Appendix Table 1. Selected laboratory characteristics of the study population by quartiles of mineral metabolites

	Glomerular filtration rate (ml/min/1.73m^2) Mean ± SD	Urine protein to creatinine ratio Median (IQR)	Serum albumin (g/dl) Mean ± SD	Fibroblast growth factor 23 (pg/ml) Median (IQR)	Parathyroid hormone (pg/ml) Median (IQR)	Serum phosphate (mg/dl) Mean ± SD	25-OH vitamin D (ng/ml) Median (IQR)	Serum calcium (mg/dl) Mean ± SD
Fibroblast Growth Factor 23 (pg/ml)								
≤30.7	54.6 ± 14.8	0.05 (0.02, 0.15)	4.2 ± 0.4	--	27.5 (19.9, 38.3)	3.4 ± 0.5	11.3 (8.5, 16.8)	9.0 ± 0.5
30.8–44.2	50.6 ± 15.0	0.05 (0.02, 0.16)	4.1 ± 0.3	--	33.9 (24.5, 46.9)	3.4 ± 0.6	12.9 (8.8, 18.2)	8.9 ± 0.5
44.3–64.3	43.3 ± 16.5	0.08 (0.03, 0.36)	4.1 ± 0.3	--	43.1 (26.8, 65.0)	3.6 ± 0.6	14.3 (9.4, 20.0)	8.9 ± 0.4
≥64.4	32.5 ± 16.9	0.20 (0.05, 1.00)	4.1 ± 0.4	--	58.4 (36.4, 99.6)	3.8 ± 0.8	14.5 (9.8, 20.5)	8.9 ± 0.6
p-trend†	<0.001	<0.001	0.001	--	<0.001	<0.001	0.001	0.02
Parathyroid Hormone (pg/ml)								
≤24.0	55.7 ± 15.2	0.04 (0.02, 0.11)	4.2 ± 0.3	36.2 (25.5, 49.6)	--	3.4 ± 0.5	15.1 (10.3, 22.8)	9.1 ± 0.5
24.1–37.0	49.9 ± 15.1	0.05 (0.02, 0.14)	4.2 ± 0.3	36.9 (27.3, 50.4)	--	3.4 ± 0.5	14.3 (9.6, 19.9)	9.0 ± 0.4
37.1–60.7	44.4 ± 16.2	0.09 (0.03, 0.36)	4.1 ± 0.3	45.6 (35.2, 66.1)	--	3.5 ± 0.6	12.0 (8.3, 16.8)	8.9 ± 0.5
≥60.8	31.0 ± 15.0	0.21 (0.05, 1.00)	4.0 ± 0.4	61.9 (45.1, 93.0)	--	3.8 ± 0.8	11.8 (8.0, 17.3)	8.6 ± 0.6
p-trend†	<0.001	<0.001	<0.001	<0.001	--	<0.001	<0.001	<0.001
Serum Phosphate (mg/dl)								
≤3.1	51.4 ± 15.9	0.05 (0.02, 0.12)	4.1 ± 0.3	38.6 (29.0, 57.3)	33.0 (22.5, 50.2)	--	14.1 (9.0, 21.2)	8.9 ± 0.5
3.2–3.5	48.0 ± 16.0	0.06 (0.03, 0.27)	4.1 ± 0.3	41.0 (29.6, 56.1)	33.9 (22.5, 54.8)	--	13.3 (8.8, 19.2)	8.9 ± 0.5
3.6–3.9	44.4 ± 17.5	0.08 (0.03, 0.39)	4.1 ± 0.3	45.5 (30.7, 61.8)	38.5 (25.3, 62.9)	--	13.5 (9.4, 17.7)	8.9 ± 0.4
≥4.0	34.9 ± 18.6	0.14 (0.04, 1.02)	4.1 ± 0.4	58.0 (38.1, 103.7)	54.9 (28.1, 99.1)	--	12.4 (8.9, 19.0)	8.8 ± 0.6
p-trend†	<0.001	<0.001	0.4	<0.001	<0.001	--	0.2	0.3
25-hydroxyvitamin D (ng/ml)‡								
Quartile 1	44.6 ± 18.4	0.10 (0.03, 0.45)	4.1 ± 0.4	38.1 (28.2, 58.6)	45.5 (29.0, 74.3)	3.5 ± 0.7	--	8.8 ± 0.6
Quartile 2	46.0 ± 18.6	0.08 (0.03, 0.42)	4.2 ± 0.3	42.3 (30.0, 62.9)	37.4 (24.5, 62.9)	3.6 ± 0.7	--	8.9 ± 0.5
Quartile 3	45.8 ± 18.9	0.07 (0.03, 0.27)	4.1 ± 0.3	46.7 (32.3, 69.3)	34.7 (23.2, 58.9)	3.5 ± 0.6	--	8.9 ± 0.5
Quartile 4	44.6 ± 15.5	0.05 (0.02, 0.19)	4.1 ± 0.3	49.1 (35.0, 66.7)	29.8 (20.9, 53.3)	3.5 ± 0.6	--	9.0 ± 0.5
p-trend†	0.9	0.001	0.1	0.009	<0.001	0.5	--	0.01

