**Supplementary Table S1.** Age-adjusted characteristics according to frequency of artificially sweetened beverage (ASB) intake among participants free of diabetes and cardiovascular disease in the Nurses’ Health Study at baseline (1 serving = 1 glass, bottle or can) (*n*=8,492).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Never or almost never** | **Less than once per week** | **Once to twice per week** | **Three to six times per week** | **One or more times per day** |
| **(n=3,204)** | **(n=1,394)** | **(n=799)** | **(n=1,979)** | **(n=1,116)** |
| Age at blood draw, years, mean (SD)\* | 61.0 (7.8) | 60.3 (7.7) | 59.8 (7.8) | 58.4 (7.3) | 55.8 (7.4) |
| BMI, kg/m2, mean (SD) | 24.6 (4.5) | 25.3 (4.4) | 25.9 (4.6) | 26.1 (4.6) | 27.6 (5.6) |
| Postmenopausal hormone use (%) | 41.8 | 39.5 | 39.8 | 39.4 | 41.0 |
| Smoking status (%) |  |  |  |  |  |
| Never | 48.7 | 46.4 | 46.1 | 41.6 | 36.9 |
| Former | 34.6 | 41.7 | 44.3 | 49.3 | 50.3 |
| Current | 16.7 | 11.9 | 9.6 | 9.2 | 12.8 |
| Alcohol intake, g/d, mean (SD) | 5.19 (9.66) | 5.26 (9.41) | 5.31 (9.88) | 5.82 (9.68) | 5.27 (9.18) |
| Physical activity, metabolic equivalent-h/wk, mean (SD) | 16.2 (21.9) | 16.7 (22.9) | 16.4 (17.7) | 17.9 (24.0) | 17.0 (19.3) |
| Total energy intake, kcal/d, mean (SD) | 1798 (528) | 1767 (480) | 1804 (510) | 1752 (501) | 1748 (524) |
| Alternative Healthy Eating Index, mean (SD)† | 49.8 (10.1) | 50.6 (9.7) | 50.9 (9.4) | 51.2 (9.7) | 49.4 (9.3) |
| Hypertension (%) | 27.8 | 28.9 | 31.6 | 30.1 | 35.4 |
| Hypercholesterolemia (%) | 41.3 | 43.8 | 46.7 | 45.1 | 47.1 |
| Fetuin-A, μg/ml, mean (SD)‡ | 457.2 (105.4) | 465.5 (90.9) | 468.6 (91.7) | 462.3 (116.6) | 478.0 (110.6) |
| Alanine transaminase, U/l, mean (SD)‡ | 19.1 (9.7) | 19 (8.6) | 18.8 (8.1) | 19 (8.8) | 19.5 (8.5) |
| Gamma-glutamyl transferase, U/l, mean (SD)‡ | 23.9 (31.9) | 23.2 (22.9) | 20.9 (23.9) | 23.0 (26.8) | 24.5 (23.9) |
| Triglyceride, mmol/l, median (IQR)‡ | 2.66 (1.96) | 2.73 (1.83) | 2.96 (2.09) | 2.78 (1.89) | 2.74 (1.90) |
| Total cholesterol/high-density lipoprotein cholesterol ratio, mean (SD)‡ | 3.77 (1.29) | 3.76 (1.47) | 3.91 (1.38) | 3.91 (1.54) | 3.84 (1.30) |
| High-density lipoprotein cholesterol, mmol/l, median (IQR)‡ | 1.56 (0.54) | 1.5 (0.53) | 1.48 (0.57) | 1.52 (0.59) | 1.52 (0.50) |
| Low-density lipoprotein cholesterol, mmol/l, median (IQR)‡ | 3.35 (1.28) | 3.27 (1.30) | 3.38 (1.05) | 3.43 (1.39) | 3.19 (1.17) |
| Total cholesterol, mmol/l, median (IQR)‡ | 5.59 (1.36) | 5.53 (1.27) | 5.54 (1.41) | 5.57 (1.34) | 5.49 (1.32) |
| C-reactive protein, mg/l, median (IQR)‡ | 1.75 (2.85) | 1.75 (2.81) | 1.66 (2.95) | 1.72 (3.15) | 2.21 (3.71) |
| Intracellular adhesion molecule 1, ng/ml, median (IQR)‡ | 233.4 (72.9) | 229.1 (69.9) | 230.5 (66.7) | 222.7 (57.0) | 227.5 (66.1) |
| Vascular cell adhesion protein 1, ng/ml, median (IQR)‡ | 607.7 (184.9) | 597.1 (151.8) | 594.6 (206.7) | 590.6 (148.6) | 596.5 (175.0) |
| Adiponectin, μg/ml, mean (SD)‡ | 10.8 (5.2) | 11.1 (5.5) | 10.9 (5.4) | 10.9 (5.5) | 10.1 (5.5) |
| Insulin, μU/ml, median (IQR)‡ | 5.52 (3.60) | 5.90 (4.16) | 6.11 (4.64) | 5.93 (4.22) | 6.07 (4.26) |
| Hemoglobin A1c, %, mean (SD)‡ | 5.40 (0.32) | 5.39 (0.30) | 5.38 (0.32) | 5.36 (0.34) | 5.39 (0.32) |

\* Baseline defined as the time of blood draw (1990 or 2000).

† SSB intake was excluded in the calculation.

‡ Not age-adjusted.

