

Supplementary Material for Online Publication

Supplementary Table S1. Pearson Coefficient Correlation Matrix

	β -Trace Protein	β -2 Microglobulin	Standardized Cystatin C	Standardized Creatinine
β -Trace Protein	1.00			
β -2 Microglobulin	0.85	1.00		
Standardized Cystatin C	0.73	0.82	1.00	
Standardized Creatinine	0.65	0.68	0.67	1.00

Supplementary Table S2. Adjusted ORs and 95% CIs of Elevated β -Trace Protein (≥ 0.81 mg/L) and Elevated $\beta 2$ -Microglobulin (≥ 2.80 mg/L) in Persons 20-59 Years-old

	β -Trace Protein (≥ 0.81 mg/L)						$\beta 2$ -Microglobulin (≥ 2.80 mg/L)					
	20-59 years (n = 2,756 [68])						20-59 years (n = 2,758 [101])					
	Model 1*			Model 2*			Model 1*			Model 2*		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age (y)	1.00	0.95-1.06	0.91	0.97	0.90-1.05	0.42	1.06	1.02-1.10	<0.01	1.05	1.01-1.08	0.01
Female sex	0.85	0.31-2.36	0.75	0.90	0.29-2.79	0.86	1.52	0.73-3.19	0.26	1.69	0.67-4.29	0.26
Non-Hispanic black†	0.85	0.34-2.11	0.72	0.53	0.16-1.78	0.30	1.91	0.97-3.77	0.06	1.53	0.75-3.13	0.24
Mexican American†	0.76	0.33-1.73	0.50	0.47	0.16-1.37	0.16	1.43	0.70-2.94	0.32	1.06	0.48-2.33	0.88
BMI (per 5kg/m ² increase)				1.13	0.79-1.60	0.50				0.64	0.46-0.89	0.01
Hypertension				4.78	1.3-17.56	0.02				1.86	0.87-3.98	0.11
Diabetes				0.68	0.20-2.37	0.54				2.84	0.79-10.21	0.11
Current smoker				0.83	0.26-2.65	0.75				0.85	0.42-1.70	0.63
CRP (0.22-1.0 mg/dL)‡				0.93	0.23-3.70	0.91				2.34	0.85-6.50	0.10
CRP (>1.0 mg/dL)‡				1.73	0.45-6.63	0.41				4.99	1.55-15.99	0.01
Triglycerides (mg/dL)				1.23	0.29-5.30	0.78				0.74	0.36-1.51	0.40
HDL (per 10 mg/dL increase)				1.02	0.71-1.48	0.90				0.76	0.52-1.10	0.14
Education ≥ 12 y				0.42	0.18-1.00	0.05				0.63	0.31-1.27	0.19

Note: Numbers in brackets represent participants with an elevated β -trace protein (≥ 0.81 mg/L) and elevated $\beta 2$ -microglobulin (≥ 2.80 mg/L). ORs in bold are statistically significant at $\alpha = 0.05$. Triglycerides were analyzed on a logarithmic scale (ln). Triglycerides may be converted from mg/dL to mmol/L by multiplying by 0.0113; HDL may be converted from mg/dL to mmol/L by multiplying by 0.0259.

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein.

*Model 1 is adjusted for age, sex, and race/ethnicity. Model 2 is adjusted for all covariates listed.

†Reference group is non-Hispanic whites.

‡Reference group is participants with CRP < 0.22 mg/dL

Supplementary Table S3. Adjusted ORs and 95% CIs of Elevated Standardized Cystatin C (≥ 1.03 mg/L) and Elevated Standardized Creatinine (Males ≥ 1.0 mg/dL; Females ≥ 1.2 mg/dL) in Persons 20-59 Years-old

	Cystatin C (≥ 1.03 mg/L)						Creatinine (Males ≥ 1.0 mg/dL; Females ≥ 1.2 mg/dL)					
	20-59 years (n = 2,776 [134])						20-59 years (n = 2,776 [259])					
	Model 1*			Model 2*			Model 1*			Model 2*		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age (y)	1.07	1.03-1.12	<0.01	1.05	0.99-1.10	0.10	1.05	1.03-1.07	<0.01	1.02	1.00-1.04	0.02
Female sex	0.91	0.44-1.87	0.80	0.91	0.39-2.13	0.82	0.48	0.29-0.79	0.01	0.46	0.27-0.81	0.01
Non-Hispanic black†	1.12	0.58-2.16	0.73	0.87	0.37-2.03	0.74	4.16	2.95-5.88	<0.01	3.61	2.49-5.25	<0.01
Mexican American†	1.44	0.75-2.79	0.27	1.14	0.46-2.83	0.77	0.45	0.25-0.83	0.01	0.36	0.20-0.67	<0.01
BMI (per 5kg/m ² increase)				1.28	1.02-1.60	0.04				1.08	0.91-1.29	0.36
Hypertension				1.93	0.68-5.49	0.21				2.20	1.36-3.54	<0.01
Diabetes				1.75	0.70-4.38	0.23				0.77	0.33-1.82	0.54
Current smoker				1.16	0.55-2.41	0.69				0.65	0.40-1.04	0.07
CRP (0.22-1.0 mg/dL)‡				0.77	0.31-1.96	0.58				1.13	0.73-1.74	0.59
CRP (>1.0 mg/dL)‡				2.78	1.05-7.39	0.04				1.05	0.39-2.81	0.92
Triglycerides (mg/dL)				1.58	0.72-3.48	0.25				1.57	1.01-2.44	0.05
HDL (per 10 mg/dL increase)				0.94	0.73-1.20	0.60				1.09	0.91-1.30	0.35
Education ≥ 12 y				0.77	0.38-1.56	0.46				0.79	0.49-1.30	0.35