† p-trend by univariate linear regression. Skewed outcome variables (urine protein to creatinine ratio, fibroblast growth factor 23, parathyroid hormone and 25-hydroxyvitamin D) were log transformed prior to testing

‡ranges for 25-hydroxyvitamin D quartiles (Q) are season specific, as follows: winter (Q1, ≤8.4; Q2, 8.5–10.9; Q3, 11.0–16.2; Q4, ≥16.3 ng/ml); spring (Q1, ≤7.9; Q2, 8.0–10.9; Q3, 11.0–16.5; Q4, ≥16.6 ng/ml); summer (Q1, ≤10.0; Q2, 10.1–15.2; Q3, 15.3–20.6; Q4, ≥20.7 ng/ml); fall (Q1, ≤11.0; Q2, 11.1–14.7; Q3, 14.8–22.8; Q4, ≥22.9 ng/ml)

Appendix Table 2. Baseline characteristics by total number of mineral metabolite abnormalities

Characteristic: Mean ± SD or n(%)	Number of Mineral Metabolism Abnormalities 0 N=420	1 N=248	2 N=108	3 N=26	p-value†
Age (years)	56 ± 10	55 ± 11	54 ± 10	50 ± 11	0.002
Female sex	171 (40.7%)	83 (33.5%)	50 (46.3%)	12 (46.2%)	0.09
Income‡					0.4
<$15,000 per yr	205 (48.8%)	124 (50.0%)	44 (40.7%)	15 (57.7%)	
≥$15,000 per yr	142 (33.8%)	76 (30.7%)	36 (33.3%)	8 (30.8%)	
Prior cardiovascular disease	219 (52.1%)	135 (54.4%)	59 (54.6%)	14 (53.9%)	0.9
Smoking					0.6
Current	137 (32.6%)	64 (25.8%)	30 (27.8%)	7 (26.9%)	
Past	119 (28.3%)	78 (31.5%)	29 (26.9%)	8 (30.8%)	
Never	164 (39.1%)	106 (42.7%)	49 (45.4%)	11 (42.3%)	
Body mass index (kg/m^2)	30.1 ± 6.2	30.3 ± 6.7	31.6 ± 6.7	30.5 ± 7.5	0.08
Glomerular filtration rate (ml/min/1.73 m^2)§	53.4 ± 14.8	42.3 ± 16.1	28.0 ± 12.4	16.8 ± 8.9	<0.001
Stage of chronic kidney disease					<0.001
2 (GFR ≥ 60 ml/min/1.73 m^2)	136 (32.4%)	34 (13.7%)	2 (1.9%)	0 (0%)	
3a (GFR 45–59 ml/min/1.73 m^2)	156 (37.1%)	70 (28.2%)	10 (9.3%)	1 (3.9%)	
3b (GFR 30–44 ml/min/1.73 m^2)	103 (24.5%)	83 (33.5%)	25 (23.2%)	2 (7.7%)	
4–5 (GFR < 30 ml/min/1.73 m^2)	22 (5.2%)	61 (24.6%)	71 (65.7%)	23 (88.5%)	
Urine protein to creatinine ratio§*	0.05 (0.02, 0.15)	0.08 (0.03, 0.36)	0.21 (0.07, 1.05)	1.30 (0.98, 2.32)	<0.001
Serum albumin (mg/dl)	4.2 ± 0.3	4.1 ± 0.3	4.0 ± 0.4	4.0 ± 0.4	<0.001
Serum fibroblast growth factor 23 (pg/ml) *	32.5 (24.4, 40.0)	60.6 (51.6, 82.0)	71.6 (59.7, 109.4)	180.5 (103.2, 427.8)	<0.001
Fibroblast growth factor 23 >50 pg/ml	0 (0%)	195 (78.6%)	107 (99.1%)	26 (100%)	
Parathyroid hormone (pg/ml) *	28 (21, 39)	43 (28, 61)	93 (74, 128)	153 (105, 183)	<0.001
Parathyroid hormone >65 pg/ml	0 (0%)	51 (20.6%)	99 (91.7%)	26 (100%)	
Serum phosphate (mg/dl)	3.4 ± 0.5	3.5 ± 0.6	3.8 ± 0.6	5.3 ± 0.7	<0.001
Phosphate >4.6 mg/dl	0 (0%)	2 (0.8%)	10 (9.3%)	26 (100%)	
25-hydroxyvitamin D (ng/ml) *	13.0 (8.8, 18.5)	14.3 (9.4, 21.4)	12.8 (8.7, 18.3)	11.8 (9.0, 17.6)	0.8
Serum calcium (mg/dl)	9.0 ± 0.5	8.9 ± 0.5	8.7 ± 0.5	8.4 ± 0.8	<0.001

