SUPPLEMENTAL TABLES

Supplemental Table 1. Cross-sectional associations of clinical characteristics with vitamin D metabolic ratio ($24,25(OH)_2D_3/25(OH)D_3$)

Characteristic	N	Unadjusted ratio mean (SD)	Adjusted* mean difference (95% CI)	p-values
Age				
<50 years	190	36.5 (21.4)	0 (reference)	
50-<60 years	287	38.0 (19.6)	3.53 (0.41, 6.64)	0.026
60-<70 years	432	39.6 (19.8)	6.86 (3.92, 9.79)	<0.001
≥70 years	171	34.1 (16.2)	4.54 (0.97, 8.12)	0.013
Age (per 10 years)			1.43 (0.45, 2.41)	0.004
Sex				
Male	616	37.9 (19.4)	0 (reference)	
Female	464	37.6 (19.9)	-0.64 (-2.68, 1.41)	0.543
Race/ethnicity				
White	463	43.6 (19.8)	0 (reference)	
Black	457	32.7 (18.9)	-8.41 (-10.58, -6.24)	<0.001
Hispanic	124	33.8 (15.6)	-3.06 (-6.44, 0.32)	0.076
Other	36	41.1 (18.4)	-1.56 (-7.20, 4.07)	0.587
Diabetes				
No	546	42.0 (21.3)	0 (reference)	
Yes	534	33.5 (16.6)	-6.04 (-8.11, -3.97)	<0.001
Prevalent CVD				
No	718	38.9 (20.0)	0 (reference)	
Yes	362	35.5 (18.5)	-0.006 (-2.29, 2.27)	0.996
Active smoking				
No	967	38.4 (19.7)	0 (reference)	
Yes	113	32.1 (17.9)	-5.99 (-9.28, -2.69)	<0.001
Calciferol use				
No	944	36.7 (19.1)	0 (reference)	
Yes	132	44.9 (22.0)	6.86 (3.70, 10.02)	<0.001

Vitamin D Receptor Agonists use				
No	1007	38.5 (19.8)	0 (reference)	
Yes	69	26.9 (11.6)	-0.45 (-4.77, 3.88)	0.839
Cinacalcet use				
No	1074	37.8 (19.6)	0 (reference)	
Yes	2	14.8 (4.2)	-15.74 (-39.28, 7.80)	0.190
Phosphate binder use				
No	1008	38.0 (19.4)	0 (reference)	
Yes	68	34.2 (21.8)	0.88 (-3.35, 5.11)	0.684
Body mass index				
<30 kg/m^2	477	41.5 (21.1)	0 (reference)	
30-<35 kg/m^2	278	37.3 (17.4)	-3.47 (-5.98, -0.95)	0.007
≥35 kg/m^2	319	32.7 (17.9)	-7.28 (-9.79, -4.78)	<0.001
Body mass index (per 5 kg/m^2)			-2.05 (-2.71, -1.40)	<0.001
Estimated GFR				
≥60 mL/min/1.73m^2	152	53.4 (21.7)	0 (reference)	
45-<60 mL/min/1.73m^2	307	43.4 (18.8)	-9.64 (-13.05, -6.23)	<0.001
30-<45 mL/min/1.73m^2	377	34.8 (16.6)	-18.05 (-21.42, -14.68)	<0.001
<30 mL/min/1.73m^2**	238	25.7 (13.5)	-26.60 (-30.21, -23.00)	<0.001
Estimated GFR (per 15 decrease mL/min/1.73m^2)***			-8.53 (-9.54, -7.51)	<0.001
Urine protein				
<30 mg/d	682	40.4 (19.9)	0 (reference)	
30-<300 mg/d	285	33.4 (18.3)	1.85 (-0.81, 4.50)	0.172
≥300 mg/d	35	29.7 (19.8)	3.24 (-2.88, 9.37)	0.299
Urine protein (per doubling)			0.22 (-0.33, 0.76)	0.434
PTH (per doubling)	1076		-6.16 (-7.25, -5.06)	<0.001
FGF-23 (per doubling)	1040		-0.46 (-1.49, 0.57)	0.380

*adjusted for age (continuous), sex, race/ethnicity (4 categories), diabetes (Y/N), and eGFR (continuous)

Supplemental Table 2. Association of baseline clinical characteristics with change in vitamin D metabolic ratio ($24,25(OH)_2D_3/25(OH)D_3$)