Note: Numbers in brackets represent participants with an elevated cystatin C (≥ 1.03 mg/L) and elevated creatinine (males ≥ 1.0 mg/dL; females ≥ 1.2 mg/dL). ORs in bold are statistically significant at $\alpha = 0.05$. Triglycerides were analyzed on a logarithmic scale (ln). Triglycerides may be converted from mg/dL to mmol/L by multiplying by 0.0113; HDL may be converted from mg/dL to mmol/L by multiplying by 0.0259.

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein.

*Model 1 is adjusted for age, sex, and race/ethnicity. Model 2 is adjusted for all covariates listed.

†Reference group is non-Hispanic whites.

‡Reference group is participants with CRP < 0.22 mg/dL

Supplementary Table S4. Adjusted ORs and 95% CIs of Elevated β -Trace Protein (≥ 0.81 mg/L) and Elevated $\beta 2$ - Microglobulin (≥ 2.80 mg/L) in Persons 60 Years and Older

	β -Trace Protein (≥ 0.81 mg/L)						$\beta 2$ -Microglobulin (≥ 2.80 mg/L)					
	≥ 60 years (n = 3,926 [1,152])						≥ 60 years (n = 3,930 [1,103])					
	Model 1*			Model 2*			Model 1*			Model 2*		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age (y)	1.12	1.11-1.14	<0.01	1.12	1.10-1.13	<0.01	1.11	1.10-1.13	<0.01	1.12	1.11-1.13	<0.01
Female sex	0.52	0.43-0.62	<0.01	0.52	0.42-0.65	<0.01	0.96	0.81-1.14	0.63	1.01	0.83-1.22	0.92
Non-Hispanic black†	0.60	0.48-0.76	<0.01	0.50	0.39-0.64	<0.01	0.92	0.72-1.17	0.48	0.87	0.66-1.15	0.32
Mexican American†	0.64	0.52-0.80	<0.01	0.52	0.39-0.70	<0.01	0.78	0.58-1.05	0.10	0.64	0.44-0.93	0.02
BMI (per 5kg/m ² increase)				0.93	0.84-1.03	0.18				1.00	0.90-1.11	0.99
Hypertension				1.91	1.52-2.40	<0.01				1.73	1.41-2.13	<0.01
Diabetes				1.13	0.78-1.65	0.51				1.13	0.77-1.67	0.52
Current smoker				1.10	0.80-1.52	0.53				1.21	0.89-1.64	0.23
CRP (0.22-1.0 mg/dL)‡				1.40	1.11-1.77	0.01				1.61	1.30-2.00	<0.01
CRP (>1.0 mg/dL)‡				2.32	1.68-3.20	<0.01				4.35	3.02-6.27	<0.01
Triglycerides (mg/dL)				0.87	0.70-1.09	0.21				1.37	1.10-1.69	0.01
HDL (per 10 mg/dL increase)				0.87	0.80-0.94	<0.01				0.82	0.75-0.89	<0.01
Education ≥ 12 y				0.76	0.60-0.95	0.02				0.82	0.66-1.02	0.08

Note: Numbers in brackets represent participants with an elevated β -trace protein (≥ 0.81 mg/L) and elevated $\beta 2$ -microglobulin (≥ 2.80 mg/L). ORs in bold are statistically significant at $\alpha = 0.05$. Triglycerides were analyzed on a logarithmic scale (ln). Triglycerides may be converted from mg/dL to mmol/L by multiplying by 0.0113; HDL may be converted from mg/dL to mmol/L by multiplying by 0.0259.

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein.

*Model 1 is adjusted for age, sex, and race/ethnicity. Model 2 is adjusted for all covariates listed.

†Reference group is non-Hispanic whites.

