Supplementary Materials

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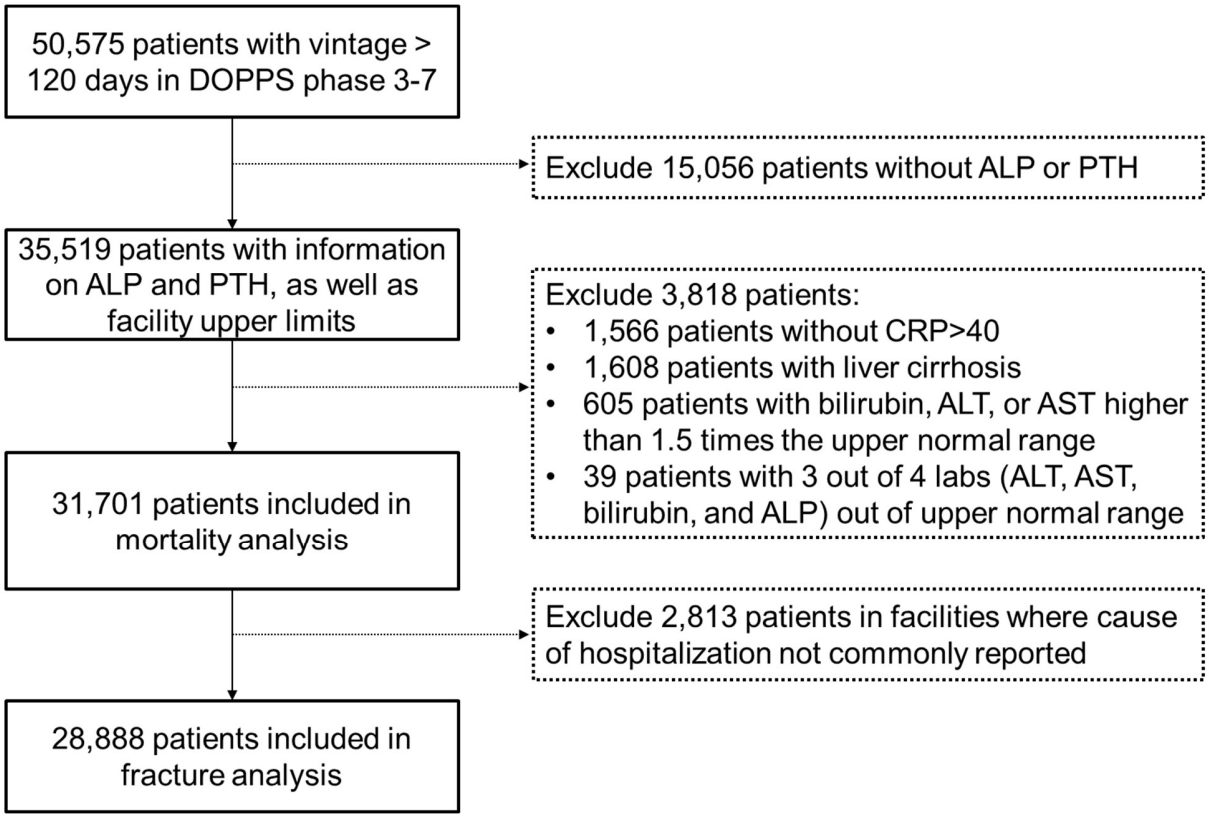
Supplementary Figure S1

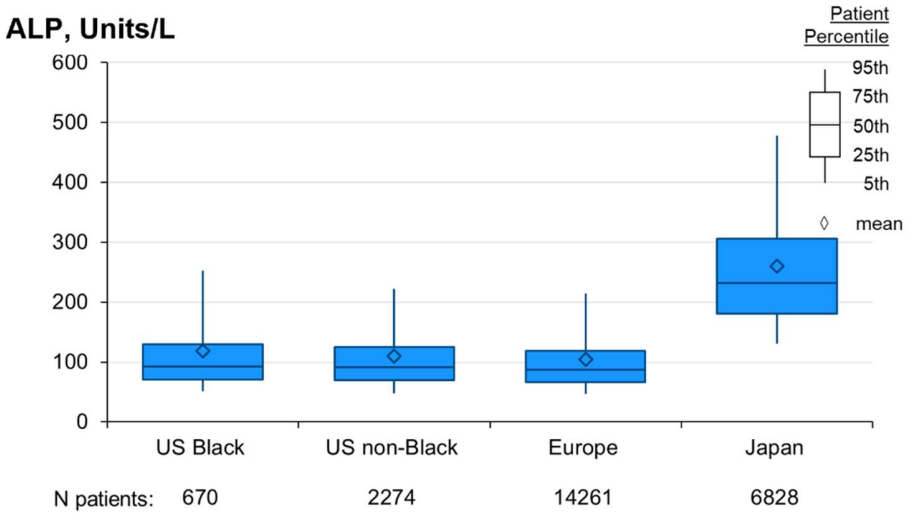
Flow chart of inclusion/exclusion criteria. DOPPS = Dialysis Outcomes and Practice Patterns Study; phase 3-7: 2005-2022; vintage = time since dialysis initiation; ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate transferase; CRP = C-reactive protein; PTH = parathyroid hormone.



