**Supplementary Table 1.** Baseline participant characteristics in the whole analytic sample and subsamples of the Women's Health Initiative

| | **Whole analytic sample (*n* = 155,925)** | **CVD Biomarker Study (*n* = 22,561)** | **DXA Study (*n* = 10,894)** |
|---|---|---|---|
| Age, y | 63.2 | 63.9 | 63.3 |
| Race/ethnicity, % | | | |
| White | 82.8 | 46.8 | 77.8 |
| Black/African-American | 8.9 | 35.5 | 13.7 |
| Hispanic/Latino | 3.9 | 15.3 | 6.3 |
| Other/unknown | 4.4 | 2.4 | 2.2 |
| College degree or above, % | 39.7 | 32.3 | 30.6 |
| Annual family income ≥$50,000, % | 40.5 | 28.8 | 29.3 |
| Smoking status, % | | | |
| Never | 51.2 | 52.5 | 54.8 |
| Former | 41.9 | 38.3 | 37.2 |
| Current | 6.9 | 9.2 | 8.0 |
| Moderate alcohol consumption (5-15 g/d), % | 16.8 | 12.6 | 13.1 |
| Recreational physical activity, MET-h/wk | 12.5 | 10.7 | 13.9 |
| AHEI-2010 (excluding alcohol) | 47.3 | 45.5 | 45.3 |
| Hormone replacement therapy, % | | | |
| Never | 43.6 | 60.6 | 47.4 |
| Former | 16.0 | 20.2 | 15.9 |
| Current | 40.2 | 19.2 | 36.8 |
| Hypertension, % | 38.8 | 46.7 | 40.2 |
| Dyslipidemia, % | 14.3 | 15.5 | 14.0 |
| Reported diabetes, % | 5.7 | 9.3 | 7.5 |
| Reported CHD or stroke, % | 4.1 | 5.1 | 4.9 |
| Study group, % | | | |
| WHI Observational Study | 57.5 | 24.9 | 56.1 |
| Control of WHI clinical trials | 16.5 | 25.0 | 17.2 |
| Active arms of WHI clinical trials | 26.0 | 50.1 | 26.6 |
| Anthropometric measures | | | |
| Body mass index, $kg/m^2$ | 27.9 | 29.6 | 28.2 |
| Waist circumference, cm | 86.3 | 89.7 | 85.7 |
| Hip circumference, cm | 106.3 | 108.7 | 106.5 |
| Waist-to-hip ratio | 0.81 | 0.82 | 0.80 |
| Height, cm | 161.8 | 161.1 | 161.7 |

AHEI, alternate Healthy Eating Index; CHD, coronary heart disease; CVD, cardiovascular disease; DXA, dual energy X-ray absorptiometry; MET, metabolic equivalent; WHI, Women's Health Initiative.

**Supplementary Table 2.** Procedures for identification and adjudication of incident cases of lower-extremity arterial disease in the Women's Health Initiative

| No. | Procedures | Details | N (%*) |
|---|---|---|---|
| 1 | Surgery, angioplasty, or thrombolysis | Surgery, angioplasty, or thrombolysis for lower-extremity arterial disease | 923 (80.1) |
| 2 | Ultrasonography or angiography | Obstruction or ulcerated plaque (≥50% of the diameter or ≥75% of the cross-sectional area) demonstrated on ultrasound or angiogram of the iliac arteries or below | 779 (67.6%) |
| 3 | Exertional leg pain | Exertional leg pain relieved by rest in combination with: *1)* claudication diagnosed by physician; and/or *2)* ankle-arm systolic blood pressure ratio ≤0.80 | 326 (28.3%) |
| 4 | No doppler pulse in vessels | Absence of pulse by doppler in any major vessel of lower extremities | 114 (9.9%) |
| 5 | Amputation of one or more toes | Amputation of one or more toes or part of the lower extremity because of ischemia or gangrene | 75 (6.5) |
| 6 | Positive exercise test | Exercise test that is positive for lower extremity claudication | 19 (1.6%) |
| | | | |
| By 1 or 2 | | | 1083 (94.0%) |
| By 1 or 2 or 3 | | | 1104 (95.8%) |
| By at least two procedures | | | 778 (67.5%) |

*Percent cases among 1152 incident cases of lower-extremity arterial disease included in the analysis.