‡Reference group is participants with CRP <0.22 mg/dL

Supplementary Table S5. Adjusted ORs and 95% CIs of Elevated Cystatin C (≥ 1.03 mg/L) and Elevated Creatinine (Males ≥ 1.2 mg/dL; Females ≥ 1.0 mg/dL) in Persons 60 Years and Older

	Cystatin C (≥ 1.03 mg/L)						Creatinine (Males ≥ 1.2 mg/dL; Females ≥ 1.0 mg/dL)					
	≥ 60 years (n = 3,966 [1,546])						≥ 60 years (n = 3,966 [707])					
	Model 1*			Model 2*			Model 1*			Model 2*		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age (y)	1.10	1.09-1.11	<0.01	1.12	1.10-1.13	<0.01	1.08	1.06-1.09	<0.01	1.08	1.06-1.10	<0.01
Female sex	0.78	0.66-0.93	0.01	0.81	0.67-0.97	0.03	0.68	0.54-0.87	<0.01	0.61	0.47-0.78	<0.01
Non-Hispanic black†	0.79	0.66-0.94	0.01	0.72	0.57-0.91	0.01	2.33	1.89-2.86	<0.01	2.58	2.11-3.15	<0.01
Mexican American†	0.74	0.60-0.91	0.01	0.58	0.43-0.78	<0.01	0.60	0.45-0.81	<0.01	0.50	0.35-0.71	<0.01
BMI (per 5kg/m ² increase)				1.25	1.11-1.42	<0.01				1.03	0.86-1.24	0.74
Hypertension				1.72	1.40-2.11	<0.01				2.38	1.79-3.16	<0.01
Diabetes				1.02	0.72-1.44	0.92				1.25	0.89-1.76	0.20
Current smoker				1.84	1.32-2.57	<0.01				0.98	0.72-1.34	0.91
CRP (0.22-1.0 mg/dL)‡				1.29	1.06-1.56	0.01				1.22	0.95-1.57	0.11
CRP (>1.0 mg/dL)‡				2.25	1.74-2.93	<0.01				2.13	1.35-3.37	<0.01
Triglycerides (mg/dL)				1.62	1.30-2.02	<0.01				2.14	1.59-2.89	<0.01
HDL (per 10 mg/dL increase)				0.85	0.79-0.90	<0.01				0.92	0.84-1.00	0.06
Education ≥ 12 y				0.78	0.63-0.97	0.02				0.86	0.66-1.12	0.26

Note: Numbers in brackets represent participants with an elevated cystatin C (≥ 1.03 mg/L) and elevated creatinine (males ≥ 1.2 mg/dL; females ≥ 1.0 mg/dL). ORs in bold are statistically significant at $\alpha = 0.05$. Triglycerides were analyzed on a logarithmic scale (ln). Triglycerides may be converted from mg/dL to mmol/L by multiplying by 0.0113; HDL may be converted from mg/dL to mmol/L by multiplying by 0.0259.

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein.

*Model 1 is adjusted for age, sex, and race/ethnicity. Model 2 is adjusted for all covariates listed.

†Reference group is non-Hispanic whites.

‡Reference group is participants with CRP <0.22 mg/dL

Supplementary Table S6. Adjusted ORs and 95% CIs of Elevated Serum β -Trace Protein (≥ 0.81 mg/L), Elevated Serum $\beta 2$ -Microglobulin (≥ 2.80 mg/L), and Elevated Serum Cystatin C (≥ 1.03 mg/L) in Persons 20 Years and Older

