| 1 | 73 | 1.00 (ref) |   | 65 | 1.00 (ref) |
| 2 | 100 | 1.27 (0.90-1.82) |   | 74 | 1.09 (0.75-1.59) |
| 3 | 82 | 1.08 (0.75-1.56) |   | 94 | 1.27 (0.89-1.82) |
| 4 | 94 | 1.28 (0.89-1.84) |   | 112 | 1.55 (1.09-2.21) |
| 5 | 102 | 1.37 (0.96-1.97) |   | 106 | 1.72 (1.21-2.46) |
| *Ptrend* |  | *0.09* |  |  | *0.0003* |
| *Pheterogeneity* |  | *ref* |  |  | *ref* |
| *≥ 1 cm* |   |   |   |   |   |
| 1 | 41 | 1.00 (ref) |   | 27 | 1.00 (ref) |
| 2 | 39 | 0.93 (0.57-1.51) |   | 29 | 1.08 (0.62-1.90) |
| 3 | 48 | 1.12 (0.70-1.79) |   | 55 | 1.83 (1.13-3.04) |
| 4 | 54 | 1.19 (0.75-1.90) |   | 57 | 1.90 (1.17-3.16) |
| 5 | 62 | 1.38 (0.88-2.18) |   | 76 | 2.84 (1.79-4.65) |
| *Ptrend* |  | *0.10* |  |  | *<0.0001* |
| *Pheterogeneity* |  | *0.45* |  |  | *0.09* |
| Degree of atypia |   |   |   |   |   |
| *Mild*  |   |   |   |   |   |
| 1 | 58 | 1.00 (ref) |   | 47 | 1.00 (ref) |
| 2 | 73 | 1.19 (0.80-1.76) |   | 46 | 0.90 (0.57-1.41) |
| 3 | 67 | 1.08 (0.72-1.62) |   | 73 | 1.40 (0.94-2.12) |
| 4 | 58 | 0.96 (0.63-1.45) |   | 77 | 1.44 (0.96-2.17) |
| 5 | 67 | 1.08 (0.72-1.62) |   | 80 | 1.70 (1.14-2.56) |
| *Ptrend* |  | *0.97* |  |  | *0.002* |
| *Pheterogeneity* |  | *ref* |  |  | *ref* |
| *Moderate to severe* |   |   |   |   |   |
| 1 | 68 | 1.00 (ref) |   | 54 | 1.00 (ref) |
| 2 | 80 | 1.11 (0.77-1.62) |   | 70 | 1.36 (0.91-2.02) |
| 3 | 76 | 1.08 (0.74-1.58) |   | 91 | 1.52 (1.04-2.22) |
| 4 | 96 | 1.38 (0.96-2.00) |   | 102 | 1.73 (1.19-2.52) |
| 5 | 108 | 1.55 (1.08-2.24) |   | 111 | 2.23 (1.55-3.25) |
| *Ptrend* |  | *0.01* |  |  | *<0.0001* |
| *Pheterogeneity* |  | *0.20* |  |  | *0.37* |

Abbreviations: BMI, body mass index; CI, confidence interval; CPRU, Cancer Prevention Research Unit; DIS, dietary inflammation score; LIS, lifestyle inflammation score; MAP, Markers of Adenomatous Polyps; MET, metabolic equivalents of task; OR, odds ratio

a For construction of the inflammation scores, see text and Table 1; higher scores indicate a higher balance of pro- versus anti-inflammatory exposures

b Covariates in the DIS unconditional logistic regression models were: age, sex, education (less than college graduate or college graduate or higher), NSAID/aspirin use (</≥ once/week), hormone therapy use (among women), family history of colorectal cancer in a first degree relative (yes/no), smoking status (never, former, or current smoker), BMI (kg/m2), alcohol intake (non-drinker, moderate drinker, or heavy drinker), physical activity (categorized into tertiles of MET-hours/wk), total energy intake (kcal/day), and study (MAP I, MAP II, or CPRU)

c Covariates in the LIS unconditional logistic regression models were: age, sex, NSAID/aspirin use (</≥ once/week), hormone therapy use (among women), family history of colorectal cancer in a first degree relative (yes/no), former smoking status (former smoker or non-former smoker), total energy intake (kcal/day), study (MAP I, MAP II, or CPRU), and the equally-weighted DIS

**Supplemental Table 3.** Multivariable-adjusted associations of the dietary (DIS) and lifestyle (LIS) inflammation scores with incident, sporadic colorectal adenoma in three pooled case-control studies (CPRU Study, 1991 – 1994; MAP I Study, 1994 – 1997; and MAP II Study, 2002), according to selected participant characteristics