**Supplementary Table 3.** Information on fasting measures of biomarkers in subsets of the Women's Health Initiative*

| Biomarker | Lab | Specimen | *n* | Mean | SD | Units | Quality Control | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Dups (*n*) | Corr (*r*) | Mean CV (%) | Min Pull Corr (*r*) |
| MUFA | Tufts | Citrate | 2437 | 12.32 | 1.66 | % | 123 | 0.82 | 3.67 | 0.72 |
| PUFA | Tufts | Citrate | 2437 | 41.60 | 2.06 | % | 123 | 0.81 | 1.66 | 0.70 |
| SFA | Tufts | Citrate | 2437 | 46.09 | 1.29 | % | 123 | 0.77 | 1.09 | 0.71 |
| Apolipoprotein (a) | Harvard-Rifai | EDTA | 3989 | 25.39 | 31.63 | mg/dL | 200 | 0.98 | 8.95 | 0.95 |
| Apolipoprotein A1 | Harvard-Rifai | EDTA | 3996 | 178.69 | 41.97 | mg/dL | 201 | 0.84 | 4.56 | 0.53 |
| Apolipoprotein B | Harvard-Rifai | EDTA | 3996 | 101.21 | 26.96 | mg/dL | 201 | 0.90 | 4.9 | 0.76 |
| Apolipoprotein E | Robinson Lab | EDTA | 2988 | 325.61 | 90.15 | RFU | 153 | 0.70 | 4.02 | 0.49 |
| Total LDL | LipoScience | EDTA | 4485 | 1509.92 | 436.25 | nmol/L | 245 | 0.94 | 6.02 | 0.70 |
| Large LDL | LipoScience | EDTA | 4485 | 593.77 | 270.29 | nmol/L | 245 | 0.83 | 14.88 | 0.73 |
| Medium-Small LDL | LipoScience | EDTA | 3964 | 174.07 | 96.31 | nmol/L | 218 | 0.89 | 16.82 | 0.72 |
| Small LDL | LipoScience | EDTA | 4485 | 798.13 | 495.61 | nmol/L | 245 | 0.91 | 17.73 | 0.69 |
| Very-Small LDL | LipoScience | EDTA | 3964 | 725.01 | 392.23 | nmol/L | 218 | 0.91 | 16.28 | 0.67 |
| LDL Size | LipoScience | EDTA | 4484 | 21.05 | 0.68 | nm | 245 | 0.83 | 0.89 | 0.63 |
| Total HDL | LipoScience | EDTA | 4485 | 33.12 | 6.78 | umol/L | 245 | 0.92 | 4.16 | 0.76 |
| Large HDL | LipoScience | EDTA | 4485 | 5.89 | 3.24 | umol/L | 245 | 0.93 | 12.71 | 0.65 |
| Medium HDL | LipoScience | EDTA | 4485 | 4.57 | 5.16 | umol/L | 245 | 0.89 | 43.26 | 0.39 |
| Small HDL | LipoScience | EDTA | 4485 | 22.67 | 5.73 | umol/L | 245 | 0.89 | 6.53 | 0.73 |
| HDL Size | LipoScience | EDTA | 4485 | 9.03 | 0.54 | nm | 245 | 0.96 | 0.78 | 0.91 |
| Triglyceride | UMMC | Serum | 24,207 | 137.5 | 83.16 | mg/dL | 1075 | 1.00 | 1.92 | 0.92 |
| HDL Cholesterol | UMMC | Serum | 24,206 | 53.91 | 13.53 | mg/dL | 1075 | 0.97 | 3.07 | 0.83 |
| LDL Cholesterol | UMMC | Serum | 23,904 | 148.96 | 37.68 | mg/dL | 1050 | 0.96 | 2.95 | 0.74 |
| Glucose | UMMC | Serum | 24,208 | 103.61 | 34.79 | mg/dL | 1075 | 0.99 | 1.55 | 0.77 |
| Insulin | UMMC | Serum | 23,420 | 68.27 | 102.22 | pmol/L | 1031 | 0.99 | 4.86 | 0.87 |
| hs-CRP | UMMC | Serum | 24,205 | 5.07 | 7.50 | mg/L | 1075 | 1.00 | 2.27 | 0.99 |
| SHBG | Hormone Lab | Serum | 11,900 | 52.28 | 32.33 | nmol/L | 645 | 0.99 | 5.18 | 0.53 |
| Adiponectin | Harvard-Rifai | EDTA | 2543 | 8479.98 | 4264.26 | ng/mL | 101 | 0.90 | 12.3 | 0.78 |