**Supplementary Table S2.** Age-adjusted characteristics according to frequency of fruit juice intake among participants free of diabetes and cardiovascular disease in the Nurses’ Health Study at baseline (1 serving = 1 glass, bottle or can) (*n*=8,492).1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Never or almost never** | **Less than once per week** | **Once to twice per week** | **Three to six times per week** | **One or more times per day** |
| **(n=731)** | **(n=1,039)** | **(n=945)** | **(n=3,141)** | **(n=2,636)** |
| Age at blood draw, years, mean (SD)1 | 59.3 (7.5) | 58.5 (8.0) | 58.7 (7.8) | 59.4 (7.8) | 60.3 (7.7) |
| BMI, kg/m2, mean (SD) | 25.7 (5.0) | 25.8 (5.0) | 25.8 (4.7) | 25.8 (4.9) | 25.2 (4.5) |
| Postmenopausal hormone use (%) | 38.9 | 41.0 | 40.3 | 40.8 | 40.5 |
| Smoking status (%) |  |  |  |  |  |
| Never | 39.5 | 38.1 | 42.6 | 45.0 | 49.8 |
| Former | 46.4 | 44.9 | 44.4 | 41.9 | 39.5 |
| Current | 14.1 | 16.9 | 13.0 | 13.1 | 10.6 |
| Alcohol intake, g/d, mean (SD) | 4.34 (9.22) | 5.35 (10.29) | 5.54 (10.39) | 5.63 (9.75) | 5.43 (8.84) |
| Physical activity, metabolic equivalent-h/wk, mean (SD) | 18.4 (21.5) | 14.2 (17.0) | 16.1 (19.2) | 16.9 (19.7) | 17.5 (27.0) |
| Total energy intake, kcal/d, mean (SD) | 1511 (470) | 1588 (496) | 1695 (480) | 1788 (499) | 1927 (504) |
| Alternative Healthy Eating Index, mean (SD)2 | 50.9 (9.9) | 49.1 (10.6) | 49.8 (9.7) | 50.4 (9.7) | 51.0 (9.6) |
| Hypertension (%) | 29.4 | 28.6 | 29.6 | 30.3 | 30.4 |
| Hypercholesterolemia (%) | 42.4 | 43.1 | 43.1 | 44.4 | 43.5 |
| Fetuin-A, μg/ml, mean (SD)3 | 468.8 (116.7) | 475.3 (122.9) | 456.3 (93.6) | 461.8 (100.9) | 460.8 (103.5) |
| Alanine transaminase, U/l, mean (SD)3 | 19.2 (6.9) | 18.0 (6.7) | 19.7 (7.9) | 19.6 (11.2) | 18.7 (7.7) |
| Gamma-glutamyl transferase, U/l, mean (SD)3 | 24.6 (29.9) | 22.2 (24.6) | 20.9 (15.0) | 24.4 (35.0) | 23.2 (21.6) |
| Triglyceride, mmol/l, median (IQR)3 | 2.51 (1.84) | 2.56 (1.84) | 2.65 (1.96) | 2.77 (1.94) | 2.82 (1.93) |
| Total cholesterol/high-density lipoprotein cholesterol ratio, mean (SD)3 | 3.68 (1.29) | 3.77 (1.32) | 3.94 (1.75) | 3.87 (1.43) | 3.78 (1.25) |
| High-density lipoprotein cholesterol, mmol/l, median (IQR)3 | 1.61 (0.48) | 1.55 (0.55) | 1.48 (0.53) | 1.53 (0.56) | 1.54 (0.56) |
| Low-density lipoprotein cholesterol, mmol/l, median (IQR)3 | 3.39 (1.17) | 3.32 (1.31) | 3.27 (1.33) | 3.38 (1.3) | 3.35 (1.16) |
| Total cholesterol, mmol/l, median (IQR)3 | 5.57 (1.38) | 5.48 (1.4) | 5.47 (1.36) | 5.62 (1.32) | 5.56 (1.33) |
| C-reactive protein, mg/l, median (IQR)3 | 1.76 (2.96) | 1.78 (3.01) | 1.73 (2.80) | 1.82 (3.02) | 1.77 (3.06) |
| Intracellular adhesion molecule 1, ng/ml, median (IQR)3 | 227.0 (77.0) | 227.8 (77.3) | 226.9 (75.5) | 229.0 (64.0) | 230.3 (65.6) |
| Vascular cell adhesion protein 1, ng/ml, median (IQR)3 | 615.7 (184.5) | 594.6 (146.4) | 586.1 (180.4) | 595.6 (194.5) | 599.8 (158.7) |
| Adiponectin, μg/ml, mean (SD)3 | 11.5 (5.7) | 10.7 (5.2) | 10.7 (5.5) | 10.7 (5.3) | 10.8 (5.3) |
| Insulin, μU/ml, median (IQR)3 | 5.48 (3.79) | 5.53 (4.43) | 6.09 (4.43) | 5.90 (3.88) | 5.74 (3.82) |
| Hemoglobin A1c, %, mean (SD)3 | 5.38 (0.36) | 5.37 (0.29) | 5.38 (0.31) | 5.38 (0.30) | 5.40 (0.35) |

1 Baseline defined as the time of blood draw (1990 or 2000).

2 SSB intake was excluded in the calculation.

3 Not age-adjusted.

**Supplementary Table S3.** Least-squares mean (95% CI) concentrations of biomarkers by frequency of sugar sweetened beverage (SSB) intake among participants free of diabetes and cardiovascular disease whose blood samples were collected in 1989-1990 (biospecimen collection cycle 1) in the Nurses’ Health Study (*n*=6,961).1

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker Concentration** | **Frequency of SSB Intake** | | | | |  |
| **Never or almost never** | **Less than once per week** | **Once to twice per week** | **Three to six times per week** | **Once per day or more** | ***P* for trend** |
| **Hepatic Biomarkers** | | | | | | |
| **Fetuin-A (μg/ml)** | | | | | | |
| N | 352 | 232 | 113 | 118 | 38 |  |
| Model 1 | 459.5 (5.8) | 458.8 (7.2) | 457.2 (10.3) | 458.8 (10.1) | 506.4 (17.9) | 0.03 |
| Model 2 | 460.8 (6.3) | 456.8 (7.3) | 456.7 (10.4) | 454.1 (10.5) | 504.9 (18.7) | 0.07 |
| **Alanine transaminase (U/l)** | | | | | |  |
| N | 323 | 243 | 112 | 129 | 44 |  |
| Model 1 | 20.0 (0.6) | 18.7 (0.6) | 17.4 (1.0) | 18.9 (0.9) | 20.0 (1.5) | 0.94 |
| Model 2 | 20.0 (0.6) | 18.6 (0.7) | 17.5 (1.0) | 18.9 (0.9) | 19.0 (1.6) | 0.67 |
| **Gamma-glutamyl transferase (U/l)** | | | | | |  |
| N | 323 | 241 | 112 | 129 | 44 |  |
| Model 1 | 23.6 (1.7) | 22.7 (2.0) | 19.7 (2.9) | 24.0 (2.7) | 21.4 (4.7) | 0.79 |
| Model 2 | 23.0 (1.8) | 22.7 (2.0) | 20.3 (2.9) | 23.7 (2.8) | 19.5 (4.8) | 0.73 |
| **Lipid Biomarkers** | | | | | | |
| **Triglyceride (mmol/l)** | | | | | | |
| N | 846 | 619 | 284 | 358 | 100 |  |
| Model 1 | 2.50 (0.04) | 2.65 (0.05) | 2.52 (0.07) | 2.81 (0.07) | 3.03 (0.14) | <0.0001 |
| Model 2 | 2.53 (0.05) | 2.67 (0.05) | 2.55 (0.07) | 2.80 (0.07) | 2.90 (0.14) | 0.003 |
| **Total cholesterol/high-density lipoprotein cholesterol ratio** | | | | | | |
| N | 1,073 | 779 | 361 | 423 | 119 |  |
| Model 1 | 3.76 (0.04) | 3.77 (0.05) | 3.72 (0.07) | 3.93 (0.07) | 4.41 (0.12) | <0.0001 |
| Model 2 | 3.90 (0.04) | 3.91 (0.05) | 3.80 (0.07) | 3.96 (0.06) | 4.32 (0.12) | 0.002 |
| **High-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 1,103 | 802 | 377 | 448 | 125 |  |
| Model 1 | 1.55 (0.01) | 1.53 (0.02) | 1.56 (0.02) | 1.46 (0.02) | 1.36 (0.03) | <0.0001 |
| Model 2 | 1.51 (0.01) | 1.49 (0.01) | 1.53 (0.02) | 1.46 (0.02) | 1.41 (0.03) | 0.005 |
| **Low-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 596 | 415 | 196 | 236 | 73 |  |
| Model 1 | 3.20 (0.04) | 3.28 (0.05) | 3.32 (0.07) | 3.23 (0.06) | 3.17 (0.1) | 0.79 |
| Model 2 | 3.22 (0.04) | 3.31 (0.05) | 3.34 (0.07) | 3.26 (0.06) | 3.09 (0.1) | 0.19 |
| **Total cholesterol (mmol/l)** | | | | | | |
| N | 1,351 | 983 | 437 | 555 | 160 |  |
| Model 1 | 5.49 (0.03) | 5.48 (0.03) | 5.46 (0.05) | 5.47 (0.04) | 5.57 (0.08) | 0.50 |
| Model 2 | 5.51 (0.03) | 5.52 (0.03) | 5.51 (0.05) | 5.51 (0.04) | 5.61 (0.08) | 0.37 |
| **Inflammatory Biomarkers** | | | | | | |
| **C-reactive protein (mg/l)** | | | | | | |
| N | 1,837 | 1,385 | 604 | 831 | 235 |  |
| Model 1 | 1.54 (0.04) | 1.55 (0.04) | 1.54 (0.07) | 1.72 (0.06) | 2.26 (0.15) | <0.0001 |
| Model 2 | 1.54 (0.04) | 1.61 (0.04) | 1.58 (0.06) | 1.66 (0.06) | 2.07 (0.13) | 0.0001 |
| **Intracellular adhesion molecule 1 (ng/ml)** | | | | | | |
| N | 627 | 450 | 189 | 268 | 65 |  |
| Model 1 | 224.7 (2.2) | 230.3 (2.7) | 230.7 (4.2) | 228.5 (3.5) | 247.7 (7.6) | 0.01 |
| Model 2 | 231.5 (2.4) | 236.8 (2.7) | 238.6 (4.2) | 235.3 (3.6) | 247.7 (7.5) | 0.09 |
| **Vascular cell adhesion protein 1 (ng/ml)** | | | | | | |
| N | 460 | 341 | 138 | 214 | 52 |  |
| Model 1 | 588.6 (6.5) | 595.9 (7.6) | 607.4 (12.1) | 595.6 (9.6) | 640.0 (20.5) | 0.03 |
| Model 2 | 585.3 (6.9) | 591.3 (7.5) | 609.1 (12.1) | 589.6 (10.0) | 638.7 (21.0) | 0.09 |
| **Metabolic Biomarkers** | | | | | | |
| **Adiponectin (μg/ml)** | | | | | | |
| N | 2,039 | 1,491 | 632 | 868 | 238 |  |
| Model 1 | 11.2 (0.1) | 10.9 (0.1) | 10.5 (0.2) | 10.0 (0.2) | 9.5 (0.4) | <0.0001 |
| Model 2 | 11.0 (0.1) | 10.6 (0.1) | 10.4 (0.2) | 10.1 (0.2) | 9.8 (0.4) | <0.0001 |
| **Insulin (μU/ml)** | | | | | | |
| N | 588 | 440 | 192 | 282 | 70 |  |
| Model 1 | 4.43 (0.14) | 4.87 (0.18) | 4.57 (0.25) | 6.09 (0.28) | 5.12 (0.45) | 0.0009 |
| Model 2 | 4.42 (0.16) | 4.88 (0.19) | 4.55 (0.25) | 5.65 (0.26) | 4.43 (0.38) | 0.20 |
| **Hemoglobin A1c (%)** | | | | | | |
| N | 1,420 | 991 | 457 | 588 | 167 |  |
| Model 1 | 5.36 (0.01) | 5.37 (0.01) | 5.37 (0.01) | 5.40 (0.01) | 5.41 (0.02) | 0.01 |
| Model 2 | 5.38 (0.01) | 5.38 (0.01) | 5.38 (0.01) | 5.40 (0.01) | 5.39 (0.02) | 0.21 |