Characteristic	N	Unadjusted absolute change** in ratio 24,25(OH)2D3/25(OH)D3 (pg/ng)	Adjusted* difference in change (pg/ng)	
		mean (SD)	(95% CI)	p-values
Age				
<50 years	138	-1.48 (15.62)	0 (reference)	
50-<60 years	214	-0.58 (16.45)	0.90 (-2.44, 4.24)	0.596
60-<70 years	311	-1.60 (14.99)	0.002 (-3.15, 3.15)	0.999
≥70 years	114	-2.42 (14.77)	-0.77 (-4.70, 3.17)	0.702
Age (per 10 years)			-0.07 (-1.13, 1.00)	0.905
Sex				
Male	432	-1.71 (15.93)	0 (reference)	
Female	345	-1.05 (14.89)	0.68 (-1.53, 2.88)	0.547
Race/ethnicity				
White	347	-1.15 (15.54)	0 (reference)	
Black	319	-1.33 (15.35)	-0.03 (-2.43, 2.38)	0.981
Hispanic	88	-3.65 (15.76)	-2.19 (-5.92, 1.54)	0.249
Other	23	1.87 (14.67)	3.01 (-3.55, 9.57)	0.368
Diabetes				
No	413	-1.05 (16.39)	0 (reference)	
Yes	364	-1.83 (14.36)	-0.64 (-2.87, 1.59)	0.572
Prevalent cardiovascular disease				
No	530	-1.29 (15.97)	0 (reference)	
Yes	247	-1.69 (14.35)	-0.05 (-2.55, 2.44)	0.967
Active smoking				
No	715	-1.36 (15.51)	0 (reference)	
Yes	62	-2.04 (15.12)	-0.74 (-4.80, 3.31)	0.719
Calciferol use				

No	674	-1.34 (15.34)	0 (reference)	
Yes	102	-2.01 (16.40)	-0.96 (-4.30, 2.38)	0.574
Vitamin D receptor activator use				
No	731	-1.55 (15.50)	0 (reference)	
Yes	45	0.61 (15.02)	3.07 (-1.85, 7.98)	0.221
Cinacalcet use				
No	775	-1.43 (15.47)	0 (reference)	
Yes	1	18.2	20.63 (-9.94, 51.20)	0.186
Phosphate binder use				
No	729	-1.62 (15.40)	0 (reference)	
Yes	47	1.58 (16.53)	3.61 (-1.10, 8.31)	0.133
Body mass index				
<30 kg/m^2	353	-0.96 (16.59)	0 (reference)	
30-<35 kg/m^2	197	-1.45 (14.65)	-0.28 (-3.05, 2.49)	0.844
≥35 kg/m^2	224	-1.96 (14.33)	-0.83 (-3.60, 1.94)	0.558
Body mass index (per 5 kg/m^2)			0.16 (-5.73, 0.90)	0.663
Estimated GFR				
≥60 mL/min/1.73m^2	118	0.42 (17.85)	0 (reference)	
45-<60 mL/min/1.73m^2	244	-0.57 (15.19)	-1.05 (-4.55, 2.45)	0.556
30-<45 mL/min/1.73m^2	258	-3.26 (14.75)	-3.70 (-7.22, -0.17)	0.040
<30 mL/min/1.73m^2**	154	-0.90 (15.04)	-1.31 (-5.14, 2.51)	0.500
Estimated GFR (per 15 decrease mL/min/1.73m^2)***			-0.41 (-1.50, 0.68)	0.460
Urine protein				
<30 mg/d	504	-0.11 (15.01)	0 (reference)	
30-<300 mg/d	195	-4.66 (15.44)	-5.02 (-7.96, -2.07)	0.001
≥300 mg/d	22	-1.66 (25.93)	-2.36 (-9.40, 4.67)	0.510
Urine protein (per doubling)			-1.08 (-1.68, -0.48)	<0.001
PTH (per doubling)	757		1.54 (0.26, 2.81)	0.018
FGF-23 (per doubling)	773		0.64 (-0.58, 1.85)	0.306

*adjusted for age (continuous), sex, race/ethnicity (4 categories), diabetes (Y/N), and eGFR (continuous)

Supplemental Table 3. Association of change in baseline clinical characteristics with change in vitamin D metabolic ratio ($24,25(OH)_2D_3/25(OH)D_3$)