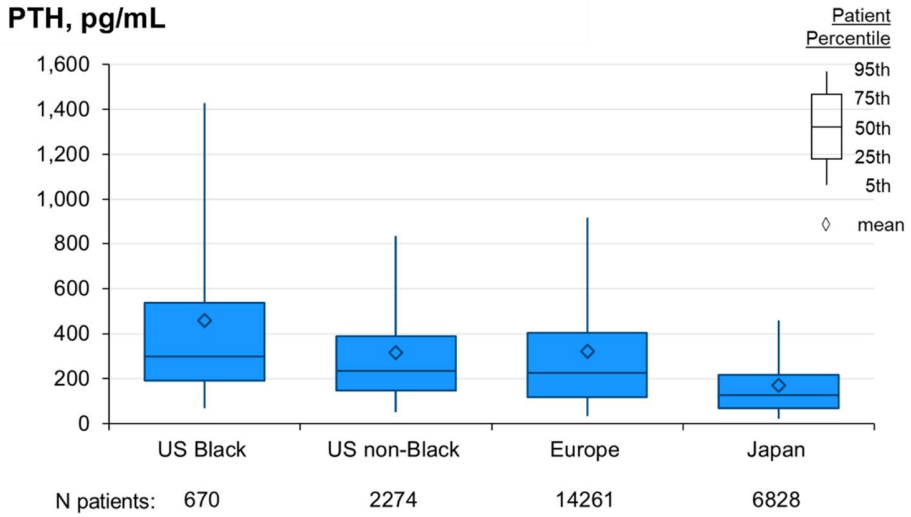
Supplementary Figure S2

Distribution of raw (not normalized) values of (A) ALP, and (B) PTH, by region and race. ALP = alkaline phosphatase; PTH = parathyroid hormone.