†p-value by Chi square (categorical variables) or p-trend by univariate linear regression (continuous variables). Skewed outcome variables (urine protein to creatinine ratio, fibroblast growth factor 23, parathyroid hormone and 25-hydroxyvitamin D) were log transformed prior to testing

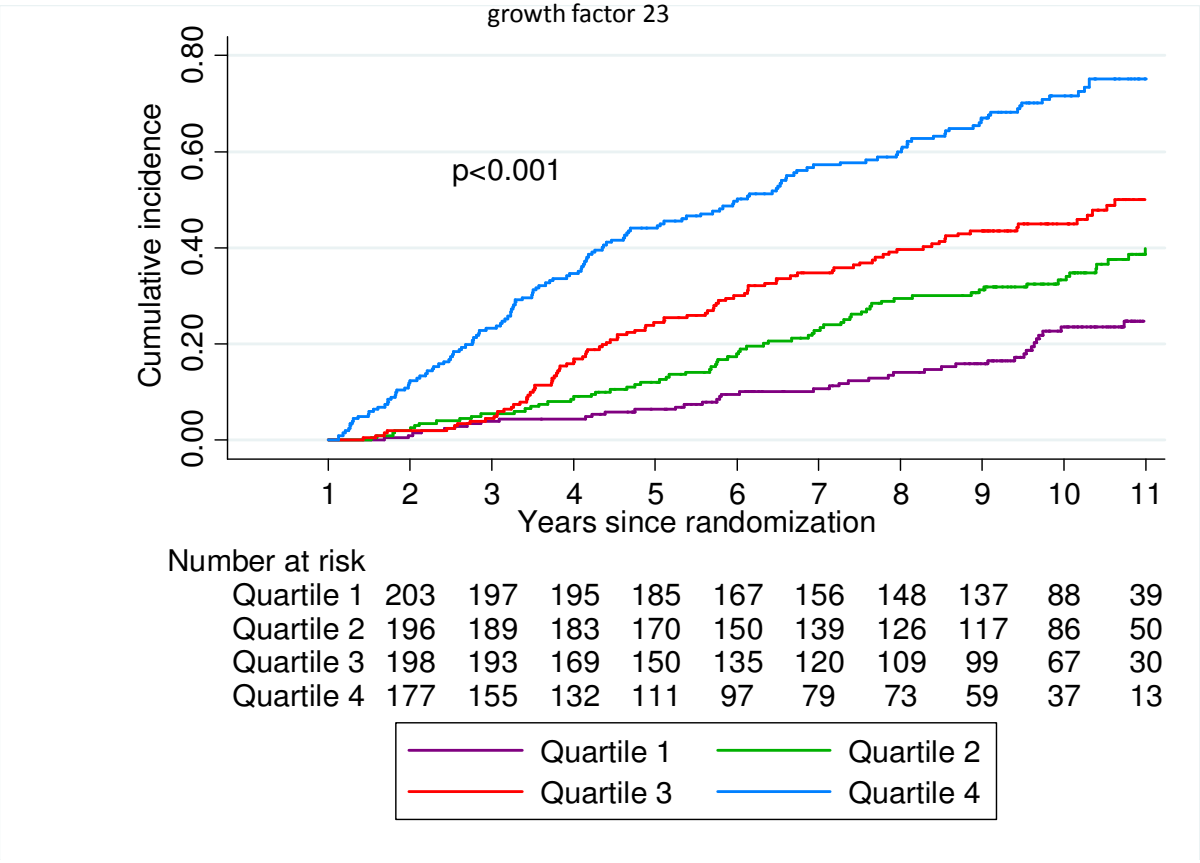
‡total does not sum to 100% due to participant non-response