1 Biomarker sample sizes vary: fetuin-A (n = 853), alanine transaminase (n = 851), gamma-glutamyl transferase (n = 849), triglyceride (n = 2,207), total cholesterol/high-density lipoprotein cholesterol ratio (n = 2,755), high-density lipoprotein cholesterol (n = 2,855), low-density lipoprotein cholesterol (n = 1,516), total cholesterol (n = 3,486), C-reactive protein (n = 4,892), intracellular adhesion molecule 1 (n = 1,599), vascular cell adhesion protein 1 (n = 1,205), adiponectin (n = 5,268), insulin (n = 1,572), hemoglobin A1c (n = 3,623). Values were determined using general linear models. Model 1 was adjusted for age at blood draw, fasting status (yes / no), and time of blood draw (blood collection cycle 1/2). Model 2 was adjusted for the variables in Model 1 plus smoking status (current / former / never), alcohol intake (continuous), physical activity (tertile), total energy intake (tertile), Alternate Healthy Eating Index score excluding sugar sweetened beverage (tertile), postmenopausal hormone use (yes / no), and BMI (continuous).

**Supplementary Table S4.** Least-squares mean (95% CI) concentrations of biomarkers by frequency of sugar sweetened beverage (SSB) intake among participants free of diabetes and cardiovascular disease whose blood samples were collected in 2000-2001 (biospecimen collection cycle 2) in the Nurses’ Health Study (*n*=1,531).1