A

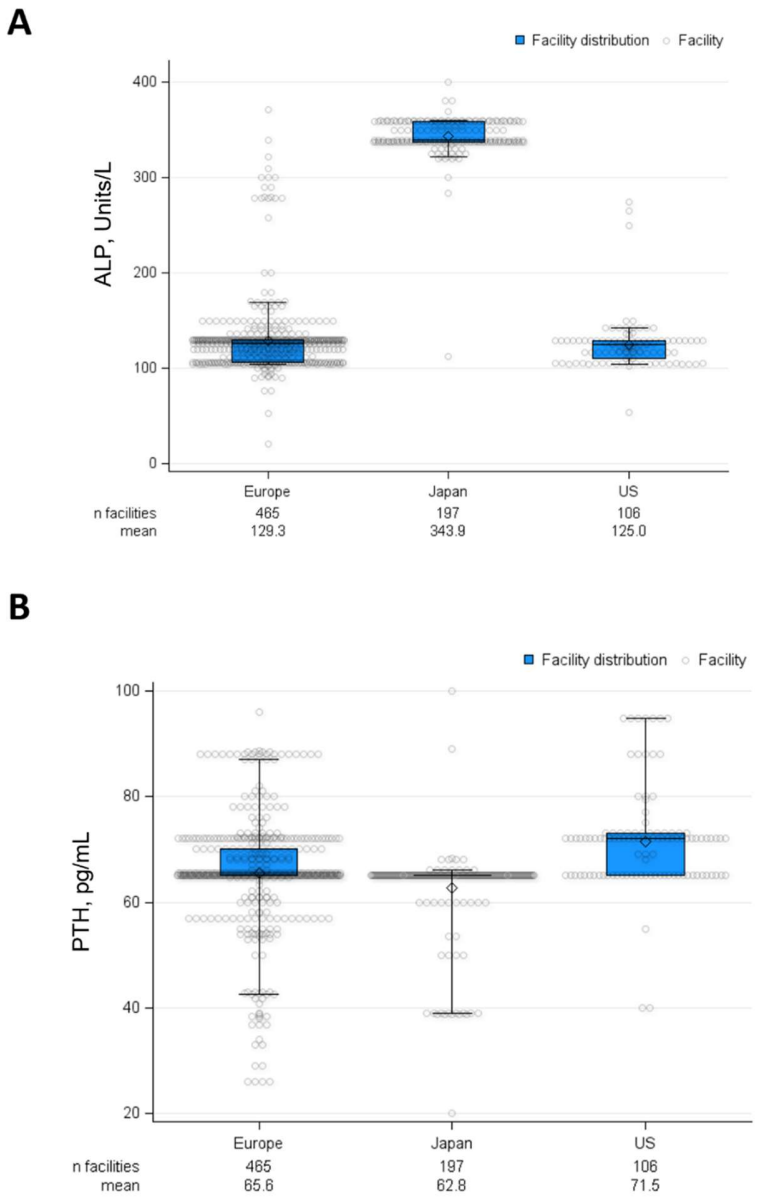


B



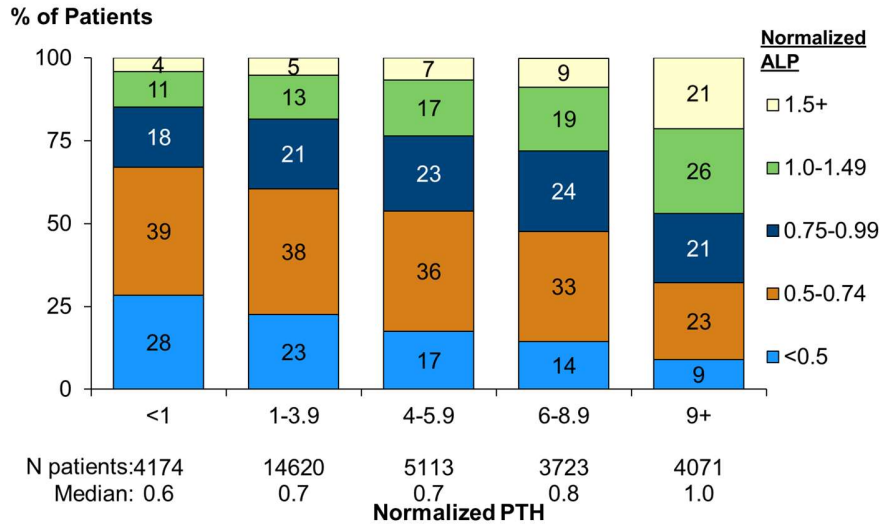
Supplementary Figure S3

Distribution of facility upper normal limit of (A) ALP, and (B) PTH by region. ALP = alkaline phosphatase; PTH = parathyroid hormone.