CV, Coefficient of variation; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; LDL, Low-density lipoprotein; MUFA, monounsaturated fatty acids; PUFA, Polyunsaturated fatty acids; SFA, saturated fatty acids; SHBG, sex hormone-binding globulin.
*Biomarkers highlighted in yellow contributed to the WHI CVD Biomarker Study.

**Supplementary Table 4.** Measures of predicated waist and hip circumference and risk of lower-extremity arterial disease in the Women's Health Initiative (*n* = 155,925)

| | Quartile | | | | P-trend |
|---|---|---|---|---|---|
| | **Q1** | **Q2** | **Q3** | **Q4** | |
| **Predicated waist circumference*** | | | | | |
| No. of cases | 209 | 243 | 307 | 393 | |
| No. of person-years | 640,234 | 630,514 | 615,212 | 583,996 | |
| Model 1 (HR [95% CI]) | 1.00 (Referent) | 1.20 (1.00-1.45) | 1.48 (1.24-1.77) | 1.91 (1.61-1.77) | <0.0001 |
| Model 2 (HR [95% CI]) | 1.00 (Referent) | 1.19 (0.98-1.43) | 1.43 (1.20-1.71) | 1.79 (1.51-2.12) | <0.0001 |
| Model 2 + metabolic factors† | 1.00 (Referent) | 1.11 (0.92-1.34) | 1.24 (1.04-1.48) | 1.30 (1.09-1.54) | 0.0019 |
| **Predicated hip circumference*** | | | | | |
| No. of cases | 391 | 281 | 252 | 228 | |
| No. of person-years | 598,935 | 622,987 | 629,399 | 618,635 | |
| Model 1 (HR [95% CI]) | 1.00 (Referent) | 0.73 (0.63-0.86) | 0.65 (0.55-0.76) | 0.57 (0.49-0.67) | <0.0001 |
| Model 2 (HR [95% CI]) | 1.00 (Referent) | 0.74 (0.63-0.87) | 0.66 (0.56-0.77) | 0.57 (0.48-0.67) | <0.0001 |
| Model 2 + metabolic factors† | 1.00 (Referent) | 0.83 (0.71-0.97) | 0.77 (0.66-0.90) | 0.65 (0.55-0.76) | <0.0001 |

Model 1 was adjusted for age (y), race/ethnicity (White, Black/African-American, Hispanic/Latino, other/unknown), education (at most high school, some college, college or above), annual family income (<20,000, 20,000-<50,000, 50,000-<75,000, ≥75,000 USD), and study group (3 variables with each being classified as observational, control, and intervention).

Model 2 was adjusted for covariates in the model 1 plus smoking status (never, former, current), pack-years of smoking (for current smokers), alcohol consumption (0, 0-<5, 5-<15, 15-<25, ≥25 g/day), recreational physical activity (MET-h/week), diet-quality score (AHEI-2010 excluding alcohol), hormone replacement therapy (never, former, current [<5, 5-<10, 10-<15, ≥15 y]), aspirin use (never, ever), use of nonsteroidal anti-inflammatory drug (never, ever), history of CHD or stroke (yes, no), and height

*Predicated waist circumference was residuals from a multivariable linear regression model in which waist circumference was regressed against hip circumference and other covariates including age, study group, race, smoking status, and baseline hormone use. Predicted hip circumference was residuals from a multivariable linear regression model in which hip circumference was regressed against waist circumference and these covariates. Predicted waist circumference was moderately correlated with absolute waist circumference (Pearson's r = 0.60) and was not correlated with absolute hip circumference (Pearson's r <0.0001). Predicted hip circumference was moderately correlated with absolute hip circumference (Pearson's r = 0.59) and was not correlated with absolute waist circumference (Pearson's r <0.0001).

†Including reported diabetes (yes, no), dyslipidemia (yes, no), use of antihypertensive drugs (yes, no), and systolic blood pressure (mmHg).