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker Concentration** | **Frequency of SSB Intake** | | | | |  |
| **Never or almost never** | **Less than once per week** | **Once to twice per week** | **Three to six times per week** | **Once per day or more** | ***P* for trend** |
| **Hepatic Biomarkers** | | | | | | |
| **Fetuin-A (μg/ml)** | | | | | | |
| N | 157 | 167 | 86 | 116 | 30 |  |
| Model 1 | 457.5 (7.8) | 474.0 (7.6) | 469.1 (10.6) | 463.8 (9.2) | 475.8 (18.0) | 0.64 |
| Model 2 | 453.0 (9.9) | 467.6 (9.5) | 462.9 (12.0) | 459.5 (10.1) | 482.4 (19.6) | 0.38 |
| **Alanine transaminase (U/l)** | | | | | |  |
| N | 133 | 139 | 75 | 93 | 27 |  |
| Model 1 | 19.1 (0.6) | 19.1 (0.6) | 19.1 (0.8) | 19.4 (0.7) | 17.2 (1.3) | 0.31 |
| Model 2 | 19.0 (0.7) | 19.2 (0.7) | 18.6 (0.9) | 19.4 (0.8) | 17.8 (1.4) | 0.59 |
| **Gamma-glutamyl transferase (U/l)** | | | | | |  |
| N | 133 | 139 | 75 | 93 | 27 |  |
| Model 1 | 24.8 (1.8) | 23.2 (1.8) | 26.8 (2.4) | 23.3 (2.1) | 27.3 (4.0) | 0.63 |
| Model 2 | 25.5 (2.3) | 24.6 (2.2) | 27.4 (2.7) | 25.1 (2.4) | 29.8 (4.3) | 0.49 |
| **Lipid Biomarkers** | | | | | | |
| **Triglyceride (mmol/l)** | | | | | | |
| N | 312 | 334 | 162 | 232 | 82 |  |
| Model 1 | 2.96 (0.07) | 2.97 (0.07) | 3.13 (0.11) | 3.20 (0.09) | 3.33 (0.16) | 0.005 |
| Model 2 | 2.96 (0.09) | 2.96 (0.08) | 3.07 (0.11) | 3.14 (0.10) | 3.23 (0.16) | 0.06 |
| **Total cholesterol/high-density lipoprotein cholesterol ratio** | | | | | | |
| N | 25 | 29 | 11 | 24 | 3 |  |
| Model 1 | 3.64 (0.46) | 3.80 (0.42) | 3.79 (0.69) | 4.77 (0.46) | 3.22 (1.30) | 0.41 |
| Model 2 | 3.74 (0.56) | 3.72 (0.53) | 3.29 (0.79) | 4.95 (0.55) | 3.61 (1.70) | 0.55 |
| **High-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 54 | 52 | 17 | 40 | 18 |  |
| Model 1 | 1.65 (0.06) | 1.51 (0.06) | 1.64 (0.11) | 1.45 (0.06) | 1.43 (0.09) | 0.07 |
| Model 2 | 1.54 (0.06) | 1.50 (0.06) | 1.61 (0.10) | 1.47 (0.07) | 1.46 (0.09) | 0.49 |
| **Low-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 54 | 52 | 17 | 40 | 18 |  |
| Model 1 | 3.27 (0.12) | 3.22 (0.12) | 3.51 (0.23) | 3.38 (0.14) | 2.92 (0.19) | 0.25 |
| Model 2 | 3.33 (0.14) | 3.23 (0.14) | 3.52 (0.24) | 3.44 (0.17) | 2.97 (0.2) | 0.28 |
| **Total cholesterol (mmol/l)** | | | | | | |
| N | 153 | 158 | 74 | 126 | 37 |  |
| Model 1 | 5.77 (0.08) | 5.64 (0.08) | 5.70 (0.11) | 5.73 (0.09) | 5.62 (0.15) | 0.66 |
| Model 2 | 5.71 (0.1) | 5.61 (0.09) | 5.65 (0.12) | 5.68 (0.10) | 5.64 (0.16) | 0.94 |
| **Inflammatory Biomarkers** | | | | | | |
| **C-reactive protein (mg/l)** | | | | | | |
| N | 290 | 293 | 137 | 197 | 78 |  |
| Model 1 | 2.40 (0.13) | 2.26 (0.13) | 2.44 (0.19) | 2.49 (0.17) | 2.39 (0.24) | 0.71 |
| Model 2 | 2.40 (0.15) | 2.27 (0.14) | 2.43 (0.20) | 2.50 (0.17) | 2.47 (0.25) | 0.55 |
| **Intracellular adhesion molecule 1 (ng/ml)** | | | | | | |
| N | 185 | 206 | 99 | 134 | 48 |  |
| Model 1 | 228.3 (3.7) | 223.2 (3.4) | 242.9 (5.3) | 239.5 (4.5) | 236.2 (7.3) | 0.04 |
| Model 2 | 242.2 (4.5) | 236.2 (4.3) | 253.1 (5.9) | 247.8 (5.0) | 246.6 (8.1) | 0.24 |
| **Metabolic Biomarkers** | | | | | | |
| **Adiponectin (μg/ml)** | | | | | | |
| N | 215 | 220 | 107 | 153 | 45 |  |
| Model 1 | 11.7 (0.3) | 11.3 (0.3) | 10.8 (0.4) | 10.6 (0.4) | 8.7 (0.7) | <0.0001 |
| Model 2 | 11.5 (0.4) | 11.0 (0.4) | 10.8 (0.5) | 10.4 (0.4) | 8.5 (0.7) | <0.0001 |
| **Insulin (μU/ml)** | | | | | | |
| N | 324 | 337 | 164 | 244 | 84 |  |
| Model 1 | 4.63 (0.16) | 4.97 (0.17) | 5.64 (0.27) | 5.10 (0.20) | 5.54 (0.36) | 0.008 |
| Model 2 | 4.55 (0.17) | 5.04 (0.19) | 5.49 (0.26) | 5.26 (0.21) | 5.65 (0.35) | 0.009 |
| **Hemoglobin A1c (%)** | | | | | | |
| N | 207 | 213 | 106 | 150 | 59 |  |
| Model 1 | 5.42 (0.02) | 5.42 (0.02) | 5.51 (0.03) | 5.47 (0.03) | 5.46 (0.04) | 0.21 |
| Model 2 | 5.46 (0.03) | 5.46 (0.03) | 5.52 (0.03) | 5.49 (0.03) | 5.47 (0.05) | 0.51 |

1 Biomarker sample sizes vary: fetuin-A (n = 556), alanine transaminase (n = 467), gamma-glutamyl transferase (n = 467), triglyceride (n = 1,122), total cholesterol/high-density lipoprotein cholesterol ratio (n = 92), high-density lipoprotein cholesterol (n = 181), low-density lipoprotein cholesterol (n = 181), total cholesterol (n = 548), C-reactive protein (n = 995), intracellular adhesion molecule 1 (n =672), adiponectin (n = 740), insulin (n = 1,153), hemoglobin A1c (n = 735). Values were determined using general linear models. Model 1 was adjusted for age at blood draw, fasting status (yes / no), and time of blood draw (blood collection cycle 1/2). Model 2 was adjusted for the variables in Model 1 plus smoking status (current / former / never), alcohol intake (tertile), physical activity (tertile), total energy intake (continuous), Alternate Healthy Eating Index score excluding sugar sweetened beverage (tertile), postmenopausal hormone use (yes / no), and BMI (continuous).

**Supplementary Table S5.** Least-squares mean (95% CI) concentrations of biomarkers by frequency of cola intake among participants free of diabetes and cardiovascular disease in the Nurses’ Health Study (*n*=8,492).1

