

**Table S1: Baseline characteristics of the total CHS cohort at year 1996-1997, as well as the subgroups with and without serum uromodulin measurement**

	Total Cohort (n=4413)	Group without sUMOD measurement (n=3480)	Random Subcohort with sUMOD measured (n=933)	p-value
<b>Demographics</b>				
Age (ys)	78.6 (4.8)	78.7 (5.2)	78.1 (4.8)	<0.001
Male	38.3	38.0	39.7	0.4
Race Black	16.7	17.1	15.3	0.2
Site				0.1
Wake Forest	26.0	26.8	23.2	
UC Davis	26.4	25.9	28.5	
Johns Hopkins	21.3	21.1	21.8	
Pittsburgh	26.3	26.2	26.6	
<b>Laboratory Measures</b>				
eGFR <60 ml/min/1.73 m <sup>2</sup>	43.2	43.7	41.7	0.3
eGFR (ml/min per 1.73 m <sup>2</sup> )	63.0 (18.6)	62.8 (18.6)	63.4 (18.6)	0.4
Albuminuria (ACR>30 mg/g Cr)	654 (21.0)	481 (21.2)	173 (20.5)	0.7
(log <sub>2</sub> ) ACR (mg/g)	3.8 (1.9)	3.8 (1.9)	3.8 (1.9)	0.9
Fasting glucose (mg/dl)	106.6 (32.3)	106.3 (31.4)	107.4 (34.6)	0.4
(log <sub>2</sub> ) CRP (mg/dl)	1.3 (1.6)	1.3 (1.6)	1.3 (1.6)	0.4
Total cholesterol (mg/dl)	202.0 (39.7)	202.2 (40.0)	201.4 (38.8)	0.6
Serum albumin (g/dl)	3.8 (0.3)	3.8 (0.3)	3.8 (0.3)	0.7
<b>CVD risk factors and prevalent CVD</b>				
Systolic BP (mmHg)	136.9 (20.7)	136.9 (20.6)	137.0 (21.0)	0.9
Diastolic BP (mmHg)	69.8 (11.3)	69.9 (11.4)	69.8 (11.0)	0.8
BMI (kg/m <sup>2</sup> )	26.9 (4.7)	26.9 (4.7)	26.9 (4.7)	0.8
Diabetes mellitus	17.2	18.4	13.8	0.06
Hypertension	65.0	66.5	60.0	<0.001
Heart Failure	11.0	11.4	9.2	0.06
Cardiovascular Disease	18.7	19.0	17.5	0.3
<b>Lifestyle factors</b>				
Smoking				0.08
Current	7.7	7.8	7.4	
Former	44.6	45.4	41.6	
Never	47.7	46.8	51.0	

Continuous variables in mean (SD=standard deviation), categorical variables in percentage of total population. Cardiovascular Disease is defined as history of myocardial infarction and/or stroke prior to baseline assessment. Abbreviations: sUMOD=serum uromodulin, eGFR=estimated glomerular filtration rate, CRP=C-reactive protein, ACR=albumin/creatinine ratio, CVD=cardiovascular disease, Cr=creatinine, BP=blood pressure, BMI=body mass index.

**Table S2: Baseline characteristics of participants from the random subcohort with an eGFR measurement available at 2005-2006 visit, compared to the remaining patients that returned to this visit**