**Supplementary 5.** Associations of trunk and leg fat mass with risk of lower-extremity arterial disease in the Women's Health Initiative ($n$ = 10,894), by smoking status

| **Smoking status** | **No. of cases** | **Trunk fat mass** | | **Leg fat mass** | |
|---|---|---|---|---|---|
| | | HR (95% CI), per 5 kg | P-interaction | HR (95% CI), per 5 kg | P-interaction |
| Never smoker | 39 | 1.17 (0.83-1.66) | 0.17 | 0.72 (0.44-1.18) | 0.0034 |
| Former smoker | 46 | 1.22 (0.87-1.73) | | 0.65 (0.38-1.14) | |
| Current smoker | 34 | 1.63 (1.06-2.50) | | 0.19 (0.09-0.42) | |

Results were adjusted for covariates listed for model 2 of Table 3 in the article except smoking status.

**Supplementary Table 6.** Associations of whole-body fat mass and the ratio of trunk-to-leg fat mass with risk of lower-extremity arterial disease in the Women's Health Initiative (*n* = 10,894)

| | Quartile | | | | P-trend | Continuous* |
|---|---|---|---|---|---|---|
| | Q1 | Q2 | Q3 | Q4 | | |
| **Whole-body fat mass** | | | | | | |
| Median (range), kg | 20.5 (<24.3) | 27.7 (24.5-30.8) | 34.5 (30.9-38.8) | 45.8 (≥38.9) | | |
| No. of cases | 31 | 30 | 29 | 29 | | |
| No. of person-years | 43,300 | 43,312 | 42,607 | 41,146 | | |
| Model 1 (HR [95% CI]) | 1.00 (Referent) | 0.91 (0.55-1.50) | 0.81 (0.55-1.50) | 0.77 (0.46-1.31) | 0.32 | 0.86 (0.72-1.02) |
| Model 2 (HR [95% CI]) | 1.00 (Referent) | 0.92 (0.55-1.54) | 0.91 (0.53-1.55) | 0.90 (0.48-1.68) | 0.75 | 0.88 (0.71-1.08) |
| Model 2 + metabolic factors† | 1.00 (Referent) | 0.85 (0.50-1.43) | 0.82 (0.47-1.43) | 0.77 (0.41-1.45) | 0.45 | 0.84 (0.68-1.03) |
| **Ratio of trunk-to-leg fat mass** | | | | | | |
| Median (range) | 0.83 (<0.99) | 1.10 (0.99-1.21) | 1.34 (1.22-1.47) | 1.69 (≥1.48) | | |
| No. of cases | 21 | 30 | 23 | 45 | | |
| No. of person-years | 44,447 | 43,336 | 42,328 | 40,253 | | |
| Model 1 (HR [95% CI]) | 1.00 (Referent) | 1.45 (0.83-2.54) | 1.07 (0.59-1.93) | 2.23 (1.32-3.87) | 0.0036 | 1.49 (1.24-1.79) |
| Model 2 (HR [95% CI]) | 1.00 (Referent) | 1.63 (0.92-2.87) | 1.25 (0.68-2.30) | 2.72 (1.58-4.69) | 0.0004 | 1.55 (1.29-1.86) |
| Model 2 + metabolic factors† | 1.00 (Referent) | 1.38 (0.78-2.45) | 1.03 (0.56-1.89) | 1.61 (0.91-2.85) | 0.15 | 1.23 (1.01-1.51) |

Model 1 was adjusted for age (y), race/ethnicity (White, Black/African-American, Hispanic/Latino, other/unknown), education (at most high school, some college, college or above), annual family income (<20,000, 20,000-<50,000, 50,000-<75,000, ≥75,000 USD), and study group (3 variables with each being classified as observational, control, and intervention).

