Supplements

Supplementary Table S1. Quality control metrics of urinary assays

	IsoP		IsoP-M	
	Control Set 1	**Control Set 2**	**Control Set 1**	**Control Set 2**
Number of Sample Runs, *n*	56	50	50	50
Concentration (mean ± SD), ng/ml	4.1 ± 0.9	17.8 ± 3.9	3.6 ± 0.9	13.7 ± 3.1
Intra-assay CV*	6.7%	5.2%	6.5%	6.5%
Inter-assay CV*	21.7%	21.7%	24.1%	22.9%

For each isoprostane entity, 2 pools of quality control samples with low and high concentration were included as duplicates in each run/batch. For each run, standard deviation of each duplicated sample divided by duplicate mean yielded sample specific intra-assay CV. Mean sample specific intraassay CV for each control set is reported as pool intra-assay CV. Sample specific Inter-assay CV was calculated as the standard deviation for mean concentration of each sample across the batches/runs divided by mean for that sample across the batches. Control set inter-assay CV was then calculated as mean of sample specific inter-assay CVs in each pool.

* CV: Coefficient of variance

Supplementary Table S2. Characteristics of participants at CARDIA Y15 exam

	Female (*n*= 1623)	**Male (*n*= 1376)**	***p***
Age, years	40.3 ± 3.6	40.2 ± 3.6	0.40
Postmenopausal	12.1%	-	-
Black Race	47.3%	42.1%	<0.01
Body Mass Index (BMI; kg/m^2)	28.9 ± 7.2	28.0 ± 4.9	<0.01
≥ College degree	48.5%	45.6%	0.15
Smoking			
Never	59.8%	61.8%	<0.01
Former	20.8%	16.0%	
Current	19.4%	22.2%	
Cumulative Pack-Years	Not Available	Not available	-
Physical Activity, EU *	290 ± 249	429 ± 307	<0.01
Systolic Blood Pressure, mmHg	111 ± 15	115 ± 14	<0.01
Total Cholesterol, mg/dl	182 ± 32	189 ± 38	<0.01
HDL Cholesterol, mg/dl	55 ± 14	45 ± 13	<0.01
Triglycerides, mg/dl	89 ± 58	126 ± 124	<0.01
Serum Creatinine, mg/dl	0.76 ± 0.24	1.00 ± 0.50	<0.01
Diabetes Medication Use	2.3%	2.0%	0.65
Fasting Glucose, mg/dl	92 ± 20	96 ± 19	<0.01
Antihypertensive Medication Use	7.4%	7.3%	0.95
Cholesterol Lowering Medication Use	3.9%	1.0%	<0.01
Plasma IsoP, ng/L†	57.2 [41.8, 80.9]	45.9 [36.9, 59.5]	<0.01

Data presented as mean ± SD, median [IQR], or percentage of participants
*** EU:** Exercise units **†** **IsoP:** 8-isoprostane

Supplementary Table S3. Replacing different diabetes-related variables into the models