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Quintiles** |  |  |
| **Characteristics** | **N cases** | **1 (ref)** | **2** | **3** | **4** | **5** | ***Ptrend*** | ***Pinteraction*** |
| ***DIS****a,b* |  |  |  |  |  |  |  |  |
| Age, y |  |  |  |  |  |  |  |  |
| < 57 | 260 | 1.00 | 1.17 (0.72-1.92) | 0.97 (0.59-1.62) | 1.02 (0.62-1.67) | 1.21 (0.74-1.98) | 0.64 |   |
| ≥ 57 | 505 | 1.00 | 1.15 (0.80-1.66) | 1.07 (0.74-1.54) | 1.23 (0.85-1.79) | 1.32 (0.92-1.91) | 0.12 | 0.99 |
| Sex |  |  |  |  |  |  |  |   |
| Men | 469 | 1.00 | 1.12 (0.75-1.69) | 1.30 (0.88-1.94) | 1.42 (0.95-2.11) | 1.67 (1.13-2.48) | 0.01 |   |
| Women  | 303 |  1.00 | 1.12 (0.73-1.70) | 0.75 (0.48-1.18) | 0.96 (0.62-1.49) | 0.92 (0.59-1.43) | 0.52 | 0.28 |
| Aspirin or other NSAID use |  |   |  |  |  |  |  |   |
| Takes aspirin or NSAID < once/wk | 493 | 1.00 | 1.06 (0.73-1.54) | 0.83 (0.57-1.22) | 1.07 (0.74-1.57) | 1.31 (0.91-1.89) | 0.17 |   |
| Take aspirin or NSAID ≥ once/wk | 272 | 1.00 | 1.33 (0.84-2.13) | 1.51 (0.94-2.44) | 1.25 (0.77-2.04) | 1.19 (0.73-1.96) | 0.41 | 0.23 |
| Family history of CRCc |  |   |  |  |  |  |  |   |
| No | 635 | 1.00 | 1.12 (0.82-1.54) | 1.02 (0.74-1.42) | 1.13 (0.82-1.57) | 1.34 (0.98-1.85) | 0.08 |   |
| Yes | 130 | 1.00 | 1.49 (0.70-3.20) | 1.18 (0.56-2.52) | 1.49 (0.71-3.16) | 1.08 (0.50-2.35) | 0.94 | 0.81 |
| Tobacco use |  |   |   |   |   |   |   |   |
| Never smoker | 234 | 1.00 | 1.56 (0.96-2.55) | 1.09 (0.64-1.85) | 1.31 (0.79-2.19) | 1.64 (1.00-2.73) | 0.12 |   |
| Former or current smoker | 531 | 1.00 | 1.05 (0.73-1.52) | 1.12 (0.78-1.61) | 1.25 (0.87-1.8) | 1.33 (0.93-1.9) | 0.07 | 0.57 |
| Body mass index, kg/m2 |  |   |  |  |  |  |  |   |
| < 30 | 560 | 1.00 | 1.23 (0.88, 1.71) | 1.02 (0.73, 1.43) | 1.21 (0.86, 1.70) | 1.25 (0.89, 1.77) | 0.22 |   |
| ≥ 30 | 205 | 1.00 | 1.10 (0.59, 2.04) | 1.31 (0.70, 2.44) | 1.13 (0.62, 2.04) | 1.50 (0.85, 2.67) | 0.21 | 0.84 |
| Alcohol use |  |   |  |  |  |  |  |   |
| Former or never drinker | 273 | 1.00 | 1.08 (0.64-1.80) | 0.70 (0.39-1.22) | 1.16 (0.71-1.92) | 1.40 (0.88-2.27) | 0.12 |   |
| Current drinker | 492 | 1.00 | 1.24 (0.87-1.77) | 1.26 (0.89-1.8) | 1.17 (0.81-1.69) | 1.27 (0.87-1.86) | 0.26 | 0.19 |
| Physical activity |  |   |   |   |   |   |   |   |
| Total moderate + vigorous METs/week < 41.54 | 361 | 1.00 | 1.11 (0.72-1.74) | 1.02 (0.65-1.58) | 0.95 (0.61-1.48) | 1.31 (0.85-2.02) | 0.38 |   |
| Total moderate + vigorous METs/week ≥ 41.54 | 404 | 1.00 | 1.23 (0.83-1.83) | 1.09 (0.73-1.63) | 1.50 (1.01-2.25) | 1.32 (0.89-1.98) | 0.09 | 0.60 |
| Study |  |   |  |  |  |  |  |   |
| MAP I | 550 | 1.00 | 1.10 (0.79-1.54) | 1.11 (0.79-1.54) | 1.18 (0.85-1.65) | 1.33 (0.96-1.85) | 0.10 |   |
| MAP II | 168 | 1.00 | 1.44 (0.67-3.13) | 0.96 (0.43-2.15) | 1.39 (0.63-3.14) | 1.43 (0.65-3.20) | 0.44 |   |
| CPRU | 47 | 1.00 | 1.42 (0.46-4.52) | 0.66 (0.16-2.55) | 1.02 (0.28-3.70) | 1.47 (0.40-5.57) | 0.63 | 0.95 |
| ***LIS****a,e* |  |   |   |   |   |   |   |   |
| Age-y |  |   |   |   |   |   |   |   |
| < 57 | 260 | 1.00 | 0.84 (0.47-1.46) | 1.89 (1.19-3.02) | 1.60 (1.00-2.58) | 2.16 (1.36-3.45) | 0.0002 |   |
| ≥ 57 | 505 | 1.00 | 1.24 (0.84-1.85) | 1.22 (0.83-1.80) | 1.52 (1.04-2.23) | 1.76 (1.20-2.59) | 0.001 | 0.20 |
| Sex |  |  |  |  |  |  |  |  |
| Men | 469 | 1.00 | 1.32 (0.85-2.07) | 1.51 (0.99-2.32) | 1.50 (0.99-2.30) | 2.13 (1.40-3.28) | 0.0004 |   |
| Women | 303 | 1.00 | 0.95 (0.59-1.51) | 1.64 (1.08-2.51) | 1.95 (1.29-2.98) | 1.93 (1.27-2.95) | <0.0001 | 0.45 |
| Aspirin or other NSAID use |  |   |  |  |  |  |  |  |
| Takes aspirin or NSAID < once/wk | 493 | 1.00 | 1.23 (0.83-1.83) | 1.56 (1.08-2.26) | 1.86 (1.29-2.68) | 2.10 (1.45-3.06) | <0.0001 |  |
| Takes aspirin or NSAID ≥ once/wk | 272 | 1.00 | 0.92 (0.54-1.57) | 1.32 (0.81-2.17) | 1.16 (0.71-1.91) | 1.74 (1.09-2.82) | 0.01 | 0.77 |
| Family history of CRCc |  |  |  |  |  |  |  |  |
| No | 635 | 1.00 | 1.14 (0.81-1.63) | 1.52 (1.10-2.12) | 1.65 (1.20-2.29) | 1.99 (1.44-2.75) | <0.0001 |  |
| Yes | 130 | 1.00 | 1.19 (0.56-2.54) | 1.39 (0.71-2.79) | 1.35 (0.66-2.80) | 2.06 (1.01-4.24) | 0.07 | 0.99 |
| Study |  |  |  |  |  |  |  |  |
| MAP I | 550 | 1.00 | 1.22 (0.85-1.75) | 1.47 (1.04-2.07) | 1.69 (1.22-2.36) | 2.01 (1.45-2.82) | <0.0001 |   |
| MAP II | 168 | 1.00 | 0.95 (0.42-2.13) | 1.69 (0.79-3.64) | 1.35 (0.61-3.04) | 2.11 (0.97-4.68) | 0.03 |   |
| CPRU | 47 | 1.00 | 0.86 (0.21-3.30) | 1.50 (0.50-4.70) | 1.66 (0.53-5.41) | 1.64 (0.45-6.09) | 0.24 | 1.00 |