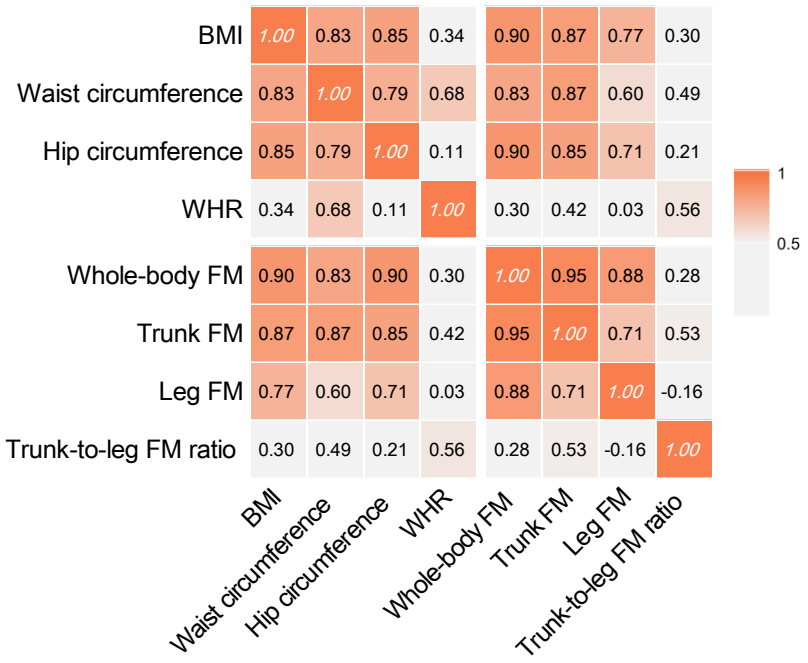
Model 2 was adjusted for covariates in the model 1 plus smoking status (never, former, current), pack-years of smoking (for current smokers), alcohol consumption (0, 0-<5, 5-<15, 15-<25, ≥25 g/day), recreational physical activity (MET-h/week), diet-quality score (AHEI-2010 excluding alcohol), hormone replacement therapy (never, former, current [<5, 5-<10, 10-<15, ≥15 y]), aspirin use (never, ever), use of nonsteroidal anti-inflammatory drug (never, ever), history of CHD or stroke (yes, no), height, and whole-body lean mass (for whole-body fat mass) or the ratio of trunk-to-leg lean mass (for the ratio of trunk-to-leg fat mass).

*Scales are 10 kg for whole-body fat mass and 0.5 unit for the ratio of trunk-to-leg fat mass.

†Including reported diabetes (yes, no), dyslipidemia (yes, no), use of antihypertensive drugs (yes, no), and systolic blood pressure (mmHg).

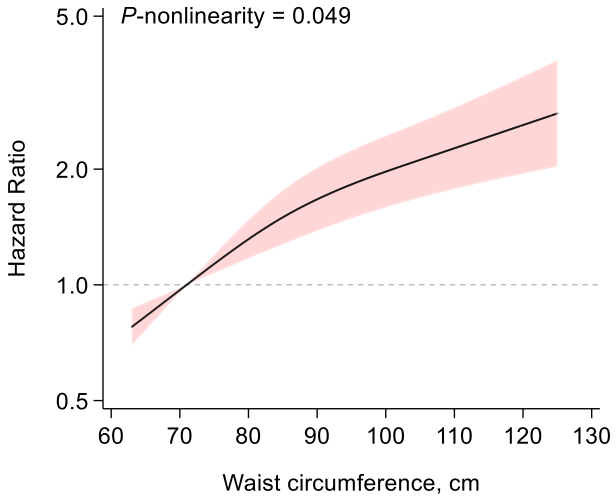
**Supplementary Figure 1. Correlations between anthropometric measures and body fat mass.**

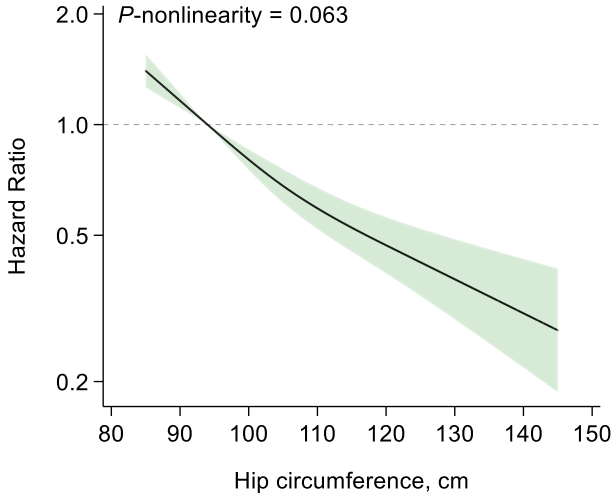
Results were Pearson partial correlation coefficients with adjustment for age, race/ethnicity, and study group. BMI, body mass index; FM, fat mass; WHR, waist-to-hip ratio.