Characteristic	N	Unadjusted absolute change** in ratio 24,25(OH)2D3:25(OH)D3 (pg/ng) mean (SD)	Adjusted difference in change in $24,25(OH)2D_3$:$25(OH)D_3$ (95% CI)* (pg/ng)	p-value
Active smoking				
None at year 1 or 4	708	-1.36 (15.57)	0 (reference)	
At year 1, but not year 4	14	-1.93 (15.64)	-0.62 (-8.86, 7.62)	0.883
At year 4, but not year 1	7	2.87 (9.19)	4.31 (-7.29, 15.92)	0.466
At year 1 and year 4	48	-2.07 (15.13)	-0.73 (-5.30, 3.85)	0.755
Calciferol use				
None at year 1 or 4	534	-2.85 (14.67)	0 (reference)	
At year 1, but not year 4	43	-4.90 (11.86)	-1.97 (-6.79, 2.85)	0.424
At year 4, but not year 1	133	5.52 (16.31)	8.45 (5.52, 11.39)	<0.001
At year 1 and year 4	59	0.17 (18.90)	3.08 (-1.16, 7.32)	0.154
VDRA use				
None at year 1 or 4	646	-1.76 (15.65)	0 (reference)	
At year 1, but not year 4	23	0.73 (17.14)	4.29 (-2.49, 11.08)	0.214
At year 4, but not year 1	78	1.60 (14.34)	4.46 (0.62, 8.31)	0.023
At year 1 and year 4	22	0.48 (12.84)	3.57 (-3.18, 10.31)	0.299
Phosphate binder use				
None at year 1 or 4	675	-1.26 (15.09)	0 (reference)	
At year 1, but not year 4	31	3.77 (15.42)	5.19 (-0.55, 10.94)	0.076
At year 4, but not year 1	47	-4.64 (19.45)	-3..07 (-7.73, 1.59)	0.197
At year 1 and year 4	16	-1.85 (18.66)	-0.58 (-8.37, 7.21)	0.884

* adjusted for age at year , sex, race/ethnicity (4 categories), diabetes at year 1 (Y/N), and eGFR at year 1 (continuous)

Supplemental Table 4. Association of time-updated vitamin D metabolic ratio ($24,25(OH)_2D_3/25(OH)D_3$) with risk of ESRD and death

	24,25(OH)2D3/25(OH)D3 Ratio				
	Tertiles			Linear model	
	1	2	3	Per SD decrease = 20 units	p-value‡
	ESRD (case-cohort)				
Unadjusted	5.82 (4.55, 7.44)	2.63 (2.02, 3.41)	1.00 (ref)	2.26 (2.01, 2.54)	<0.001
model 1	4.12 (2.58, 6.58)	2.25 (1.42, 3.57)	1.00 (ref)	1.93 (1.54, 2.44)	<0.001
model 2	0.98 (0.56, 1.72)	1.03 (0.58, 1.86)	1.00 (ref)	0.88 (0.69, 1.13)	0.327
model 3	0.74 (0.43, 1.30)	0.81 (0.45, 1.45)	1.00 (ref)	0.75 (0.58, 0.97)	0.031
	Death (case-cohort)				
Unadjusted	1.81 (1.45, 2.26)	1.61 (1.27, 2.03)	1.00 (ref)	1.36 (1.23, 1.51)	<0.001
model 1	1.72 (1.20, 2.47)	1.44 (1.01, 2.07)	1.00 (ref)	1.28 (1.08, 1.51)	0.004
model 2	1.33 (0.88, 2.03)	1.32 (0.89, 1.95)	1.00 (ref)	1.16 (0.96, 1.41)	0.118
model 3	1.21 (0.77, 1.92)	1.45 (0.95, 2.19)	1.00 (ref)	1.07 (0.87, 1.31)	0.515

Model 1: Adjusted for age, gender, race, diabetes, systolic blood pressure, number of anti-hypertensive medication classes, prevalent cardiovascular disease, smoking status, RAAS inhibtors, statin use, calciferol use, and Vit D receptor activators

Model 2: Model 1 + eGFR and PCR

Model 3: Model 2 + PTH and FGF23

Supplemental Table 5. Associations of $24,25(OH)_2D_3$ with risk of ESRD and death in case-cohort