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker Concentration** | **Frequency of Cola Intake** | | | | |  |
| **Never or almost never** | **Less than once per week** | **Once to twice per week** | **Three to six times per week** | **Once per day or more** | ***P* for trend** |
| **Hepatic Biomarkers** | | | | | | |
| **Fetuin-A (μg/ml)** | | | | | | |
| N | 866 | 342 | 87 | 91 | 23 |  |
| Model 1 | 459.7 (3.6) | 467.1 (5.7) | 476.0 (11.3) | 458.4 (11.1) | 509.2 (22.0) | 0.05 |
| Model 2 | 458.1 (4.2) | 465.5 (6.0) | 467.8 (11.6) | 460.2 (11.4) | 517.3 (22.9) | 0.03 |
| **Alanine transaminase (U/l)** | | | | | |  |
| N | 799 | 302 | 97 | 98 | 22 |  |
| Model 1 | 19.3 (0.3) | 19.2 (0.5) | 17.0 (0.9) | 19.1 (0.9) | 17.7 (1.9) | 0.27 |
| Model 2 | 19.1 (0.4) | 18.9 (0.5) | 17.2 (0.9) | 19.2 (1.0) | 18.6 (2.0) | 0.75 |
| **Gamma-glutamyl transferase (U/l)** | | | | | |  |
| N | 797 | 302 | 97 | 98 | 22 |  |
| Model 1 | 23.4 (1.0) | 25.0 (1.6) | 19.6 (2.8) | 22.2 (2.8) | 24.5 (6.0) | 0.78 |
| Model 2 | 23.5 (1.1) | 25.7 (1.6) | 20.4 (2.8) | 21.2 (2.9) | 27.6 (6.0) | 0.98 |
| **Lipid Biomarkers** | | | | | | |
| **Triglyceride (mmol/l)** | | | | | | |
| N | 2,045 | 744 | 207 | 271 | 62 |  |
| Model 1 | 2.69 (0.03) | 2.86 (0.05) | 2.70 (0.09) | 2.99 (0.09) | 3.07 (0.18) | 0.001 |
| Model 2 | 2.72 (0.03) | 2.89 (0.05) | 2.73 (0.09) | 3.01 (0.09) | 2.97 (0.17) | 0.02 |
| **Total cholesterol/high-density lipoprotein cholesterol ratio** | | | | | | |
| N | 1,726 | 686 | 185 | 200 | 50 |  |
| Model 1 | 3.79 (0.03) | 3.82 (0.05) | 3.73 (0.10) | 4.04 (0.10) | 4.41 (0.20) | 0.0003 |
| Model 2 | 3.94 (0.08) | 3.94 (0.08) | 3.80 (0.12) | 4.03 (0.11) | 4.45 (0.20) | 0.008 |
| **High-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 1,826 | 728 | 196 | 228 | 58 |  |
| Model 1 | 1.55 (0.01) | 1.51 (0.02) | 1.57 (0.03) | 1.41 (0.03) | 1.35 (0.05) | <0.0001 |
| Model 2 | 1.50 (0.02) | 1.48 (0.02) | 1.55 (0.03) | 1.42 (0.03) | 1.37 (0.05) | 0.002 |
| **Low-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 1,017 | 399 | 112 | 135 | 34 |  |
| Model 1 | 3.25 (0.03) | 3.27 (0.05) | 3.26 (0.09) | 3.10 (0.07) | 3.27 (0.15) | 0.49 |
| Model 2 | 3.23 (0.05) | 3.24 (0.06) | 3.25 (0.09) | 3.07 (0.08) | 3.23 (0.15) | 0.41 |
| **Total cholesterol (mmol/l)** | | | | | | |
| N | 2,453 | 933 | 257 | 314 | 77 |  |
| Model 1 | 5.53 (0.02) | 5.49 (0.03) | 5.5 (0.06) | 5.47 (0.05) | 5.50 (0.11) | 0.48 |
| Model 2 | 5.55 (0.03) | 5.53 (0.04) | 5.55 (0.07) | 5.49 (0.06) | 5.56 (0.12) | 0.80 |
| **Inflammatory Biomarkers** | | | | | | |
| **C-reactive protein (mg/l)** | | | | | | |
| N | 3,554 | 1,363 | 374 | 480 | 116 |  |
| Model 1 | 1.67 (0.03) | 1.65 (0.05) | 1.96 (0.10) | 1.94 (0.09) | 2.35 (0.21) | <0.0001 |
| Model 2 | 1.71 (0.04) | 1.78 (0.05) | 2.05 (0.11) | 1.84 (0.09) | 2.21 (0.19) | 0.002 |
| **Intracellular adhesion molecule 1 (ng/ml)** | | | | | | |
| N | 1,387 | 531 | 130 | 182 | 41 |  |
| Model 1 | 226.6 (1.5) | 229.8 (2.4) | 241.9 (5.1) | 239.9 (4.3) | 234.8 (8.6) | 0.01 |
| Model 2 | 236.4 (1.8) | 239.5 (2.6) | 252.3 (5.2) | 244.6 (4.3) | 239.6 (8.9) | 0.16 |
| **Vascular cell adhesion protein 1 (ng/ml)** | | | | | | |
| N | 726 | 274 | 72 | 110 | 23 |  |
| Model 1 | 593.4 (5.2) | 590.9 (8.4) | 617.8 (16.9) | 610.8 (13.6) | 611.2 (29.0) | 0.21 |
| Model 2 | 590.0 (5.5) | 589.7 (8.5) | 613.0 (16.8) | 605.5 (13.8) | 602.8 (29.4) | 0.45 |
| **Metabolic Biomarkers** | | | | | | |
| **Adiponectin (μg/ml)** | | | | | | |
| N | 3,675 | 1,384 | 385 | 459 | 105 |  |
| Model 1 | 11.1 (0.1) | 10.5 (0.1) | 10.5 (0.3) | 9.7 (0.2) | 9.0 (0.5) | <0.0001 |
| Model 2 | 10.8 (0.1) | 10.2 (0.2) | 10.3 (0.3) | 9.8 (0.3) | 9.0 (0.5) | <0.0001 |
| **Insulin (μU/ml)** | | | | | | |
| N | 1,682 | 594 | 158 | 236 | 55 |  |
| Model 1 | 4.75 (0.08) | 5.01 (0.15) | 5.80 (0.32) | 5.64 (0.26) | 4.78 (0.44) | 0.05 |
| Model 2 | 4.70 (0.10) | 5.09 (0.15) | 5.70 (0.30) | 5.35 (0.24) | 4.56 (0.39) | 0.25 |
| **Hemoglobin A1c (%)** | | | | | | |
| N | 2,643 | 1,017 | 266 | 353 | 79 |  |
| Model 1 | 5.38 (0.01) | 5.39 (0.01) | 5.42 (0.02) | 5.42 (0.02) | 5.39 (0.04) | 0.11 |
| Model 2 | 5.41 (0.01) | 5.42 (0.01) | 5.43 (0.02) | 5.42 (0.02) | 5.40 (0.04) | 0.59 |

1 Biomarker sample sizes vary: fetuin-A (n = 1,409), alanine transaminase (n = 1,318), gamma-glutamyl transferase (n = 1,316), triglyceride (n = 3,329), total cholesterol/high-density lipoprotein cholesterol ratio (n = 2,847), high-density lipoprotein cholesterol (n = 3,036), low-density lipoprotein cholesterol (n = 1,697), total cholesterol (n = 4,034), C-reactive protein (n = 5,887), intracellular adhesion molecule 1 (n = 2,271), vascular cell adhesion protein 1 (n = 1,205), adiponectin (n = 6,008), insulin (n = 2,725), hemoglobin A1c (n = 4,358). Values were determined using general linear models. Model 1 was adjusted for age at blood draw, fasting status (yes / no), and time of blood draw (blood collection cycle 1/2). Model 2 was adjusted for the variables in Model 1 plus smoking status (current / former / never), alcohol intake (continuous), physical activity (tertile), total energy intake (tertile), Alternate Healthy Eating Index score excluding sugar sweetened beverage (tertile), postmenopausal hormone use (yes / no), and BMI (continuous).