Abbreviations: BMI, body mass index; CI, confidence interval; CPRU, Cancer Prevention Research Unit; CRC, colorectal cancer; DIS, dietary inflammation score; LIS, lifestyle inflammation score; MAP, Markers of Adenomatous Polyps; MET, metabolic equivalent of task; NSAID, non-steroidal anti-inflammatory drug; OR, odds ratio; ref, referent

a ﻿For inflammation score construction, see text and Table 1; higher scores indicate a higher balance of pro- versus anti-inflammatory exposures

b Covariates in the DIS unconditional logistic regression models were: age, sex, education (less than college graduate or college graduate or higher), NSAID/aspirin use (</≥ once/week), hormone therapy use (among women), family history of colorectal cancer in a first degree relative (yes/no), smoking status (never, former, or current smoker), BMI (kg/m2), alcohol intake (non-drinker, moderate drinker, or heavy drinker), physical activity (categorized into tertiles of MET-hours/wk), total energy intake (kcal/day), and study (MAP I, MAP II, or CPRU)

c In a first degree relative

d Covariates in the LIS unconditional logistic regression models were: age, sex, NSAID/aspirin use (</≥ once/week), hormone therapy use (among women), family history of colorectal cancer in a first degree relative (yes/no), former smoking status (non-former smoker or former smoker), total energy intake (kcal/day), study (MAP I, MAP II, or CPRU), and the equally-weighted DIS