	Diabetes-related variable	Model 1	Model 2	Model 3	Model 4
Urinary IsoP	**Original DM variable***	0.94 (0.79 to 1.12)	0.91 (0.77 to 1.09)	0.90 (0.75 to 1.07)	0.95 (0.79 to 1.15)
	Hemoglobin A1c (per SD)	0.99 (0.93 to 1.05)	0.98 (0.92 to 1.04)	0.97 (0.91 to 1.03)	1.00 (0.92 to 1.07)
	Log HOMA-IR (per SD)	0.96 (0.90 to 1.04)	0.96 (0.89 to 1.03)	0.96 (0.90 to 1.04)	0.96 (0.88 to 1.04)
	Fasting Glucose (per SD)	1.01 (0.95 to 1.07)	1.00 (0.94 to 1.06)	0.99 (0.93 to 1.05)	1.01 (0.94 to 1.07)
	Diabetes Medication use	1.04 (0.83 to 1.30)	1.01 (0.81 to 1.27)	1.00 (0.80 to 1.25)	1.14 (0.88 to 1.46)
Urinary IsoP-M	**Original DM variable***	0.88 (0.72 to 1.08)	0.86 (0.70 to 1.06)	0.86 (0.70 to 1.06)	**0.84 (0.70 to 1.02)**
	Hemoglobin A1c (per SD)	0.99 (0.93 to 1.06)	0.99 (0.93 to 1.05)	0.98 (0.92 to 1.04)	1.00 (0.93 to 1.08)
	Log HOMA-IR (per SD)	0.94 (0.88 to 1.01)	0.94 (0.87 to 1.01)	0.95 (0.88 to 1.02)	**0.91 (0.84 to 0.99)**
	Fasting Glucose (per SD)	1.00 (0.94 to 1.06)	0.99 (0.93 to 1.05)	0.98 (0.92 to 1.04)	0.97 (0.91 to 1.03)
	Diabetes Medication use	1.01 (0.81 to 1.27)	1.00 (0.79 to 1.25)	0.99 (0.79 to 1.24)	0.91 (0.71 to 1.17)
Plasma IsoP	**Original DM variable***	**0.90 (0.84 to 0.93)**	**0.90 (0.83 to 0.97)**	**0.89 (0.83 to 0.96)**	**0.89 (0.83 to 0.96)**
	Hemoglobin A1c (per SD)	-	-	-	-
	Log HOMA-IR (per SD)	0.99 (0.97 to 1.00)	0.99 (0.97 to 1.00)	0.98 (0.97 to 1.00)	**0.98 (0.96 to 1.00)**
	Fasting Glucose (per SD)	**0.97 (0.95 to 0.98)**	**0.97 (0.95 to 0.98)**	**0.97 (0.95 to 0.98)**	**0.96 (0.95 to 0.98)**
	Diabetes Medication use	**0.87 (0.79 to 0.96)**	**0.86 (0.78 to 0.95)**	**0.86 (0.78 to 0.95)**	**0.85 (0.77 to 0.94)**

Models were constructed as described in the methods section, with each of the listed diabetes-related variables being replaced in each model separately to assess robustness of the associations to variable definition.

*** Diabetes:** use of diabetes medications or fasting glucose ≥126 mg/dL

Supplementary Table S4. Plasma Iso-P Models in Participants Also in Urine Isoprostane Analyses

	Model 1		Model 4	
	All Y15 Participants	Overlapping Participants	All Y15 Participants	Overlapping Participants
Age (per SD)	**0.98 (0.97 to 1.00)**	1.00 (0.97 to 1.04)	**0.97 (0.96 to 0.99)**	0.99 (0.96 to 1.02)
Female Sex (vs. Male Sex)	**1.26 (1.23 to 1.30)**	**1.24 (1.16 to 1.32)**	**1.21 (1.17 to 1.26)**	**1.27 (1.15 to 1.40)**
Black Race (vs. White)	**0.90 (0.87 to 0.93)**	**0.86 (0.80 to 0.93)**	**0.89 (0.86 to 0.92)**	**0.86 (0.79 to 0.93)**
BMI (per SD)	**1.16 (1.14 to 1.18)**	**1.18 (1.14 to 1.23)**	**1.18 (1.16 to 1.20)**	**1.18 (1.13 to 1.22)**
Current Smoking (vs. Never)	**1.12 (1.08 to 1.16)**	**1.10 (1.00 to 1.20)**	**1.11 (1.07 to 1.15)**	1.09 (0.99 to 1.19)
Diabetes*	**0.90 (0.84 to 0.93)**	**0.94 (0.79 to 1.11)**	**0.89 (0.83 to 0.96)**	0.95 (0.81 to 1.12)
Blood Pressure Medication	0.95 (0.90 to 1.00)	0.93 (0.82 to 1.07)	**0.92 (0.87 to 0.98)**	**0.83 (0.72 to 0.95)**
Systolic BP (per SD)	**1.02 (1.00 to 1.04)**	**1.05 (1.02 to 1.09)**	1.01 (1.00 to 1.03)	**1.05 (1.02 to 1.09)**
Cholesterol-lowering Meds	1.07 (0.97 to 1.18)	1.07 (0.82 to 1.39)	**1.11 (1.01 to 1.23)**	**1.14 (0.88 to 1.47)**
Total Cholesterol (per SD)	**1.02 (1.00 to 1.03)**	1.01 (0.98 to 1.05)	**0.98 (0.96 to 1.00)**	**0.95 (0.92 to 0.99)**
HDL Cholesterol (per SD)	**1.07 (1.05 to 1.09)**	**1.06 (1.02 to 1.10)**	**1.11 (1.09 to 1.13)**	**1.12 (1.07 to 1.17)**
Log Triglycerides (per SD)	**1.03 (1.01 to 1.04)**	**1.06 (1.02 to 1.10)**	**1.07 (1.05 to 1.10)**	**1.12 (1.07 to 1.16)**
Serum Creatinine (per SD)	1.01 (1.00 to 1.03)	1.02 (0.98 to 1.07)	**1.02 (1.00 to 1.03)**	1.04 (1.00 to 1.09)
Physical Activity (per SD)	**0.97 (0.96 to 0.99)**	0.97 (0.94 to 1.00)	**0.97 (0.95 to 0.98)**	**0.96 (0.92 to 0.99)**