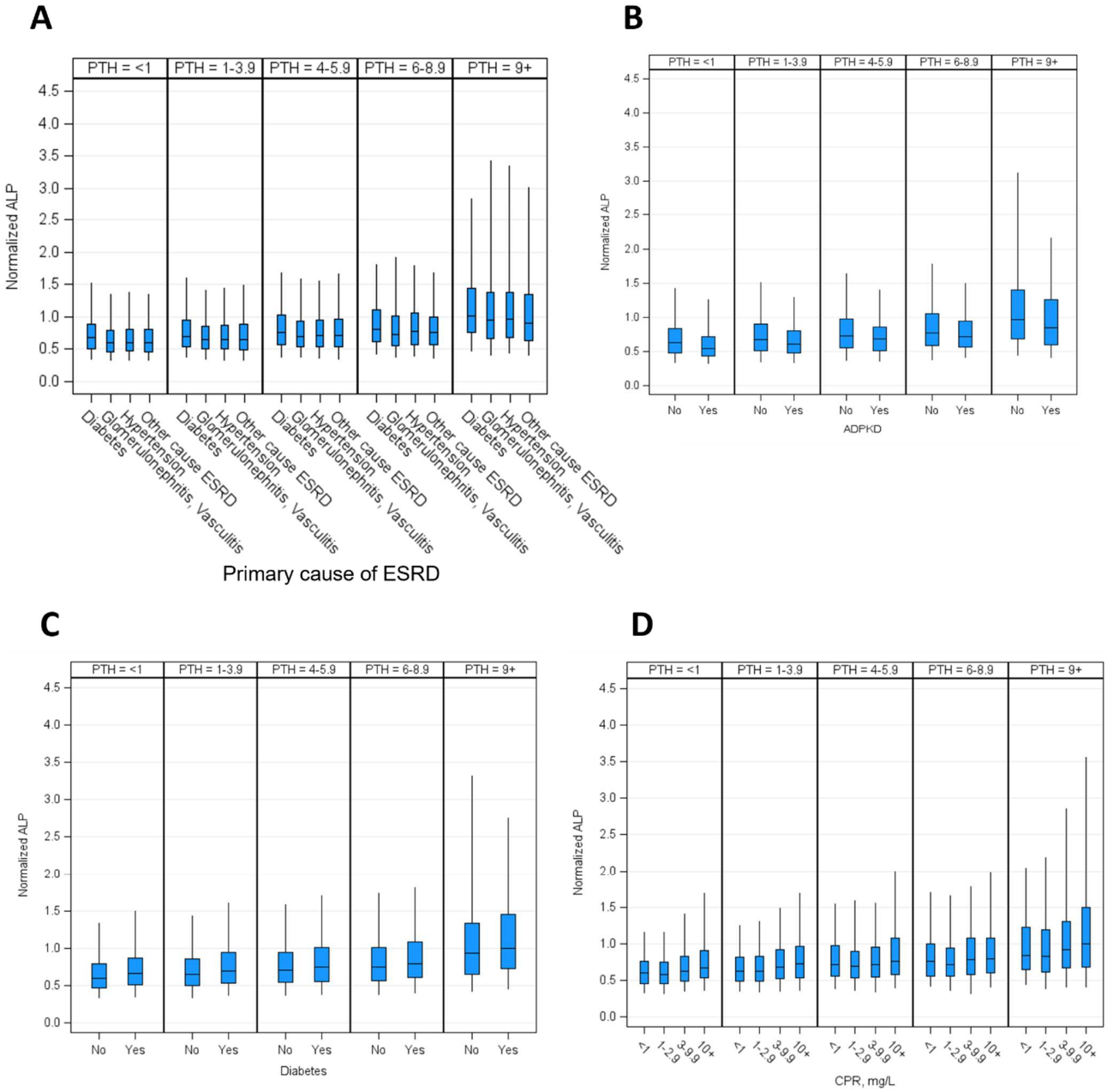
Supplementary Figure S4

Distribution of normalized ALP, by normalized PTH. ALP = alkaline phosphatase; PTH = parathyroid hormone



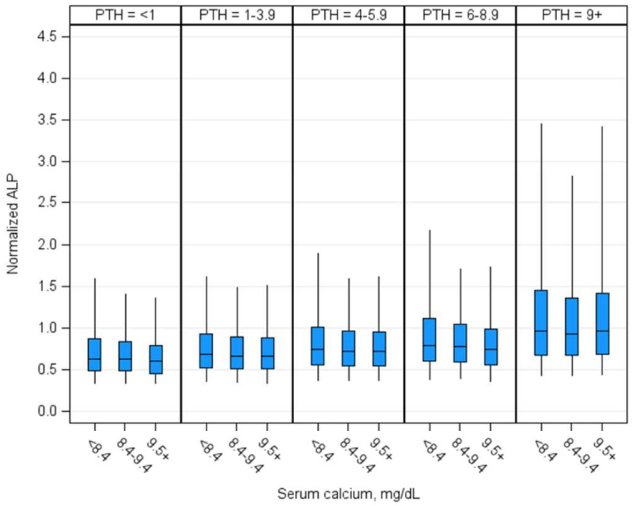
Supplementary Figure S5

Normalized ALP by categories of normalized PTH by (A) primary cause of ESRD, (B) ADPKD, (C) diabetes, (D) CRP, (E) serum calcium, (F) serum phosphorus, (G) cinacalcet, and (H) active vitamin D. ALP = alkaline phosphatase; ADPKD = adult polycystic kidney disease; CRP = C-reactive protein; ESRD = end-stage renal disease; PTH = parathyroid hormone.