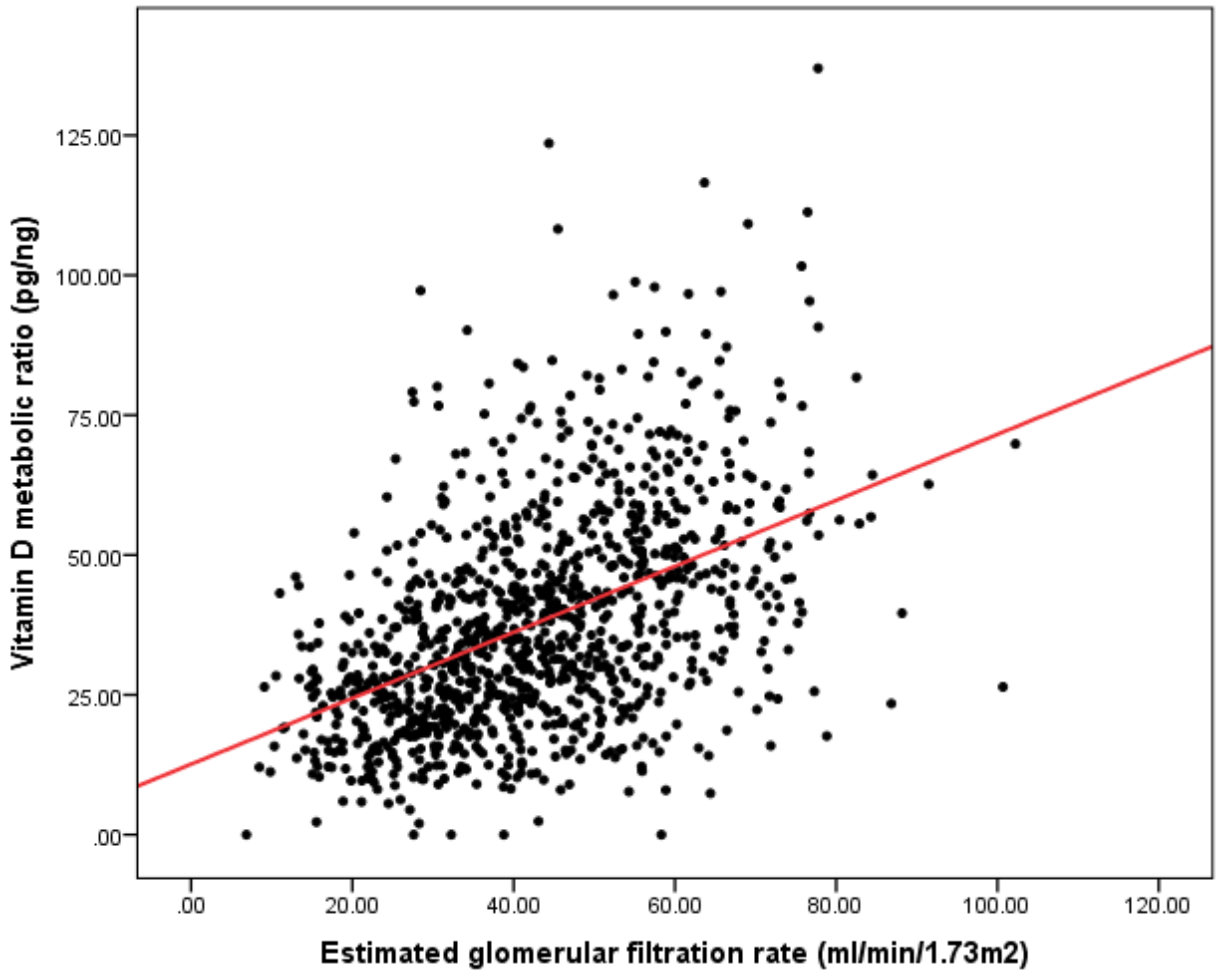
24,25(OH)2D3	N events	Incidence rate (%/yr)*	HR (95% CI) Model 1	HR (95% CI) Model 2	HR (95% CI) Model 3
ESRD					
Tertile 1	416	7.85	3.83 (2.86, 5.12)	1.42 (0.97, 2.07)	1.29 (0.83, 2.02)
Tertile 2	198	3.59	1.79 (1.34, 2.41)	1.13 (0.78, 1.62)	1.02 (0.68, 1.53)
Tertile 3	94	1.36	ref	ref	ref
Per 20 pg/ng (1 SD) decrement			1.92 (1.64, 2.25)	1.17 (1.00, 1.36)	1.12 (0.94, 1.33)
Death					
Tertile 1	327	5.18	2.08 (1.55, 2.78)	1.58 (1.14, 2.21)	1.64 (1.10, 2.45)
Tertile 2	203	2.84	1.50 (1.13, 1.99)	1.44 (1.06, 1.94)	1.46 (1.03, 2.05)
Tertile 3	120	1.45	ref	ref	ref
Per 20 pg/ng (1 SD) decrement			1.40 (1.22, 1.61)	1.27 (1.10, 1.45)	1.29 (1.09, 1.53)