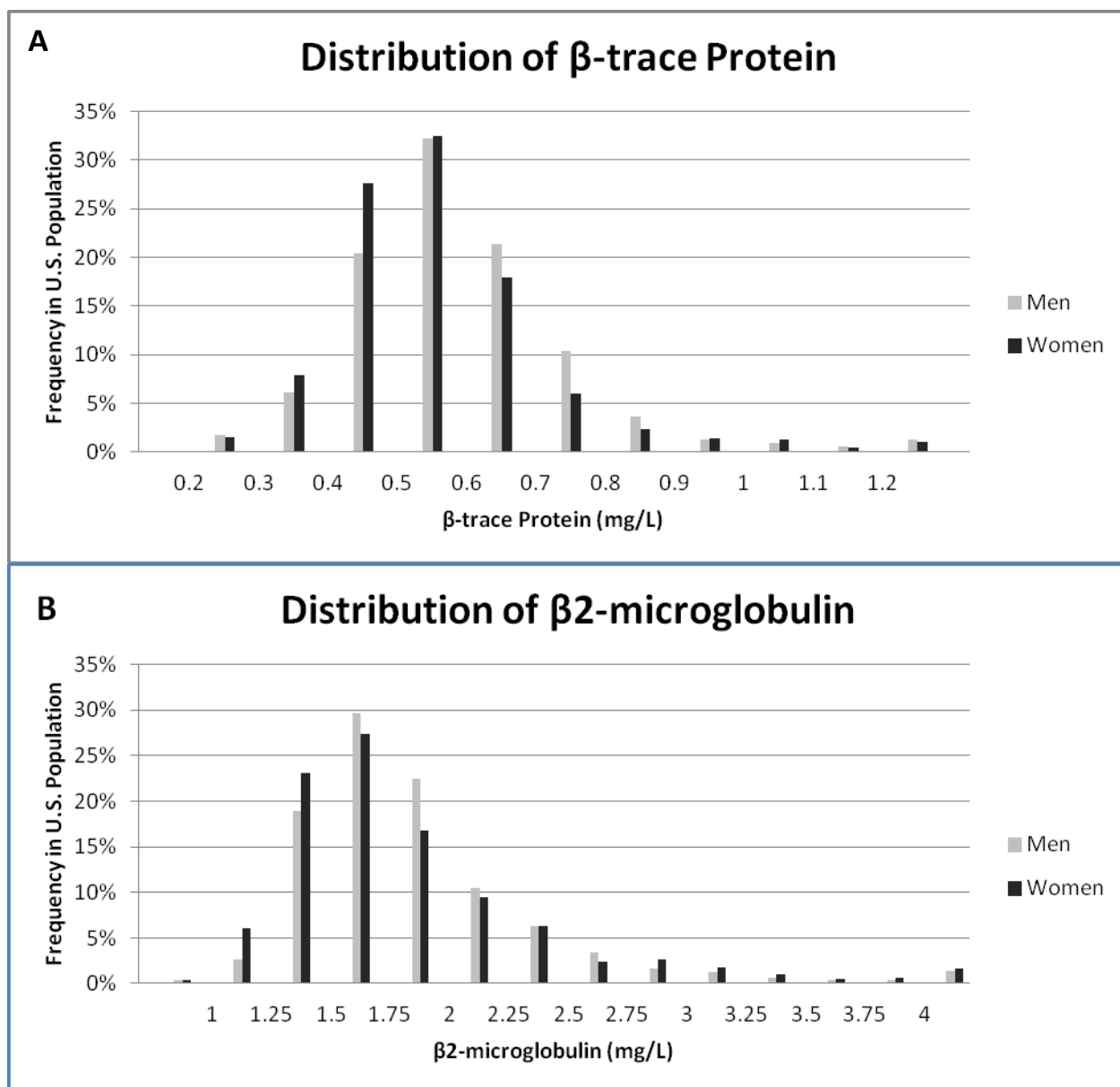
	β -Trace Protein (≥ 0.81 mg/L)			$\beta 2$ -Microglobulin (≥ 2.80 mg/L)			Standard Cystatin C (≥ 1.03 mg/L)		
	≥ 20 years (n = 6,682 [1,220])			≥ 20 years (n = 6,688 [1,204])			≥ 20 years (n = 6,742 [1,680])		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age (y)	1.03	1.00-1.06	0.05	1.03	1.02-1.04	<0.01	1.04	1.01-1.06	<0.01
Female sex	0.57	0.38-0.86	0.01	1.38	0.94-2.03	0.10	0.89	0.64-1.23	0.46
Non-Hispanic black†	0.43	0.29-0.64	<0.01	1.14	0.82-1.58	0.42	0.80	0.54-1.20	0.28
Mexican American†	0.85	0.52-1.39	0.52	1.26	0.80-1.99	0.31	1.38	0.71-2.69	0.34
eGFR	0.93	0.91-0.94	<0.01	0.94	0.93-0.95	<0.01	0.92	0.91-0.93	<0.01
BMI (per 5kg/m ² increase)	0.88	0.73-1.06	0.16	0.79	0.71-0.87	<0.01	1.22	1.04-1.44	0.02
Hypertension	1.75	1.18-2.60	0.01	1.35	1.08-1.69	0.01	1.40	0.99-1.99	0.06
Diabetes	1.02	0.69-1.52	0.92	1.39	0.86-2.23	0.17	1.28	0.85-1.92	0.23
Current smoker	1.06	0.62-1.80	0.83	1.00	0.64-1.56	1.00	1.67	1.03-2.71	0.04
CRP (0.22-1.0 mg/dL)‡	1.28	0.89-1.85	0.18	1.76	1.30-2.38	<0.01	1.07	0.82-1.41	0.61
CRP (>1.0 mg/dL)‡	2.09	1.29-3.39	<0.01	4.88	2.99-7.98	<0.01	3.21	1.85-5.58	<0.01
Triglycerides (mg/dL)	0.56	0.36-0.88	0.01	0.73	0.50-1.06	0.10	1.23	0.82-1.83	0.31
HDL (per 10 mg/dL increase)	0.88	0.78-1.00	0.05	0.76	0.65-0.89	<0.01	0.84	0.77-0.92	<0.01
Education ≥ 12 y	0.61	0.45-0.83	<0.01	0.71	0.55-0.93	0.01	0.72	0.55-0.95	0.02