**Supplementary Table S6.** Least-squares mean (95% CI) concentrations of biomarkers by frequency of non-cola carbonated beverage intake among participants free of diabetes and cardiovascular disease in the Nurses’ Health Study (*n*=8,492).1

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker Concentration** | **Frequency of Non-cola Carbonated Beverage Intake** | | | | |  |
| **Never or almost never** | **Less than once per week** | **Once to twice per week** | **Three to six times per week** | **Once per day or more** | ***P* for trend** |
| **Hepatic Biomarkers** | | | | | | |
| **Fetuin-A (μg/ml)** | | | | | | |
| N | 1,022 | 309 | 51 | 23 | 4 |  |
| Model 1 | 464.6 (3.3) | 461.2 (6.0) | 458.2 (14.8) | 445.2 (22.0) | 429.6 (52.7) | 0.25 |
| Model 2 | 463.9 (3.8) | 459.5 (6.5) | 451.8 (15.2) | 446.8 (22.5) | 423.0 (52.1) | 0.20 |
| **Alanine transaminase (U/l)** | | | | | |  |
| N | 952 | 280 | 49 | 33 | 4 |  |
| Model 1 | 19.2 (0.3) | 19.2 (0.5) | 17.9 (1.3) | 16.3 (1.6) | 22.4 (4.5) | 0.31 |
| Model 2 | 19.0 (0.3) | 18.9 (0.6) | 17.9 (1.3) | 16.9 (1.6) | 23.0 (4.5) | 0.67 |
| **Gamma-glutamyl transferase (U/l)** | | | | | |  |
| N | 951 | 279 | 49 | 33 | 4 |  |
| Model 1 | 23.5 (0.9) | 23.7 (1.7) | 19.3 (4.0) | 21.3 (4.9) | 46.7 (13.9) | 0.65 |
| Model 2 | 23.5 (1.0) | 24.5 (1.7) | 19.8 (4.0) | 22.8 (4.8) | 48.0 (13.4) | 0.37 |
| **Lipid Biomarkers** | | | | | | |
| **Triglyceride (mmol/l)** | | | | | | |
| N | 2,370 | 749 | 122 | 79 | 9 |  |
| Model 1 | 2.74 (0.03) | 2.82 (0.05) | 2.71 (0.11) | 2.78 (0.14) | 2.90 (0.40) | 0.73 |
| Model 2 | 2.78 (0.03) | 2.86 (0.05) | 2.74 (0.12) | 2.81 (0.14) | 2.82 (0.40) | 0.91 |
| **Total cholesterol/high-density lipoprotein cholesterol ratio** | | | | | | |
| N | 1,955 | 688 | 123 | 71 | 10 |  |
| Model 1 | 3.81 (0.03) | 3.79 (0.05) | 3.85 (0.13) | 4.16 (0.16) | 4.01 (0.44) | 0.10 |
| Model 2 | 3.95 (0.07) | 3.93 (0.09) | 3.97 (0.14) | 4.22 (0.17) | 4.19 (0.40) | 0.13 |
| **High-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 2,079 | 736 | 133 | 77 | 11 |  |
| Model 1 | 1.53 (0.01) | 1.53 (0.02) | 1.51 (0.04) | 1.42 (0.04) | 1.40 (0.11) | 0.02 |
| Model 2 | 1.48 (0.02) | 1.50 (0.02) | 1.49 (0.04) | 1.40 (0.04) | 1.38 (0.10) | 0.12 |
| **Low-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 1,155 | 415 | 71 | 51 | 5 |  |
| Model 1 | 3.23 (0.03) | 3.26 (0.05) | 3.26 (0.11) | 3.29 (0.13) | 3.37 (0.38) | 0.55 |
| Model 2 | 3.20 (0.04) | 3.26 (0.06) | 3.22 (0.11) | 3.32 (0.13) | 3.28 (0.36) | 0.46 |
| **Total cholesterol (mmol/l)** | | | | | | |
| N | 2,804 | 949 | 166 | 99 | 16 |  |
| Model 1 | 5.52 (0.02) | 5.50 (0.03) | 5.46 (0.07) | 5.54 (0.10) | 5.48 (0.23) | 0.80 |
| Model 2 | 5.53 (0.03) | 5.55 (0.04) | 5.51 (0.08) | 5.60 (0.1) | 5.56 (0.25) | 0.71 |
| **Inflammatory Biomarkers** | | | | | | |
| **C-reactive protein (mg/l)** | | | | | | |
| N | 4,088 | 1,392 | 238 | 149 | 20 |  |
| Model 1 | 1.72 (0.03) | 1.70 (0.05) | 1.68 (0.11) | 1.74 (0.14) | 1.85 (0.36) | 0.83 |
| Model 2 | 1.77 (0.04) | 1.80 (0.06) | 1.76 (0.11) | 1.70 (0.13) | 1.55 (0.28) | 0.48 |
| **Intracellular adhesion molecule 1 (ng/ml)** | | | | | | |
| N | 1,612 | 518 | 83 | 51 | 7 |  |
| Model 1 | 228.8 (1.4) | 231.4 (2.5) | 229.2 (6.0) | 228.0 (7.6) | 238.2 (20.1) | 0.78 |
| Model 2 | 238.4 (1.7) | 241.4 (2.7) | 237.5 (6.1) | 230.9 (7.5) | 246.4 (19.9) | 0.76 |
| **Vascular cell adhesion protein 1 (ng/ml)** | | | | | | |
| N | 819 | 292 | 53 | 37 | 4 |  |
| Model 1 | 591.8 (4.9) | 604.5 (8.3) | 600.8 (19.0) | 609.4 (23.0) | 723.8 (76.9) | 0.09 |
| Model 2 | 588.2 (5.1) | 601.9 (8.6) | 599.5 (19.0) | 609.5 (22.8) | 738.4 (77.1) | 0.08 |
| **Metabolic Biomarkers** | | | | | | |
| **Adiponectin (μg/ml)** | | | | | | |
| N | 4,201 | 1,403 | 234 | 149 | 21 |  |
| Model 1 | 10.9 (0.1) | 10.4 (0.1) | 10.4 (0.3) | 10.7 (0.4) | 10.8 (1.2) | 0.29 |
| Model 2 | 10.6 (0.1) | 10.1 (0.2) | 10.1 (0.4) | 10.2 (0.4) | 10.9 (1.1) | 0.33 |
| **Insulin (μU/ml)** | | | | | | |
| N | 1,972 | 591 | 93 | 60 | 9 |  |
| Model 1 | 4.88 (0.08) | 5.13 (0.15) | 4.89 (0.35) | 4.82 (0.42) | 5.69 (1.12) | 0.69 |
| Model 2 | 4.84 (0.10) | 5.11 (0.15) | 4.74 (0.33) | 4.88 (0.41) | 5.01 (0.96) | 0.92 |
| **Hemoglobin A1c (%)** | | | | | | |
| N | 3,030 | 1,030 | 169 | 113 | 16 |  |
| Model 1 | 5.38 (0.01) | 5.39 (0.01) | 5.40 (0.02) | 5.45 (0.03) | 5.20 (0.08) | 0.96 |
| Model 2 | 5.41 (0.01) | 5.42 (0.01) | 5.43 (0.02) | 5.47 (0.03) | 5.24 (0.08) | 0.90 |

1 Biomarker sample sizes vary: fetuin-A (n = 1,409), alanine transaminase (n = 1,318), gamma-glutamyl transferase (n = 1,316), triglyceride (n = 3,329), total cholesterol/high-density lipoprotein cholesterol ratio (n = 2,847), high-density lipoprotein cholesterol (n = 3,036), low-density lipoprotein cholesterol (n = 1,697), total cholesterol (n = 4,034), C-reactive protein (n = 5,887), intracellular adhesion molecule 1 (n = 2,271), vascular cell adhesion protein 1 (n = 1,205), adiponectin (n = 6,008), insulin (n = 2,725), hemoglobin A1c (n = 4,358). Values were determined using general linear models. Model 1 was adjusted for age at blood draw, fasting status (yes / no), and time of blood draw (blood collection cycle 1/2). Model 2 was adjusted for the variables in Model 1 plus smoking status (current / former / never), alcohol intake (continuous), physical activity (tertile), total energy intake (tertile), Alternate Healthy Eating Index score excluding sugar sweetened beverage (tertile), postmenopausal hormone use (yes / no), and BMI (continuous).