**Supplemental Table 4.** Adjusted associationsa of the Dietary Inflammation Score (DIS)b with incident, sporadic colorectal adenomas in three pooled case-control studies (CPRU Study, 1991 – 1994; MAP I Study, 1994 – 1997; and MAP II Study, 2002), with each DIS component removed one at a time and added as a covariate

|  |  |  |
| --- | --- | --- |
| **DIS component removed/reduced DIS quintiles** | **N cases** | **Adjusted OR (95% CI)** |
| Leafy greens |  |  |
| 1 | 126 | 1.00 |
| 2 | 161 | 1.22 (0.91-1.63) |
| 3 | 145 | 1.09 (0.80-1.48) |
| 4 | 150 | 1.16 (0.85-1.58) |
| 5 | 183 | 1.40 (1.03-1.91) |
|  | *Ptrend* | *0.06* |
| Tomatoes |  |  |
| 1 | 124 | 1.00 |
| 2 | 148 | 1.10 (0.81-1.48) |
| 3 | 142 | 1.12 (0.83-1.52) |
| 4 | 170 | 1.28 (0.95-1.72) |
| 5 | 181 | 1.45 (1.07-1.97) |
|  | *Ptrend* | *0.01* |
| Apples and berries |  |  |
| 1 | 134 | 1.00 |
| 2 | 153 | 1.03 (0.77-1.38) |
| 3 | 140 | 0.96 (0.71-1.29) |
| 4 | 165 | 1.13 (0.84-1.52) |
| 5 | 173 | 1.13 (0.84-1.53) |
|  | *Ptrend* | *0.30* |
| Deep yellow or orange vegetables and fruit |  |  |
| 1 | 137 | 1.00 |
| 2 | 147 | 1.00 (0.74-1.34) |
| 3 | 150 | 1.03 (0.77-1.39) |
| 4 | 156 | 1.02 (0.76-1.38) |
| 5 | 175 | 1.18 (0.87-1.59) |
|  | *Ptrend* | *0.30* |
| Other fruits and real fruit juices |  |  |
| 1 | 130 | 1.00 |
| 2 | 158 | 1.06 (0.79-1.42) |
| 3 | 145 | 0.97 (0.72-1.32) |
| 4 | 153 | 1.02 (0.75-1.38) |
| 5 | 179 | 1.14 (0.84-1.56) |
|  | *Ptrend* | *0.44* |
| Other vegetables |  |  |
| 1 | 126 | 1.00 |
| 2 | 159 | 1.19 (0.89-1.60) |
| 3 | 140 | 1.03 (0.76-1.41) |
| 4 | 156 | 1.17 (0.86-1.59) |
| 5 | 184 | 1.38 (1.02-1.89) |
|  | *Ptrend* | *0.05* |
| Legumes |  |  |
| 1 | 128 | 1.00 |
| 2 | 153 | 1.10 (0.82-1.48) |
| 3 | 149 | 1.07 (0.80-1.45) |
| 4 | 157 | 1.14 (0.84-1.54) |
| 5 | 178 | 1.26 (0.93-1.71) |
|  | *Ptrend* | *0.13* |
| Fish  |  |  |
| 1 | 130 | 1.00 |
| 2 | 154 | 1.08 (0.81-1.45) |
| 3 | 145 | 1.05 (0.78-1.41) |
| 4 | 160 | 1.16 (0.86-1.56) |
| 5 | 176 | 1.27 (0.94-1.71) |
|  | *Ptrend* | *0.11* |
| Poultry |  |  |
| 1 | 144 | 1.00 |
| 2 | 151 | 1.01 (0.76-1.35) |
| 3 | 149 | 0.95 (0.71-1.27) |
| 4 | 137 | 0.88 (0.66-1.19) |
| 5 | 184 | 1.21 (0.91-1.62) |
|  | *Ptrend* | *0.36* |
| Red and organ meats |  |  |
| 1 | 129 | 1.00 |
| 2 | 154 | 1.11 (0.83-1.48) |
| 3 | 152 | 1.10 (0.82-1.47) |
| 4 | 151 | 1.09 (0.81-1.47) |
| 5 | 179 | 1.28 (0.96-1.72) |
|  | *Ptrend* | *0.12* |
| Processed meats  |  |  |
| 1 | 133 | 1.00 |
| 2 | 155 | 1.10 (0.83-1.48) |
| 3 | 163 | 1.15 (0.86-1.54) |
| 4 | 137 | 1.02 (0.76-1.38) |
| 5 | 177 | 1.25 (0.92-1.70) |
|  | *Ptrend* | *0.25* |
| Added sugars  |  |  |
| 1 | 125 | 1.00 |
| 2 | 156 | 1.17 (0.88-1.58) |
| 3 | 145 | 1.08 (0.80-1.46) |
| 4 | 165 | 1.25 (0.93-1.68) |
| 5 | 174 | 1.21 (0.90-1.64) |
|  | *Ptrend* | *0.17* |
| High-fat dairy  |  |  |
| 1 | 132 | 1.00 |
| 2 | 154 | 1.06 (0.79-1.42) |
| 3 | 138 | 0.97 (0.72-1.31) |
| 4 | 158 | 1.12 (0.84-1.50) |
| 5 | 183 | 1.29 (0.96-1.72) |
|  | *Ptrend* | *0.08* |
| Low-fat dairy  |  |  |
| 1 | 126 | 1.00 |
| 2 | 156 | 1.16 (0.86-1.55) |
| 3 | 147 | 1.11 (0.83-1.50) |
| 4 | 159 | 1.18 (0.88-1.59) |
| 5 | 177 | 1.33 (0.99-1.78) |
|  | *Ptrend* | *0.07* |
| Coffee and tea |  |  |
| 1 | 131 | 1.00 |
| 2 | 145 | 1.04 (0.78-1.40) |
| 3 | 146 | 1.01 (0.75-1.36) |
| 4 | 154 | 1.11 (0.82-1.48) |
| 5 | 189 | 1.32 (0.99-1.77) |
|  | *Ptrend* | *0.05* |
| Nuts  |  |  |
| 1 | 118 | 1.00 |
| 2 | 169 | 1.25 (0.94-1.68) |
| 3 | 157 | 1.29 (0.96-1.74) |
| 4 | 144 | 1.10 (0.81-1.48) |
| 5 | 177 | 1.34 (0.99-1.80) |
|  | *Ptrend* | *0.15* |
| Fats  |  |  |
| 1 | 135 | 1.00 |
| 2 | 162 | 1.10 (0.82-1.46) |
| 3 | 145 | 0.93 (0.69-1.25) |
| 4 | 146 | 0.99 (0.74-1.33) |
| 5 | 177 | 1.19 (0.89-1.60) |
|  | *Ptrend* | *0.38* |
| Refined grains and starchy vegetables |  |  |
| 1 | 128 | 1.00 |
| 2 | 165 | 1.29 (0.96-1.72) |
| 3 | 136 | 0.97 (0.72-1.32) |
| 4 | 150 | 1.11 (0.82-1.50) |
| 5 | 186 | 1.33 (0.99-1.80) |
|  | *Ptrend* | *0.17* |
| Supplement score |  |  |
| 1 | 139 | 1.00 |
| 2 | 161 | 1.04 (0.78-1.39) |
| 3 | 138 | 0.94 (0.70-1.26) |
| 4 | 149 | 1.03 (0.77-1.38) |
| 5 | 178 | 1.16 (0.87-1.55) |
|   | *Ptrend* | *0.32* |