**Supplementary Figure 2. Restricted cubic spline for the association between waist or hip circumference and risk of lower-extremity arterial disease.**

Median value for the lowest quartile of waist or hip circumference was used as the referent and results were adjusted for covariates listed for model 2 of Table 2 in the article. All data were included in the analyses and results for waist or hip circumference between 1st and 99th percentile were shown for presentation purpose.



**Supplementary Figure 3. Measures of upper- and lower-body fat and multiple cardiometabolic biomarkers.**

All biomarker concentrations were transformed using a rank-based inverse normal transformation to approximate a normal distribution. Results are Pearson partial correlations with adjustment for covariates listed for model 2 of Table 2 (for waist and hip circumference) or Table 3 (for trunk and leg fat) in the article in addition to clinical risk factors including use of antihypertensive drugs, systolic blood pressure, dyslipidemia, and diabetes.

HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; LDL, Low-density lipoprotein; MUFA, monounsaturated fatty acids; PUFA, Polyunsaturated fatty acids; SFA, saturated fatty acids; SHBG, sex hormone-binding globulin.

| Biomarker | Waist | Hip | *n* | Trunk fat | Leg fat | *n* |
|---|---|---|---|---|---|---|
| MUFA | -0.08 | 0.03 | 2399 | -0.05 | 0.12 | 195 |
| PUFA | -0.06 | 0.02 | 2399 | -0.20 | 0.06 | 195 |
| SFA | 0.19 | -0.08 | 2399 | 0.33 | -0.22 | 195 |
| Apolipoprotein (a) | -0.02 | 0.04 | 3975 | -0.05 | 0.02 | 326 |
| Apolipoprotein A1 | -0.12 | 0.01 | 3982 | -0.25 | 0.11 | 328 |
| Apolipoprotein B | 0.14 | -0.07 | 3982 | 0.14 | -0.12 | 328 |
| Apolipoprotein E | -0.04 | 0.00 | 2793 | -0.01 | 0.04 | 272 |
| Total LDL | 0.16 | -0.13 | 4256 | 0.20 | -0.15 | 378 |
| Large LDL | -0.17 | 0.11 | 4256 | -0.11 | 0.09 | 378 |
| Medium-Small LDL | 0.24 | -0.16 | 3769 | 0.27 | -0.20 | 330 |
| Small LDL | 0.23 | -0.19 | 4256 | 0.23 | -0.21 | 378 |
| Very-Small LDL | 0.24 | -0.17 | 3769 | 0.28 | -0.21 | 330 |
| LDL Size | -0.24 | 0.14 | 4255 | -0.24 | 0.16 | 378 |
| Total HDL | -0.06 | 0.03 | 4256 | 0.09 | -0.07 | 378 |
| Large HDL | -0.26 | 0.11 | 4256 | -0.24 | 0.12 | 378 |
| Medium HDL | -0.02 | 0.12 | 4256 | 0.04 | 0.13 | 378 |
| Small HDL | 0.10 | -0.13 | 4256 | 0.21 | -0.24 | 378 |
| HDL Size | -0.26 | 0.16 | 4256 | -0.27 | 0.18 | 378 |
| Triglyceride | 0.27 | -0.16 | 23,320 | 0.36 | -0.29 | 2088 |
| HDL Cholesterol | -0.28 | 0.11 | 23,319 | -0.33 | 0.23 | 2088 |
| LDL Cholesterol | 0.06 | -0.04 | 23,032 | 0.04 | -0.02 | 2049 |
| Glucose | 0.25 | -0.07 | 23,321 | 0.32 | -0.19 | 2088 |
| Insulin | 0.39 | -0.02 | 22,563 | 0.52 | -0.21 | 2030 |
| HOMA-IR | 0.40 | -0.05 | 22,561 | 0.54 | -0.25 | 2030 |
| hs-CRP | 0.21 | 0.09 | 23,318 | 0.33 | 0.01 | 2088 |
| SHBG | -0.33 | 0.08 | 11,471 | -0.41 | 0.16 | 989 |
| Adiponectin | -0.28 | 0.11 | 2497 | -0.41 | 0.25 | 235 |