Note: Numbers in brackets represent individuals with an elevated β -trace protein (≥ 0.81 mg/L) and elevated $\beta 2$ -microglobulin (≥ 2.80 mg/L). ORs in bold are statistically significant at $\alpha = 0.05$. Triglycerides were analyzed on a logarithmic scale (ln). Triglycerides may be converted from mg/dL to mmol/L by multiplying by 0.0113; HDL may be converted from mg/dL to mmol/L by multiplying by 0.0259. Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein

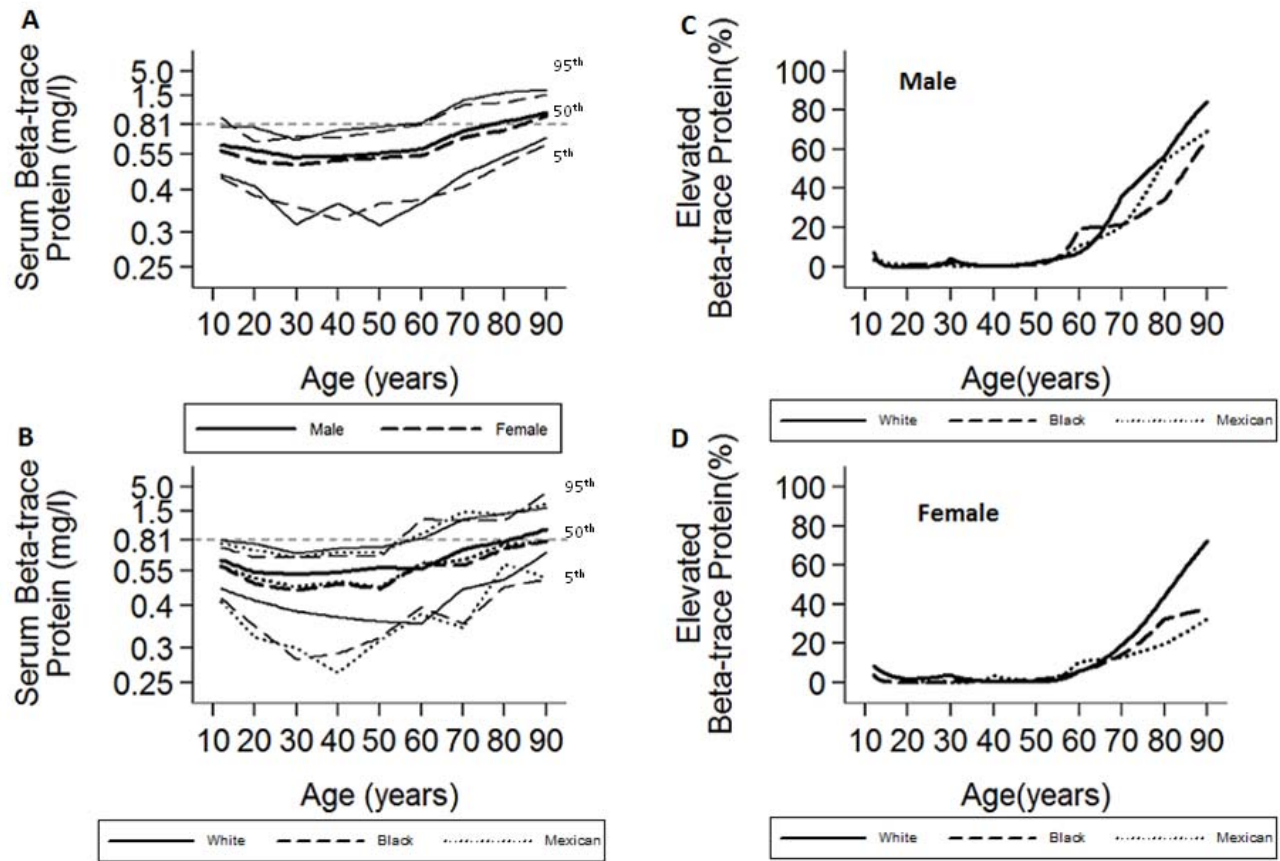
*Model 1 is adjusted for eGFR. Model 2 is adjusted for all covariates listed.

†Reference group is non-Hispanic whites.