Abbreviations: BMI, body mass index; CI, confidence interval; CPRU, Cancer Prevention Research Unit; DIS, dietary inflammation score; LIS, lifestyle inflammation score; MAP, Markers of Adenomatous Polyps; MET, metabolic equivalent of task; NSAID, non-steroidal anti-inflammatory drug; OR, odds ratio

a Covariates in the DIS unconditional logistic regression models were: age, sex, education (less than college graduate or college graduate or higher), NSAID/aspirin use (</≥ once/week), hormone therapy use (among women), family history of colorectal cancer in a first degree relative (yes/no), smoking status (never, former, or current smoker), BMI (kg/m2), alcohol intake (non-drinker, moderate drinker, or heavy drinker), physical activity (categorized into tertiles of MET-hours/wk), total energy intake (kcal/day), study (MAP I, MAP II, or CPRU), and the component removed from the DIS

b ﻿For inflammation score construction, see text and Table 1; higher scores indicate a higher balance of pro- versus anti-inflammatory exposures

**Supplemental Table 5.** Adjusted associationsa of the Lifestyle Inflammation Score (LIS)b with incident, sporadic colorectal adenomas in three pooled case-control studies (CPRU Study, 1991 – 1994; MAP I Study, 1994 – 1997; and MAP II Study, 2002), with each LIS component removed one at a time and added as a covariate