Statistically significant results ($p<0.05$) were **bold**ed. Exponentiated beta-coefficients are equivalent to geometric ratios of analyte of interest. Ratios >1 represent positive correlation and ratios <1 represent inverse correlation.

Models were progressively adjusted as follows:

Model 1—Single CV risk factor + age, sex, race, BMI, college attainment, study center;

Model 4—All CV risk factors mutually adjusted (diabetes, hypertension medication, systolic blood pressure, lipid lowering medication, total cholesterol, HDL cholesterol, fasting triglyceride concentrations [log transformed], physical activity) +serum creatinine + smoking status (current, former, or never) + Model 1;

*** Diabetes:** use of diabetes medications or fasting glucose ≥126 mg/dL

Supplementary Table S5. P values for interaction terms between each of the covariates and sex or race in the fully adjusted model

	P value for Interaction term			
	Sex		Race	
	IsoP	IsoP-M	IsoP	IsoP-M
Black Race (vs. White)	0.42	0.34	-	-
BMI (per SD)	0.02	0.28	0.07	0.05
Current Smoking (vs. Never)	0.42	0.71	0.24	0.58
Former Smoking (vs. Never)	0.03	0.50	0.84	0.48
Cumulative Pack-years	0.77	0.71	0.50	0.60
Diabetes	0.54	0.82	0.14	0.75
Blood Pressure Medication	0.99	0.49	0.07	0.12
Systolic BP (per SD)	0.26	0.29	0.25	0.02
Cholesterol-lowering Meds	0.17	0.83	0.07	0.02
Total Cholesterol (per SD)	0.06	0.11	0.17	0.27
HDL Cholesterol (per SD)	0.57	0.81	0.75	0.58
Log Triglycerides (per SD)	0.27	0.01	0.81	0.16
Serum Creatinine (per SD)	0.04	0.40	0.95	0.97
Physical Activity (per SD)	0.21	0.89	0.02	0.46

Supplementary Table S6. Interactions between Sex/Race and BMI on urinary isoprostanes

	β for Male	β for Female	*p*	β for Black	β for White	*p*
IsoP	0.89 (0.79-1.02)	1.05 (0.98-1.14)	0.02	1.09 (0.98-1.20)	0.97 (0.89-1.06)	0.07
IsoP-M	1.07 (0.94-1.22)	1.16 (1.07-1.25)	0.28	1.22 (1.11-1.35)	1.08 (0.99-1.18)	0.05