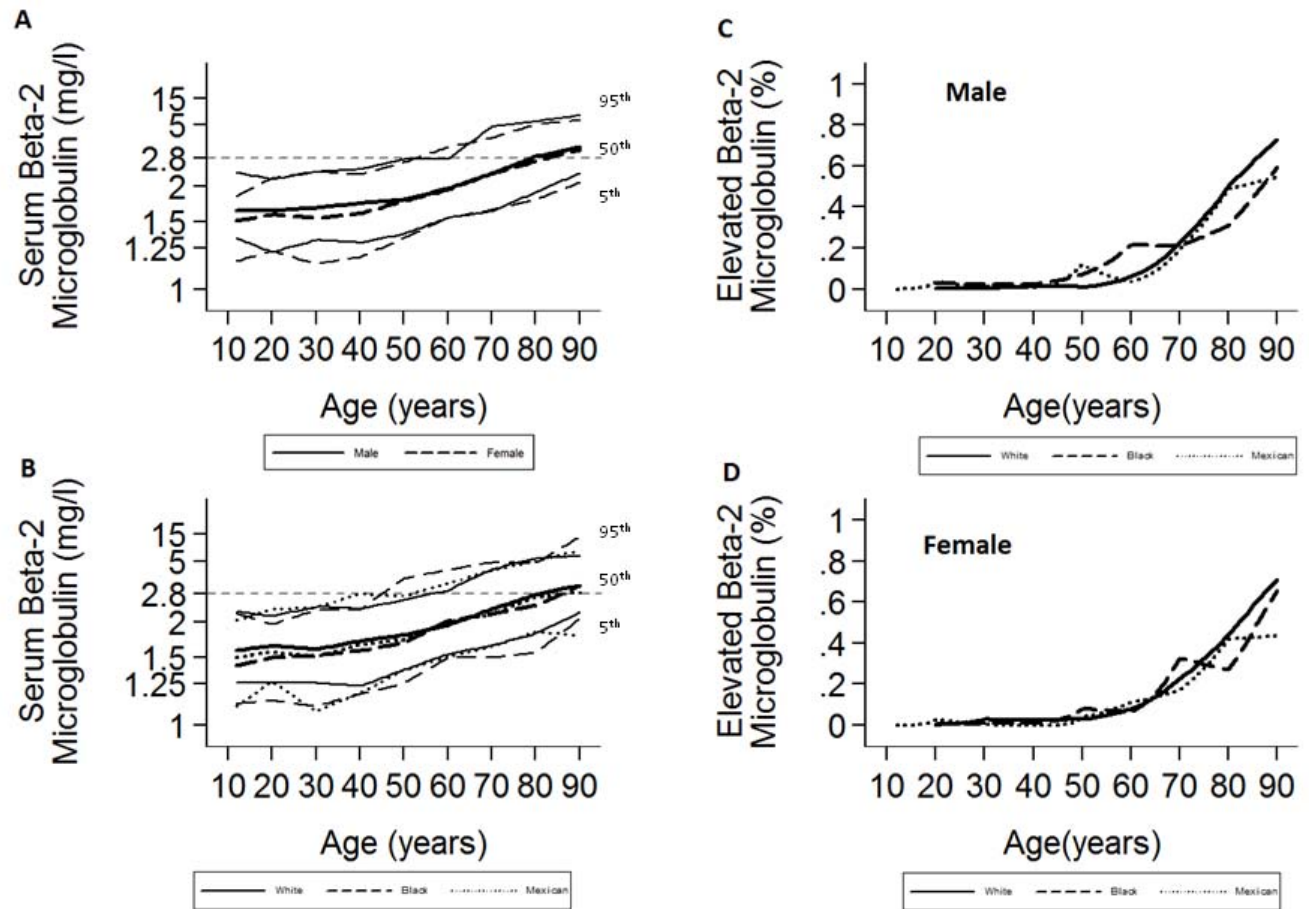
‡Reference group is individuals with CRP < 0.22 mg/dL