**Supplementary Table S7.** Least-squares mean (95% CI) concentrations of biomarkers by frequency of fruit drink and punch intake among participants free of diabetes and cardiovascular disease in the Nurses’ Health Study (*n*=8,492).1

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker Concentration** | **Frequency of Fruit Drink and Punch Intake** | | | | |  |
| **Never or almost never** | **Less than once per week** | **Once to twice per week** | **Three to six times per week** | **Once per day or more** | ***P* for trend** |
| **Hepatic Biomarkers** | | | | | | |
| **Fetuin-A (μg/ml)** | | | | | | |
| N | 723 | 420 | 122 | 111 | 33 |  |
| Model 1 | 460.4 (3.9) | 464.2 (5.2) | 472.9 (9.6) | 459.1 (10.0) | 488.5 (18.3) | 0.19 |
| Model 2 | 461.1 (4.5) | 460.2 (5.5) | 468.6 (9.6) | 458.3 (10.3) | 497.9 (20.2) | 0.12 |
| **Alanine transaminase (U/l)** | | | | | |  |
| N | 678 | 399 | 116 | 92 | 33 |  |
| Model 1 | 19.2 (0.4) | 18.6 (0.5) | 19.4 (0.8) | 19.4 (1.0) | 20.4 (1.6) | 0.34 |
| Model 2 | 19.1 (0.4) | 18.3 (0.5) | 19.1 (0.9) | 19.5 (1.0) | 19.3 (1.7) | 0.51 |
| **Gamma-glutamyl transferase (U/l)** | | | | | |  |
| N | 678 | 397 | 116 | 92 | 33 |  |
| Model 1 | 23.4 (1.1) | 22.3 (1.4) | 26.0 (2.6) | 23.4 (2.9) | 27.2 (4.9) | 0.36 |
| Model 2 | 23.5 (1.2) | 23.0 (1.4) | 26.1 (2.6) | 24.1 (2.9) | 25.5 (5.2) | 0.39 |
| **Lipid Biomarkers** | | | | | | |
| **Triglyceride (mmol/l)** | | | | | | |
| N | 1,659 | 1,035 | 277 | 281 | 77 |  |
| Model 1 | 2.69 (0.03) | 2.78 (0.04) | 2.85 (0.08) | 2.92 (0.08) | 3.13 (0.16) | 0.0005 |
| Model 2 | 2.74 (0.04) | 2.81 (0.04) | 2.82 (0.08) | 2.91 (0.08) | 3.13 (0.17) | 0.008 |
| **Total cholesterol/high-density lipoprotein cholesterol ratio** | | | | | | |
| N | 1,594 | 811 | 200 | 198 | 44 |  |
| Model 1 | 3.79 (0.03) | 3.79 (0.05) | 3.86 (0.10) | 4.15 (0.10) | 4.07 (0.21) | 0.003 |
| Model 2 | 3.94 (0.08) | 3.89 (0.08) | 3.87 (0.11) | 4.24 (0.11) | 3.77 (0.22) | 0.31 |
| **High-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 1,682 | 871 | 211 | 221 | 51 |  |
| Model 1 | 1.54 (0.01) | 1.52 (0.01) | 1.48 (0.03) | 1.45 (0.03) | 1.47 (0.06) | 0.005 |
| Model 2 | 1.49 (0.02) | 1.48 (0.02) | 1.50 (0.03) | 1.43 (0.03) | 1.55 (0.06) | 0.96 |
| **Low-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 945 | 473 | 121 | 124 | 34 |  |
| Model 1 | 3.20 (0.03) | 3.31 (0.04) | 3.33 (0.08) | 3.21 (0.08) | 3.32 (0.16) | 0.55 |
| Model 2 | 3.19 (0.05) | 3.29 (0.05) | 3.24 (0.09) | 3.15 (0.08) | 3.19 (0.15) | 0.69 |
| **Total cholesterol (mmol/l)** | | | | | | |
| N | 2,167 | 1,179 | 303 | 312 | 73 |  |
| Model 1 | 5.52 (0.02) | 5.50 (0.03) | 5.51 (0.06) | 5.52 (0.06) | 5.63 (0.12) | 0.38 |
| Model 2 | 5.53 (0.03) | 5.54 (0.04) | 5.54 (0.06) | 5.55 (0.06) | 5.66 (0.12) | 0.26 |
| **Inflammatory Biomarkers** | | | | | | |
| **C-reactive protein (mg/l)** | | | | | | |
| N | 3,070 | 1748 | 469 | 477 | 123 |  |
| Model 1 | 1.67 (0.03) | 1.68 (0.04) | 1.86 (0.09) | 1.78 (0.08) | 2.38 (0.21) | 0.0002 |
| Model 2 | 1.74 (0.04) | 1.76 (0.05) | 1.83 (0.09) | 1.81 (0.08) | 2.30 (0.20) | 0.003 |
| **Intracellular adhesion molecule 1 (ng/ml)** | | | | | | |
| N | 1,175 | 673 | 190 | 188 | 45 |  |
| Model 1 | 228.2 (1.6) | 228.0 (2.1) | 236.8 (4.1) | 233.4 (4.1) | 236.4 (8.3) | 0.08 |
| Model 2 | 237.9 (2.0) | 237.4 (2.3) | 243.5 (4.2) | 242.5 (4.3) | 243.9 (8.8) | 0.17 |
| **Vascular cell adhesion protein 1 (ng/ml)** | | | | | | |
| N | 676 | 336 | 94 | 86 | 13 |  |
| Model 1 | 592.6 (5.4) | 593.6 (7.6) | 616.9 (14.8) | 609.3 (15.3) | 617.6 (38.3) | 0.15 |
| Model 2 | 589.4 (5.7) | 590.5 (7.6) | 612.0 (14.9) | 602.7 (15.5) | 636.2 (42.0) | 0.17 |
| **Metabolic Biomarkers** | | | | | | |
| **Adiponectin (μg/ml)** | | | | | | |
| N | 3,249 | 1719 | 465 | 467 | 108 |  |
| Model 1 | 11.1 (0.1) | 10.7 (0.1) | 10.3 (0.2) | 9.8 (0.2) | 9.5 (0.5) | <0.0001 |
| Model 2 | 10.7 (0.1) | 10.4 (0.2) | 10.3 (0.3) | 9.7 (0.3) | 10.0 (0.5) | 0.0009 |
| **Insulin (μU/ml)** | | | | | | |
| N | 1,299 | 861 | 244 | 256 | 65 |  |
| Model 1 | 4.65 (0.09) | 5.02 (0.12) | 5.43 (0.25) | 5.51 (0.25) | 5.74 (0.49) | 0.0007 |
| Model 2 | 4.68 (0.11) | 4.99 (0.13) | 5.13 (0.22) | 5.36 (0.23) | 5.17 (0.43) | 0.03 |
| **Hemoglobin A1c (%)** | | | | | | |
| N | 2,347 | 1,246 | 346 | 329 | 90 |  |
| Model 1 | 5.37 (0.01) | 5.39 (0.01) | 5.42 (0.02) | 5.41 (0.02) | 5.44 (0.03) | 0.01 |
| Model 2 | 5.41 (0.01) | 5.42 (0.01) | 5.43 (0.02) | 5.42 (0.02) | 5.44 (0.03) | 0.15 |