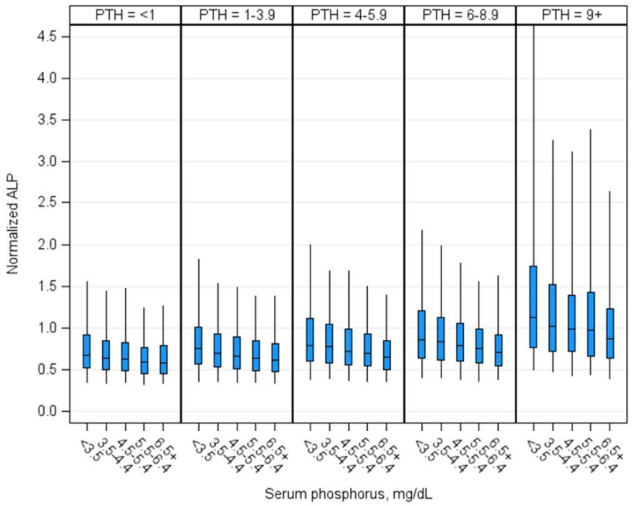


Supplementary Figure S5 (continued)

E



F



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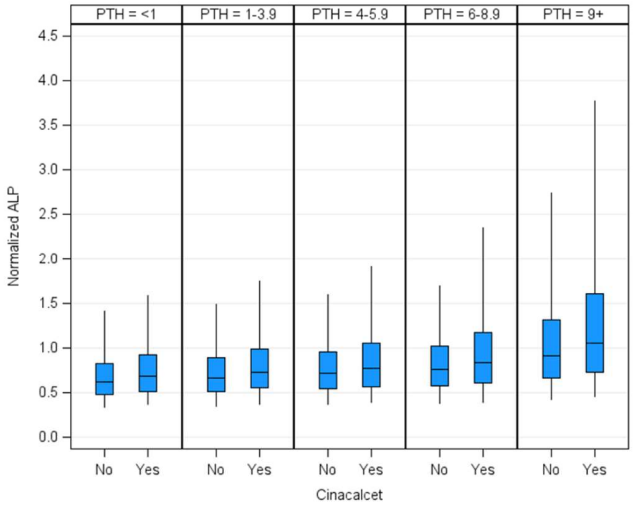
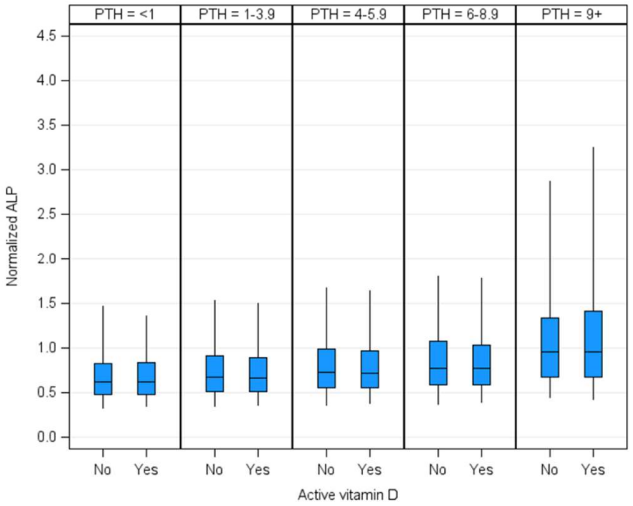


H



Supplementary Table S1

Patient characteristics, by (A) normalized ALP and (B) normalized PTH, within each region and race