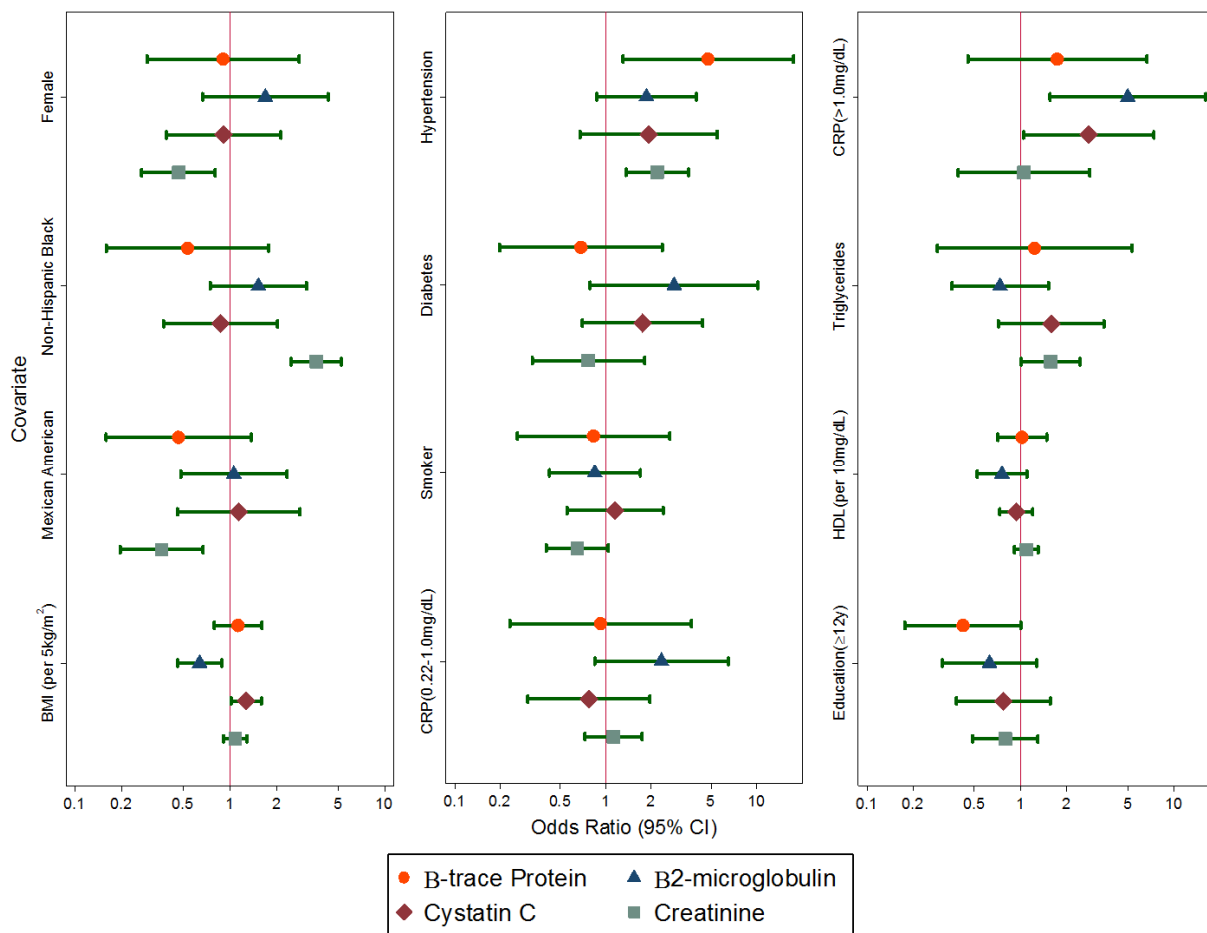
Supplementary Figure S1. Histogram Describing the Distribution of (A) β -trace Protein (mg/L) and (B) β 2-microglobulin (mg/L) in the U.S. population for males and females age 12 and over.



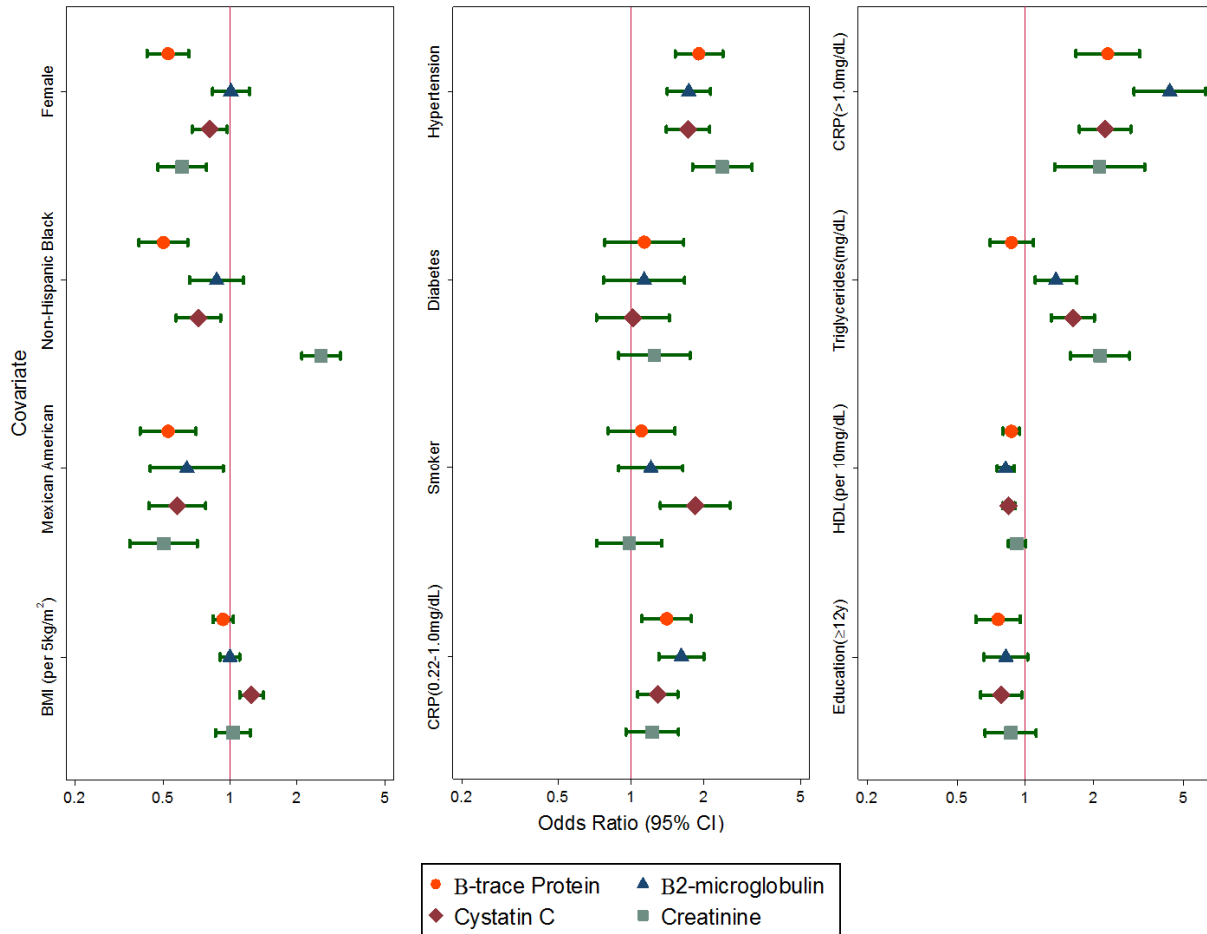
Supplementary Figure S2A-D. β -trace protein (β TP) percentiles (5th, 50th, and 95th) by age and (A) sex and (B) race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American) graphed by using an inverse transformation: $-1/\beta$ TP. Corresponding values for β TP (mg/L) are shown on the y-axis. Also, proportion of the US population 12 years and older with elevated β TP (defined as ≥ 0.81 mg/L, the 99th percentile in healthy 20-39 year olds) by age and race/ethnicity in (C) men and (D) women.