|  |  |  |
| --- | --- | --- |
| **LIS component removed/reduced LIS quintiles** | **N cases** | **Adjusted OR (95% CI)** |
| Alcohol intake |  |  |
| 1 | 131 | 1.00 |
| 2 | 136 | 1.55 (1.16-2.08) |
| 3 | 167 | 1.47 (1.12-1.93) |
| 4 | 165 | 1.70 (1.29-2.25) |
| 5 | 166 | 2.03 (1.54-2.69) |
|  | *Ptrend* | *<0.0001* |
| Physical Activity |  |  |
| 1 | 161 | 1.00 |
| 2 | 120 | 1.01 (0.76-1.34) |
| 3 | 136 | 1.41 (1.06-1.88) |
| 4 | 194 | 1.47 (1.14-1.90) |
| 5 | 154 | 1.86 (1.41-2.46) |
|  | *Ptrend* | *<0.0001* |
| Smoking |  |  |
| 1 | 132 | 1.00 |
| 2 | 139 | 1.15 (0.86-1.54) |
| 3 | 151 | 1.50 (1.12-2.01) |
| 4 | 171 | 1.53 (1.16-2.03) |
| 5 | 172 | 1.62 (1.22-2.15) |
|  | *Ptrend* | 0.0002 |
| BMI |  |  |
| 1 | 207 | 1.00 |
| 2 | 134 | 1.03 (0.79-1.34) |
| 3 | 85 | 1.12 (0.81-1.53) |
| 4 | 136 | 1.12 (0.85-1.46) |
| 5 | 203 | 1.90 (1.48-2.43) |
|  | *Ptrend* | *<0.0001* |

Abbreviations: BMI, body mass index; CI, confidence interval; CPRU, Cancer Prevention Research Unit; DIS, dietary inflammation score; LIS, lifestyle inflammation score; MAP, Markers of Adenomatous Polyps; MET, metabolic equivalent of task; NSAID, non-steroidal anti-inflammatory drug; OR, odds ratio

a Covariates in the LIS-equal weight unconditional logistic regression models were: age, sex, NSAID/aspirin use (</≥ once/week), hormone therapy use (among women), family history of colorectal cancer in a first degree relative (yes/no), former smoking status (former smoker or non-former smoker), total energy intake (kcal/day), study (MAP I, MAP II, or CPRU), the equally-weighted DIS, and the component removed from the LIS

b ﻿For inflammation score construction, see text and Table 1; higher scores indicate a higher balance of pro- versus anti-inflammatory exposures

**Supplemental References**

1. Kallio P, Kolehmainen M, Laaksonen DE, Kekäläinen J, Salopuro T, Sivenius K, *et al*. Dietary carbohydrate modification induces alterations in gene expression in abdominal subcutaneous adipose tissue in persons with the metabolic syndrome: the FUNGENUT Study. *Am J Clin Nutr* **2007**;85:1417–27.

2. Guzik T, Korbut R, Adamek-Guzik T. Nitric oxide and superoxide in inflammation and immune regulation. *J Physiol Pharmacol* **2003**;54:469–87.

3. Giugliano D, Ceriello A, Esposito K. The effects of diet on inflammation: emphasis on the metabolic syndrome. *J Am Coll Cardiol* **2006**;48:677–85.

4. Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA* **2002**;287:2414–23.

5. Prior RL, Gu L, Wu X, Jacob RA, Sotoudeh G, Kader AA, *et al*. Plasma antioxidant capacity changes following a meal as a measure of the ability of a food to alter in vivo antioxidant status. *J Am Coll Nutr* **2007**;26:170–81.

6. Espley R V, Butts CA, Laing WA, Martell S, Smith H, McGhie TK, *et al*. Dietary flavonoids from modified apple reduce inflammation markers and modulate gut microbiota in mice. *J Nutr* **2014**;144:146–54.

7. Codoñer-Franch P, Betoret E, Betoret N, López-Jaén AB, Valls-Belles V, Fito P. Dried apples enriched with mandarin juice by vacuum impregnation improve antioxidant capacity and decrease inflammation in obese children. *Nutr Hosp* **2013**;28:1177–83.

8. Dower JI, Geleijnse JM, Gijsbers L, Schalkwijk C, Kromhout D, Hollman PC. Supplementation of the pure flavonoids epicatechin and quercetin affects some biomarkers of endothelial dysfunction and inflammation in (pre)hypertensive adults: a randomized double-blind, placebo-controlled, crossover trial. *J Nutr* **2015**;145:1459–63.

9. Park JB. Javamide-II found in coffee is better than caffeine at suppressing TNF-α production in PMA/PHA-treated lymphocytic jurkat cells. *J Agric Food Chem* **2018**;66:6782–9.

10. Zitvogel L, Pietrocola F, Kroemer G. Nutrition, inflammation and cancer. *Nat Immunol* **2017**;18:843–50.

11. Kaulmann A, Bohn T. Carotenoids, inflammation, and oxidative stress—implications of cellular signaling pathways and relation to chronic disease prevention. *Nutr Res* **2014**;34:907–29.

12. Simopoulos AP. Omega-3 fatty acids in inflammation and autoimmune diseases. *J Am Coll Nutr* **2002**;21:495–505.

13. Calder PC. Omega-3 fatty Acids and inflammatory processes. *Nutrients* **2010**;2:355–74.

14. Govers MJ, Termont DS, Lapré JA, Kleibeuker JH, Vonk RJ, Van der Meer R. Calcium in milk products precipitates intestinal fatty acids and secondary bile acids and thus inhibits colonic cytotoxicity in humans. *Cancer Res* **1996**;56:3270–5.

