

Supplemental Information

Supplemental methods

Sensitivity analyses

In the first sensitivity analyses, we excluded all participants that were non-whites (n=206), because of ethnicity-related differences in vitamin D metabolism, and repeated the Cox proportional hazards regression models. Second, we examined the difference between expected and actually measured 24-hour urine volume to account for potential inadequacies in urine collections. We defined possible over or under collections as the upper and lower 2.5% of the difference between the estimated and measured volume of a subject's 24-hour urine sample.^(1,2) The estimated 24-hour urine volume was derived from the formula $\text{creatinine clearance} = (\text{urinary creatinine} \times \text{estimated 24 hour urine volume}) / \text{serum creatinine}$. Creatinine clearance was estimated using the Cockcroft–Gault formula. ⁽³⁾ We additionally adjusted for urine volume and creatinine excretion. Third, we redefined albuminuria as albuminuria >40 mg/24h (instead of >30 mg/24h). To reach this secondary endpoint, albuminuria had to increase with a minimum of 10 mg/24h, which is an increase of at least 33%. As a final sensitivity analysis, we re-analyzed the association between 25(OH)D levels and both renal outcomes in subjects followed up until the last time point by multivariable logistic regression, adjusted as in Cox regression models.

References

1. Joosten MM, Gansevoort RT, Mukamal KJ, Lambers Heerspink HJ, Geleijnse JM, Feskens EJ, Navis G, Bakker SJ, PREVEND Study Group. Sodium excretion and risk of developing coronary heart disease. *Circulation* 129(10): 1121-1128, 2014

2. Kieneker LM, Gansevoort RT, Mukamal KJ, de Boer RA, Navis G, Bakker SJ, Joosten MM. Urinary potassium excretion and risk of developing hypertension: The prevention of renal and vascular end-stage disease study. *Hypertension* 64(4): 769-776, 2014

3. Cockcroft DW, & Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 16(1): 31-41, 1976

Supplemental Table 1. Baseline characteristics of the study population compared with participants excluded due to missing follow-up data

	Study population n=5,051	Excluded n=1,084	<i>P</i>
Male sex, n (%)	2,391 (47)	493 (46)	0.26
Age, y	48.4±11.7	47.7±13.8	0.14
Body mass index, kg/m ²	25.7±3.9	25.8±4.4	0.48
Type 2 diabetes, n (%)	95 (2)	39 (4)	<0.001
History of CVD, n (%)	168 (3)	62 (6)	<0.001
Systolic blood pressure, mmHg	125.8±17.9	127.4±19.4	0.01
Diastolic blood pressure, mmHg	72.8±9.1	73.2±9.4	0.24
Blood pressure-lowering drugs, n (%)	583 (12)	151 (14)	0.03
ACEi or ARB, n (%)	160 (4)	44 (5)	0.14
Lipid-lowering drugs, n (%)	254 (5)	52 (5)	0.75
Serum total cholesterol, mg/dL	215.3±42.6	215.7±43.0	0.80
Serum HDL cholesterol, mg/dL	52.1±15.4	51.7±16.0	0.42
Plasma 25(OH)D, ng/mL	23.2±9.3	22.5±9.6	0.04
Plasma 1,25(OH) ₂ D, pg/mL	60.6±19.6	60.2±20.7	0.51
eGFR, mL/min/1.73m ²	97.3±14.6	96.3±16.2	0.08
Urinary sodium excretion, mmol/24h	141.0±49.8	136.4±51.3	0.006
Urine albumin, mmol/24h	8.1 [5.9-12.1]	8.6 [5.9-13.8]	0.03

P-values for differences in groups were assessed with T-test for normally distributed continuous data, the Mann-Whitney test for skewed distributed data, and the χ^2 test for nominal data.

Abbreviations: 1,25(OH)₂D, 1,25 dihydroxyvitamin D; 25(OH)D, 25-hydroxyvitamin D; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein.

Supplemental Table 2. Associations of 25(OH) and 1,25(OH)₂ vitamin D levels with risk of developing reduced eGFR based on CKD-EPI creatinine equation in the PREVEND study

	25-hydroxyvitamin D					
	Unadjusted HR	No. of events	P	Adjusted HR	No. of events	P
Reduced eGFR	1.12 (0.98-1.28)	192	0.11	1.02 (0.87-1.20)	181	0.82
	1,25-dihydroxyvitamin D					
	Unadjusted HR	No. of events	P	Adjusted HR	No. of events	P
Reduced eGFR	1.04 (0.90-1.19)	192	0.61	1.03 (0.89-1.20)	181	0.69

Reduced estimated glomerular filtration rate (eGFR) is defined as an eGFR <60 ml/min/1.73m². HR, hazard ratio. Multivariable model includes adjustment for age, sex, presence of type 2 diabetes, history of cardiovascular disease, current smoking, use of lipid-lowering drugs, use of blood pressure-lowering drugs, body mass index, systolic blood pressure, day of blood sampling, cholesterol - high-density lipoprotein cholesterol ratio, triglyceride level, baseline UAE and eGFR. Data are presented as hazard ratio (HR) per standard deviation increase in 25(OH)D and 1,25(OH)₂D concentrations plus 95% confidence interval (CI).

Supplemental Table 3. Other independent determinants at baseline associated with incident increased albuminuria and reduced eGFR in the PREVENT cohort

	Adjusted hazard ratio	95% CI	<i>P</i>
Albuminuria outcome			
Age	1.03	1.02-1.04	<0.001
Female sex	0.78	0.65-0.93	0.005
Blood pressure-lowering drugs	1.80	1.46-2.22	<0.001
Serum total to HDL cholesterol ratio	1.06	1.00-1.13	0.047
Albuminuria	6.44	5.39-7.70	<0.001
eGFR outcome			
Age	1.06	1.04-1.08	<0.001
Female sex	1.34	1.03-1.75	0.03
Presence of type 2 diabetes	2.37	1.35-4.13	0.002
Current smoking	1.70	1.28-2.27	<0.001
Blood pressure-lowering drugs	1.81	1.36-2.40	<0.001
Systolic blood pressure	1.02	1.01-1.03	<0.001
Triglycerides	0.66	0.45-0.97	0.04
eGFR	0.88	0.86-0.89	<0.001