§Glomerular filtration rate was missing in 3 participants; urine protein to creatinine ratio was missing in 26 participants

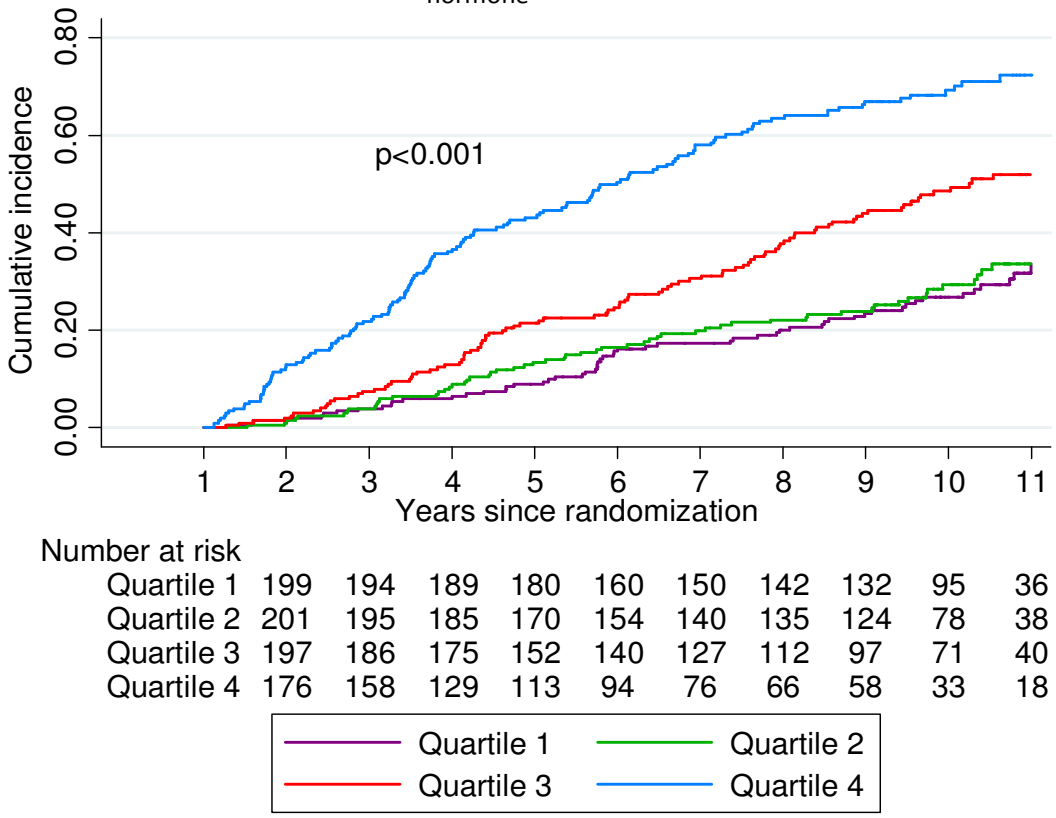
*median (interquartile range)