15. Dash C, Goodman M, Flanders WD, Mink PJ, McCullough ML, Bostick RM. Using pathway-specific comprehensive exposure scores in epidemiology: application to oxidative balance in a pooled case-control study of incident, sporadic colorectal adenomas. *Am J Epidemiol* **2013**;178:610–24.

16. Kratz M, Baars T, Guyenet S. The relationship between high-fat dairy consumption and obesity, cardiovascular, and metabolic disease. *Eur J Nutr* **2013**;52:1–24.

17. Hussain T, Tan B, Liu G, Murtaza G, Rahu N, Saleem M, *et al*. Modulatory mechanism of polyphenols and Nrf2 Signaling Pathway in LPS challenged pregnancy disorders. *Oxid Med Cell Longev* **2017**;2017:1–14.

18. Johnson M, Pace RD, Mcelhenney WH. Green leafy vegetables in diets with a 25:1 omega-6/omega-3 fatty acid ratio modify the erythrocyte fatty acid profile of spontaneously hypertensive rats. *Lipids Health Dis* **2018**;17.

19. Sommerburg O, Keunen JE, Bird AC, van Kuijk FJ. Fruits and vegetables that are sources for lutein and zeaxanthin: the macular pigment in human eyes. *Br J Ophthalmol* **1998**;82:907–10.

20. Brown AA, Hu FB. Dietary modulation of endothelial function: implications for cardiovascular disease. *Am J Clin Nutr* **2001**;73:673–86.

21. Guardia T, Rotelli AE, Juarez AO, Pelzer LE. Anti-inflammatory properties of plant flavonoids. Effects of rutin, quercetin and hesperidin on adjuvant arthritis in rat. *Farmaco* **2001**;56:683–7.

22. Obeid R, Kirsch SH, Kasoha M, Eckert R, Herrmann W. Concentrations of unmetabolized folic acid and primary folate forms in plasma after folic acid treatment in older adults. *Metabolism* **2011**;60:673–80.

23. Kelly K, Kennelly J, Ordonez M, Nelson R, Leonard K, Stabler S, *et al*. Excess folic acid increases lipid storage, weight gain, and adipose tissue inflammation in high fat diet-fed rats. *Nutrients* **2016**;8:594.

24. Du S-Y, Zhang Y-L, Bai R-X, Ai Z-L, Xie B-S, Yang H-Y. Lutein prevents alcohol-induced liver disease in rats by modulating oxidative stress and inflammation. *Int J Clin Exp Med* **2015**;8:8785–93.

25. Wang M-X, Jiao J-H, Li Z-Y, Liu R-R, Shi Q, Ma L. Lutein supplementation reduces plasma lipid peroxidation and C-reactive protein in healthy nonsmokers. *Atherosclerosis* **2013**;227:380–5.

26. Johnson EJ. Role of lutein and zeaxanthin in visual and cognitive function throughout the lifespan. *Nutr Rev* **2014**;72:605–12.

27. Nidhi B, Sharavana G, Ramaprasad TR, Vallikannan B. Lutein derived fragments exhibit higher antioxidant and anti-inflammatory properties than lutein in lipopolysaccharide induced inflammation in rats. *Food Funct* **2015**;6:450–60.

28. Hartman TJ, Albert PS, Zhang Z, Bagshaw D, Kris-Etherton PM, Ulbrecht J, *et al*. Consumption of a legume-enriched, low-glycemic index diet is associated with biomarkers of insulin resistance and inflammation among men at risk for colorectal cancer. *J Nutr* **2010**;140:60–7.

29. Wall R, Ross RP, Fitzgerald GF, Stanton C. Fatty acids from fish: the anti-inflammatory potential of long-chain omega-3 fatty acids. *Nutr Rev* **2010**;68:280–9.

30. Casas-Agustench P, Bulló M, Salas-Salvadó J. Nuts, inflammation and insulin resistance. *Asia Pac J Clin Nutr* **2010**;19:124–30.

31. Ghanim H, Mohanty P, Pathak R, Chaudhuri A, Chang LS, Dandona P. Orange juice or fructose intake does not induce oxidative and inflammatory response. *Diabetes Care* **2007**;30:1406–11.

32. Knekt P, Kumpulainen J, Järvinen R, Rissanen H, Heliövaara M, Reunanen A, *et al*. Flavonoid intake and risk of chronic diseases. *Am J Clin Nutr* **2002**;76:560–8.

33. Fortis-Barrera Á, Alarcón-Aguilar FJ, Banderas-Dorantes T, Díaz-Flores M, Román-Ramos R, Cruz M, *et al*. Cucurbita ficifolia Bouché (Cucurbitaceae) and D-chiro-inositol modulate the redox state and inflammation in 3T3-L1 adipocytes. *J Pharm Pharmacol* **2013**;65:1563–76.