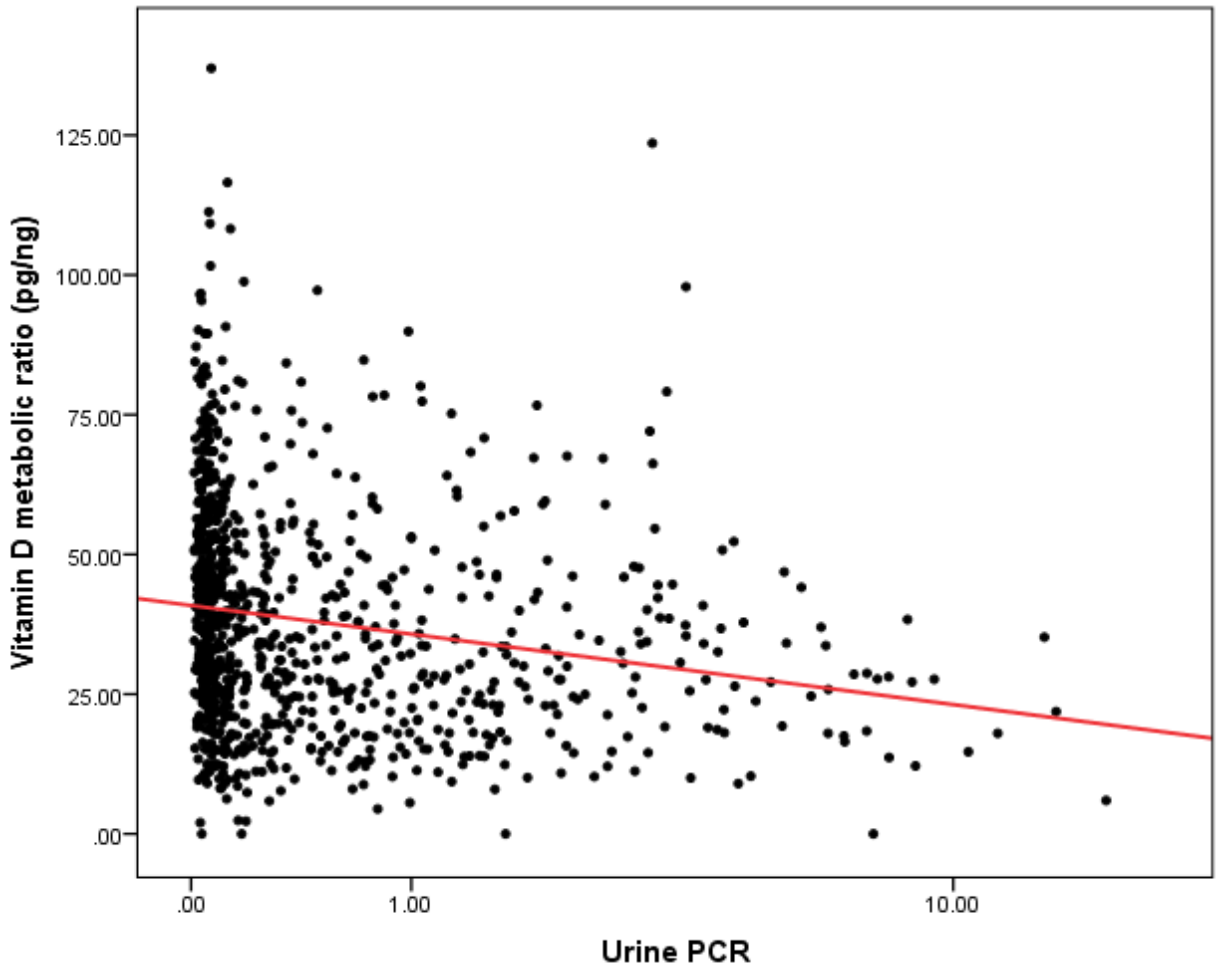
Model 1: Adjusted for age, gender, race, diabetes, systolic blood pressure, number of anti-hypertensive medication classes, prevalent cardiovascular disease, smoking status, RAAS inhibtors, statin use, calciferol use, and Vit D receptor activators

Model 2: Model 1 + eGFR and PCR

Model 3: Model 2 + PTH and FGF23

Supplemental Figure 1. Scatterplots of 24,25(OH)2D3/ 24(OH)D3 with (a) eGFR and (b) urine PCR




Vitamin D metabolic ratio (pg/ng)
125.00
100.00
75.00
50.00
25.00
.00
.00
1.00
10.00
Urine PCR

Supplemental Figure 2. Histogram of change in vitamin D metabolic ratio ($24,25(OH)_2D_3/25(OH)D_3$) from Year 1 to Year 4