GFR, glomerular filtration rate

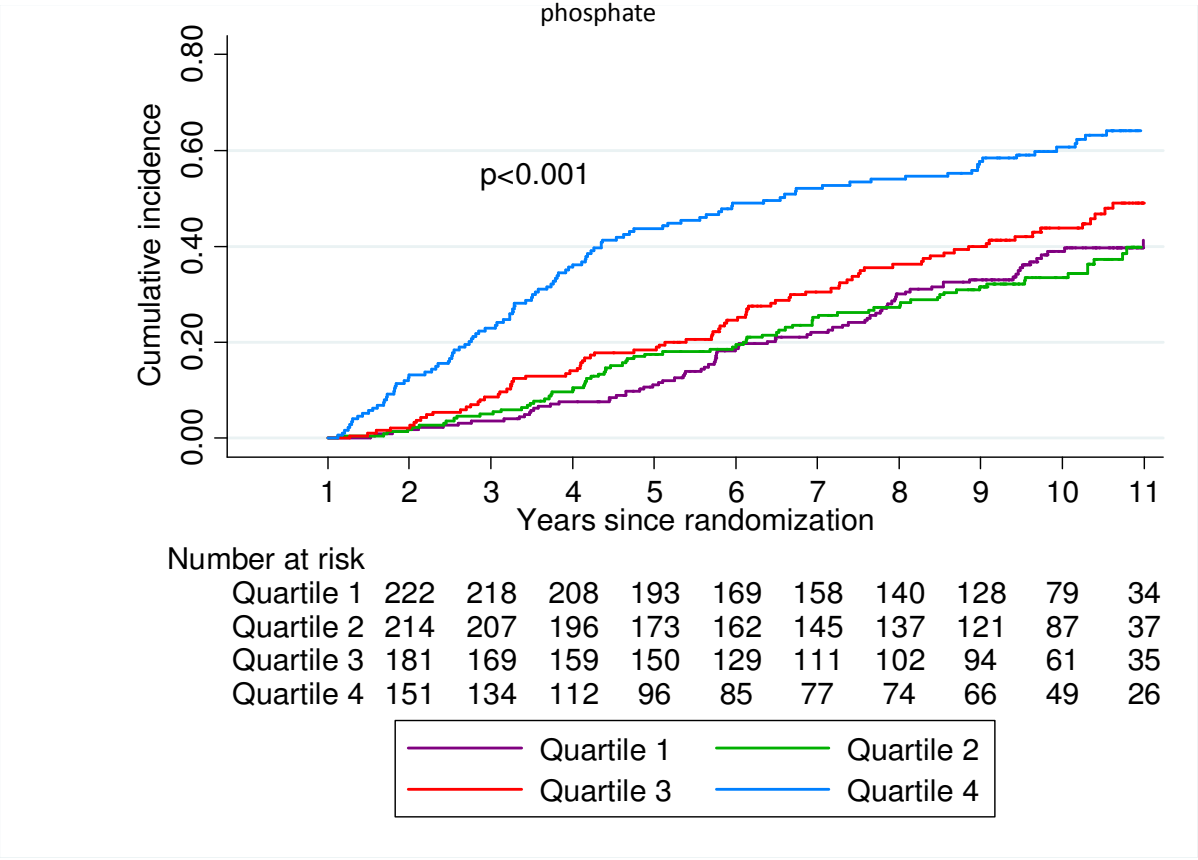
Appendix figure 1a. Cumulative incidence of end-stage renal disease or death by quartiles of fibroblast growth factor 23