1 Biomarker sample sizes vary: fetuin-A (n = 1,409), alanine transaminase (n = 1,318), gamma-glutamyl transferase (n = 1,316), triglyceride (n = 3,329), total cholesterol/high-density lipoprotein cholesterol ratio (n = 2,847), high-density lipoprotein cholesterol (n = 3,036), low-density lipoprotein cholesterol (n = 1,697), total cholesterol (n = 4,034), C-reactive protein (n = 5,887), intracellular adhesion molecule 1 (n = 2,271), vascular cell adhesion protein 1 (n = 1,205), adiponectin (n = 6,008), insulin (n = 2,725), hemoglobin A1c (n = 4,358). Values were determined using general linear models. Model 1 was adjusted for age at blood draw, fasting status (yes / no), and time of blood draw (blood collection cycle 1/2). Model 2 was adjusted for the variables in Model 1 plus smoking status (current / former / never), alcohol intake (continuous), physical activity (tertile), total energy intake (tertile), Alternate Healthy Eating Index score excluding sugar sweetened beverage (tertile), postmenopausal hormone use (yes / no), and BMI (continuous).

**Supplementary Table S8.** Least-squares mean (95% CI) concentrations of biomarkers by frequency of sugar sweetened beverage (SSB) intake among participants free of diabetes and cardiovascular disease in the Nurses’ Health Study (*n*=8,492), with adjusting for food groups instead of Alternate Healthy Eating Index score.1

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Biomarker Concentration** | **Frequency of SSB Intake** | | | | |  |
| **Never or almost never** | **Less than once per week** | **Once to twice per week** | **Three to six times per week** | **Once per day or more** | ***P* for trend** |
| **Hepatic Biomarkers** | | | | | | |
| **Fetuin-A (μg/ml)** | | | | | | |
| N | 509 | 399 | 199 | 234 | 68 |  |
| Model | 458.6 (5.4) | 462.1 (5.6) | 459.8 (7.7) | 457.4 (7.2) | 495.7 (13.6) | 0.07 |
| **Alanine transaminase (U/l)** | | | | | |  |
| N | 456 | 382 | 187 | 222 | 71 |  |
| Model | 19.7 (0.5) | 18.8 (0.5) | 17.8 (0.7) | 19.1 (0.6) | 18.8 (1.1) | 0.63 |
| **Gamma-glutamyl transferase (U/l)** | | | | | |  |
| N | 456 | 380 | 187 | 222 | 71 |  |
| Model | 24.0 (1.5) | 23.4 (1.5) | 23.1 (2.0) | 24.1 (1.9) | 23.2 (3.4) | 0.99 |
| **Lipid Biomarkers** | | | | | | |
| **Triglyceride (mmol/l)** | | | | | | |
| N | 1,158 | 953 | 446 | 590 | 182 |  |
| Model | 2.7 (0.04) | 2.8 (0.05) | 2.74 (0.06) | 2.91 (0.06) | 2.97 (0.1) | 0.004 |
| **Total cholesterol/high-density lipoprotein cholesterol ratio** | | | | | | |
| N | 1,098 | 808 | 372 | 447 | 122 |  |
| Model | 3.88 (0.09) | 3.90 (0.09) | 3.80 (0.10) | 4.00 (0.09) | 4.29 (0.14) | 0.002 |
| **High-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 1,157 | 854 | 394 | 488 | 143 |  |
| Model | 1.50 (0.02) | 1.49 (0.02) | 1.53 (0.03) | 1.46 (0.02) | 1.40 (0.03) | 0.002 |
| **Low-density lipoprotein cholesterol (mmol/l)** | | | | | | |
| N | 650 | 467 | 213 | 276 | 91 |  |
| Model | 3.20 (0.05) | 3.26 (0.05) | 3.31 (0.07) | 3.22 (0.06) | 3.04 (0.09) | 0.13 |
| **Total cholesterol (mmol/l)** | | | | | | |
| N | 1,504 | 1,141 | 511 | 681 | 197 |  |
| Model | 5.53 (0.04) | 5.53 (0.04) | 5.52 (0.05) | 5.52 (0.04) | 5.58 (0.08) | 0.62 |
| **Inflammatory Biomarkers** | | | | | | |
| **C-reactive protein (mg/l)** | | | | | | |
| N | 2,127 | 1,678 | 741 | 1,028 | 313 |  |
| Model | 1.70 (0.05) | 1.76 (0.05) | 1.73 (0.07) | 1.79 (0.06) | 2.08 (0.12) | 0.003 |
| **Intracellular adhesion molecule 1 (ng/ml)** | | | | | | |
| N | 812 | 656 | 288 | 402 | 113 |  |
| Model | 234.6 (2.3) | 237.0 (2.3) | 244.2 (3.5) | 240.1 (3.0) | 247.2 (5.6) | 0.02 |
| **Vascular cell adhesion protein 1 (ng/ml)** | | | | | | |
| N | 460 | 341 | 138 | 214 | 52 |  |
| Model | 584.7 (7.0) | 592.0 (7.6) | 609.9 (12.2) | 592.5 (10.2) | 641.7 (21.3) | 0.06 |
| **Metabolic Biomarkers** | | | | | | |
| **Adiponectin (μg/ml)** | | | | | | |
| N | 2,254 | 1,711 | 739 | 1,021 | 283 |  |
| Model | 11.0 (0.2) | 10.6 (0.2) | 10.4 (0.2) | 10.1 (0.2) | 9.6 (0.3) | <0.0001 |
| **Insulin (μU/ml)** | | | | | | |
| N | 912 | 777 | 356 | 526 | 154 |  |
| Model | 4.49 (0.12) | 4.96 (0.13) | 4.91 (0.18) | 5.42 (0.17) | 4.94 (0.27) | 0.02 |
| **Hemoglobin A1c (%)** | | | | | | |
| N | 1,627 | 1,204 | 563 | 738 | 226 |  |
| Model | 5.41 (0.01) | 5.41 (0.01) | 5.42 (0.01) | 5.43 (0.01) | 5.42 (0.02) | 0.21 |

1 Biomarker sample sizes vary: fetuin-A (n = 1,409), alanine transaminase (n = 1,318), gamma-glutamyl transferase (n = 1,316), triglyceride (n = 3,329), total cholesterol/high-density lipoprotein cholesterol ratio (n = 2,847), high-density lipoprotein cholesterol (n = 3,036), low-density lipoprotein cholesterol (n = 1,697), total cholesterol (n = 4,034), C-reactive protein (n = 5,887), intracellular adhesion molecule 1 (n = 2,271), vascular cell adhesion protein 1 (n = 1,205), adiponectin (n = 6,008), insulin (n = 2,725), hemoglobin A1c (n = 4,358). Values were determined using general linear models. Model was adjusted for age at blood draw, fasting status (yes / no), and time of blood draw (blood collection cycle 1/2), smoking status (current / former / never), alcohol intake (continuous), physical activity (tertile), total energy intake (tertile), red and processed meat intake (tertile), whole grain intake (tertile), fruit intake (tertile), vegetable intake (tertile), coffee intake (tertile), postmenopausal hormone use (yes / no), and BMI (continuous).