Supplementary Figure S3A-D. β 2-microglobulin (β 2M) percentiles (5th, 50th, and 95th) by age and (A) sex and (B) race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American) graphed by using an inverse transformation: $-1/\beta$ 2M. Corresponding values for β 2M (mg/L) are shown on the y-axis. Also, proportion of the US population 12 years and older with elevated β 2M (defined as ≥ 2.80 mg/L, the 99th percentile in healthy 20-39 year olds) by age and race/ethnicity in (C) men and (D) women.



Supplementary Figure S4. Age 20-59: odds ratios (95% confidence intervals) of an elevated concentration of β -trace protein (≥ 0.81 mg/L), β 2-microglobulin (≥ 2.80 mg/L), cystatin C (≥ 1.03 mg/L), and creatinine (Men: ≥ 1.2 mg/dL; Women: ≥ 1.0 mg/dL) after adjusting for age (per 1 year increase), female sex, non-Hispanic black race/ethnicity, Mexican American race/ethnicity, body mass index (BMI) per 5 kg/m² increase, hypertension, diabetes, current smoking status, C-reactive protein (CRP) from 0.22-1.0 mg/dL, C-reactive protein >1.0 mg/dL, triglycerides (mg/dL), high density lipoprotein (HDL) cholesterol (per 10 mg/dL increase), and education (≥ 12 years). Reference groups for categorical variables include male sex, non-Hispanic whites, no hypertension, no diabetes, no current smoking status, and an education <12 years. β -trace protein is depicted by a circle, β 2-microglobulin is depicted by a triangle, cystatin C is depicted by a diamond, and creatinine is depicted by a square. The age covariate is not shown.



Supplementary Figure S5. Age 60 years and older: odds ratios (95% confidence intervals) of an elevated concentration of β -trace protein (≥ 0.81 mg/L), $\beta 2$ -microglobulin (≥ 2.80 mg/L), cystatin C (≥ 1.03 mg/L), and creatinine (Men: ≥ 1.2 mg/dL; Women: ≥ 1.0 mg/dL) after adjusting for age (per 1 year increase), female sex, non-Hispanic black race/ethnicity, Mexican American race/ethnicity, body mass index (BMI) per 5 kg/m² increase, hypertension, diabetes, current smoking status, C-reactive protein (CRP) from 0.22-1.0 mg/dL, C-reactive protein >1.0 mg/dL, triglycerides (mg/dL), high density lipoprotein (HDL) cholesterol (per 10 mg/dL increase), and education (≥ 12 years). Reference groups for categorical variables include male sex, non-Hispanic whites, no hypertension, no diabetes, no current smoking status, and an education <12 years. β -trace protein is depicted by a circle, $\beta 2$ -microglobulin is depicted by a triangle, cystatin C is depicted by a diamond, and creatinine is depicted by a square. The age covariate is not shown.