	Total Cohort (n=1876)	Patients not from the random subcohort (n=1596)	Patients from the random subcohort (n=280)	p-value
<b>Demographics</b>				
Age at baseline (ys)	76.8 (3.9)	76.8 (3.9)	76.5(3.8)	0.1
Age at follow-up (ys)	85.7 (3.8)	85.7 (3.9)	85.4 (3.8)	0.2
Male	33.2	32.3	37.9	0.08
Race Black	17.4	17.9	14.6	0.2
Site				0.08
Wake Forest	24.3	25.3	18.6	
UC Davis	28.3	37.5	32.5	
Johns Hopkins	19.3	19.0	20.7	
Pittsburgh	28.1	28.1	28.2	
<b>Laboratory Measures</b>				
eGFR <60 ml/min/1.73 m <sup>2</sup> at baseline	31.7	32.1	30.0	0.5
eGFR at baseline (ml/min per 1.73 m <sup>2</sup> )	68.3 (16.6)	68.2 (16.5)	68.6 (17.2)	0.7
eGFR at follow-up (ml/min per 1.73 m <sup>2</sup> )	60.5 (19.6)	60.2 (19.2)	61.3 (20.6)	0.5
Albuminuria at baseline (ACR>30 mg/g Cr)	12.0	12.6	8.9	0.1
(log <sub>2</sub> ) ACR (mg/g)	3.3 (1.6)	3.3 (1.5)	3.3 (1.6)	0.9
Fasting glucose (mg/dl)	103.7 (27.0)	103.6 (26.4)	104.0 (28.8)	0.8
(log <sub>2</sub> ) CRP (mg/dl)	1.2 (1.5)	1.2 (1.5)	1.2 (1.5)	0.5
Total cholesterol (mg/dl)	204.2 (37.7)	204.2 (37.8)	204.3 (37.1)	1.0
Serum albumin (g/dl)	3.8 (0.3)	3.8 (0.3)	3.8 (0.3)	0.5
<b>CVD risk factors and prevalent CVD</b>				
Systolic BP (mmHg)	136.0 (19.7)	136.0 (19.6)	136.0 (20.2)	1.0
Diastolic BP (mmHg)	70.2 (10.9)	70.0 (10.9)	71.0 (10.8)	0.2
BMI (kg/m <sup>2</sup> )	27.3 (4.5)	27.3 (4.5)	27.4 (4.5)	0.8
Diabetes mellitus	21.5	22.5	16.6	0.05
Hypertension	62.3	63.4	56.8	0.05
Heart Failure	3.7	3.3	5.7	0.07
Cardiovascular Disease	10.4	10.5	10.0	0.9
<b>Lifestyle factors</b>				
Smoking				0.9
Current	7.3	7.3	6.9	
Former	40.7	40.9	40.0	
Never	52.0	51.8	53.1	

Continuous variables in mean (SD=standard deviation), categorical variables in percentage of total population. Cardiovascular Disease is defined as history of myocardial infarction and/or stroke prior to baseline assessment. Abbreviations: sUMOD=serum uromodulin, eGFR=estimated glomerular filtration rate, CRP=C-reactive protein, ACR=albumin/creatinine ratio, CVD=cardiovascular disease, Cr=creatinine, BP=blood pressure, BMI=body mass index.

**Table S3: Associations of serum uromodulin with kidney function decline  $\geq 40\%$**

	Cases/ Controls	Univariate	Plus adjusted for demographics <sup>b</sup>	Plus adjusted for eGFR and ACR <sup>c</sup>	Plus adjusted for CVD RF and prevalent disease <sup>d</sup>
<b>Odds ratio per SD<sup>a</sup> higher sUMOD</b>	92/311	0.76 (0.59-0.99)	0.82 (0.63-1.08)	0.94 (0.71-1.25)	0.98 (0.73-1.33)

Kidney function decline is defined a reduction of estimated glomerular filtration rate  $\geq 40\%$  from baseline (1996-1997) for the follow-up visit (2005-2006). 95%-confidence intervals for the hazards ratios are given in parentheses. Abbreviations: SD=standard deviation; eGFR=estimated glomerular filtration rate; ACR=urinary albumin/creatinine-ratio; RF=risk factors.

<sup>a</sup> SD=63.9 ng/ml

<sup>b</sup> adjusted for age, sex, race, clinic site, body-mass index, level of education

<sup>c</sup> adjusted for <sup>b</sup> + eGFR & (log<sub>2</sub>) ACR

<sup>d</sup> adjusted for <sup>c</sup> + diabetes, smoking status, systolic blood pressure, serum cholesterol, (log<sub>2</sub>) serum C-reactive protein, lipid-lowering medication, antihypertensive medication, prevalent heart failure and cardiovascular disease (CVD) at baseline