34. Sharma D, Rawat I, Goel HC. Anticancer and anti-inflammatory activities of some dietary cucurbits. *Indian J Exp Biol* **2015**;53:216–21.

35. Hale LP, Chichlowski M, Trinh CT, Greer PK. Dietary supplementation with fresh pineapple juice decreases inflammation and colonic neoplasia in IL-10-deficient mice with colitis. *Inflamm Bowel Dis* **2010**;16:2012–21.

36. Böhm F, Settergren M, Pernow J. Vitamin C blocks vascular dysfunction and release of interleukin-6 induced by endothelin-1 in humans in vivo. *Atherosclerosis* **2007**;190:408–15.

37. Alam MA, Subhan N, Rahman MM, Uddin SJ, Reza HM, Sarker SD. Effect of citrus flavonoids, naringin and naringenin, on metabolic syndrome and their mechanisms of action. *Adv Nutr* **2014**;5:404–17.

38. Jia Q, Cheng W, Yue Y, Hu Y, Zhang J, Pan X, *et al*. Cucurbitacin E inhibits TNF-α-induced inflammatory cytokine production in human synoviocyte MH7A cells via suppression of PI3K/Akt/NF-κB pathways. *Int Immunopharmacol* **2015**;29:884–90.

39. van Woudenbergh GJ, Kuijsten A, Tigcheler B, Sijbrands EJG, van Rooij FJA, Hofman A, *et al*. Meat consumption and its association with C-reactive protein and incident type 2 diabetes: the Rotterdam Study. *Diabetes Care* **2012**;35:1499–505.

40. van Bussel BC, Henry RM, Ferreira I, van Greevenbroek MM, van der Kallen CJ, Twisk JW, *et al*. A Healthy diet is associated with less endothelial dysfunction and less low-grade inflammation over a 7-Year period in adults at risk of cardiovascular disease. *J Nutr* **2015**;145:532–40.

41. White DL, Collinson A. Red meat, dietary heme iron, and risk of type 2 diabetes: the involvement of advanced lipoxidation endproducts. *Adv Nutr* **2013**;4:403–11.

42. Chassaing B, Koren O, Goodrich JK, Poole AC, Srinivasan S, Ley RE, *et al*. Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome. *Nature* **2015**;519:92–6.

43. Rao A V. Lycopene, tomatoes, and the prevention of coronary heart disease. *Exp Biol Med* **2002**;227:908–13.

44. Burton-Freeman BM, Sesso HD. Whole food versus supplement: comparing the clinical evidence of tomato intake and lycopene supplementation on cardiovascular risk factors. *Adv Nutr* **2014**;5:457–85.

45. Jacob K, Periago MJ, Böhm V, Berruezo GR. Influence of lycopene and vitamin C from tomato juice on biomarkers of oxidative stress and inflammation. *Br J Nutr* **2017**;99:137–46.

46. Markovits N, Amotz A, Levy Y. The effect of tomato-derived lycopene on low carotenoids and enhanced systemic inflammation and Oxidation in severe Obesity. *IMAJ* **2009**;11:598–601.

47. Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y, *et al*. Increased oxidative stress in obesity and its impact on metabolic syndrome. *J Clin Invest* **2004**;114:1752–61.

48. Calder PC, Ahluwalia N, Brouns F, Buetler T, Clement K, Cunningham K, *et al*. Dietary factors and low-grade inflammation in relation to overweight and obesity. *Br J Nutr* **2011**;106:S5–78.

49. Wu D, Zhai Q, Shi X. Alcohol-induced oxidative stress and cell responses. *J Gastroenterol Hepatol* **2006**;21:26–9.

50. Kumar Das S, Vasudevan DM. Alcohol-induced oxidative stress. *Life Sci* **2007**;81:177–87.

51. Mathews MJ, Liebenberg L, Mathews EH. The mechanism by which moderate alcohol consumption influences coronary heart disease. *Nutr J* **2015**;14:33.

52. McCarty M. Interleukin-6 as a central mediator of cardiovascular risk associated with chronic inflammation, smoking, diabetes, and visceral obsesity: down-regulation with essential fatty acids, ethanol and pentoxifylline. *Med Hypotheses* **1999**;52:465–77.

53. Gomez-Cabrera M-C, Domenech E, Viña J. Moderate exercise is an antioxidant: upregulation of antioxidant genes by training. *Free Radic Biol Med* **2008**;44:126–31.

54. van der Vaart H, Postma D, Timens W, Ten Hacken N. Acute effects of cigarette smoke on inflammation and oxidative stress: a review. *Thorax* **2004**;59:713–21.