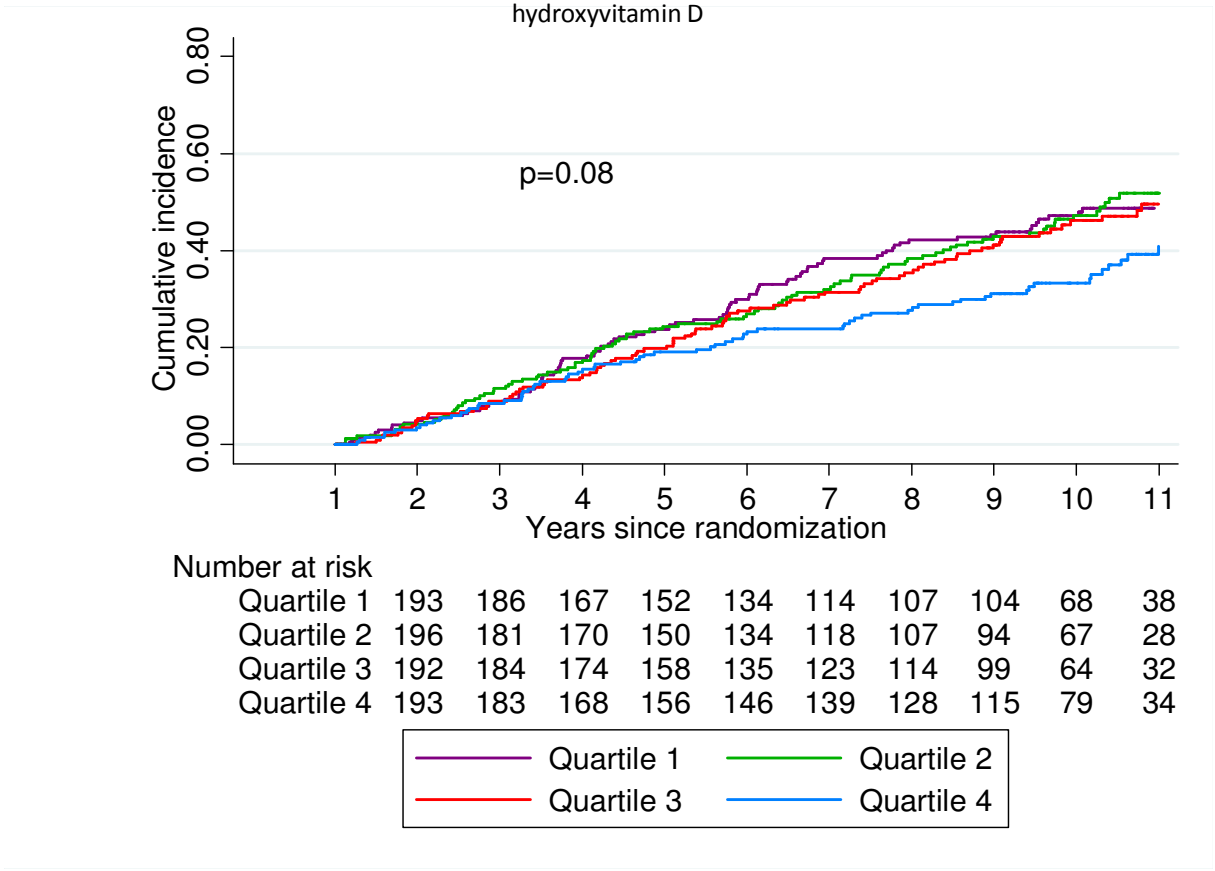
Appendix figure 1b. Cumulative incidence of end-stage renal disease or death by quartiles of parathyroid hormone



Appendix figure 1c. Cumulative incidence of end-stage renal disease or death by quartiles of serum phosphate



Appendix figure 1d. Cumulative incidence of end-stage renal disease or death by quartiles of 25-hydroxyvitamin D



Appendix Figure 1. Cumulative incidence of end-stage renal disease or death by quartiles of mineral metabolism parameters (A) fibroblast growth factor 23; (B) parathyroid hormone; (C) serum phosphate; and (D) 25-hydroxyvitamin D. Quartiles of 25-hydroxyvitamin D are season-specific. Follow-up began 1 year after randomization at the time baseline mineral metabolites were measured. P-values were derived from the log-rank test.