A

	Europe					Japan					US Black					US non-Black				
Characteristics	**<0.5**	**0.5-0.74**	**0.75-0.99**	**1.0-1.49**	**1.5+**	**<0.5**	**0.5-0.74**	**0.75-0.99**	**1.0-1.49**	**1.5+**	**<0.5**	**0.5-0.74**	**0.75-0.99**	**1.0-1.49**	**1.5+**	**<0.5**	**0.5-0.74**	**0.75-0.99**	**1.0-1.49**	**1.5+**
	(n = 3086)	**(n = 4966)**	**(n = 2977)**	**(n = 2164)**	**(n = 1068)**	**(n = 1376)**	**(n = 2758)**	**(n = 1528)**	**(n = 897)**	**(n = 269)**	**(n = 115)**	**(n = 226)**	**(n = 151)**	**(n = 112)**	**(n = 66)**	**(n = 337)**	**(n = 797)**	**(n = 505)**	**(n = 424)**	**(n = 211)**
Demographics																				
Age, y	65 ± 15	67 ± 15	67 ± 15	66 ± 15	64 ± 16	63 ± 12	65 ± 12	66 ± 12	67 ± 12	66 ± 11	57 ± 14	59 ± 14	63 ± 14	63 ± 13	52 ± 14	64 ± 16	66 ± 15	65 ± 15	65 ± 14	62 ± 15
Sex (% male)	68%	64%	58%	55%	51%	72%	68%	63%	52%	45%	58%	53%	52%	44%	48%	62%	57%	52%	53%	43%
Race (% Black)	2%	2%	3%	3%	4%	0%	0%	0.10%	0%	0%	100%	100%	100%	100%	100%	0%	0%	0%	0%	0%
Vintage, y	1.7 [0.7,4.5]	2.0 [0.8,5.0]	2.4 [0.9,5.7]	3.1 [1.1,6.9]	3.9 [1.4,8.0]	3.4 [1.1,7.9]	4.1 [1.1,9.2]	5.1 [1.4,11.0]	5.7 [1.6,12.6]	6.9 [2.3,13.2]	2.5 [0.9,5.0]	2.2 [0.9,5.1]	3.3 [1.2,6.4]	2.8 [1.2,6.3]	4.0 [2.1,8.0]	1.5 [0.6,3.6]	1.5 [0.6,3.4]	1.6 [0.8,3.6]	2.2 [0.9,4.8]	2.9 [1.0,5.2]
Comorbidity history																				
Diabetes	32%	36%	39%	41%	43%	42%	42%	43%	39%	42%	52%	53%	63%	63%	55%	54%	58%	64%	66%	64%
Hypertension	87%	88%	87%	85%	85%	82%	82%	80%	80%	78%	94%	93%	94%	98%	88%	95%	91%	91%	91%	86%
Coronary artery disease	36%	37%	37%	39%	41%	25%	31%	32%	34%	32%	55%	48%	46%	48%	41%	50%	56%	55%	62%	56%
Heart failure	23%	24%	26%	25%	25%	16%	19%	20%	23%	25%	42%	37%	38%	40%	34%	37%	37%	41%	45%	48%
Cerebrovascular disease	15%	16%	16%	17%	15%	13%	15%	17%	17%	18%	16%	15%	13%	19%	13%	19%	17%	17%	18%	20%
Peripheral vascular disease	24%	29%	30%	32%	33%	13%	15%	18%	20%	20%	18%	27%	27%	30%	23%	32%	31%	34%	39%	42%
Other cardiovascular diseases	32%	33%	35%	37%	37%	21%	26%	27%	32%	32%	28%	19%	24%	31%	22%	32%	31%	30%	37%	36%
Gastrointestinal bleeding	3%	4%	5%	5%	6%	2%	4%	4%	5%	6%	4%	5%	6%	4%	3%	5%	6%	5%	8%	8%
Lung disease	13%	14%	14%	15%	12%	3%	4%	4%	4%	6%	10%	12%	17%	12%	6%	19%	21%	19%	24%	26%
Neurologic disease	11%	12%	13%	13%	11%	5%	7%	9%	8%	12%	10%	14%	12%	13%	20%	10%	11%	12%	10%	18%
Psychiatric disorder	14%	15%	17%	15%	16%	2%	4%	4%	4%	4%	23%	23%	15%	21%	30%	26%	24%	26%	30%	36%
Cancer	18%	18%	16%	17%	16%	11%	11%	11%	12%	15%	7%	10%	9%	8%	11%	15%	16%	14%	14%	14%
Recurrent cellulitis / gangrene	6%	8%	11%	12%	14%	3%	3%	4%	5%	8%	6%	7%	9%	10%	13%	12%	9%	10%	19%	21%
HIV	0.50%	0.70%	0.40%	0.70%	0.90%	0.60%	0.60%	0.40%	0.90%	0%	9%	6%	3%	5%	10%	1%	0.40%	0%	2%	0%
ADPKD	7%	7%	5%	5%	4%	5%	4%	5%	3%	2%	1%	1%	0.70%	0%	0%	7%	4%	3%	2%	3%
Dialysis treatments																				
Vascular access type																				
Catheter	24%	27%	27%	29%	30%	0.80%	1%	1%	1%	3%	24%	28%	29%	22%	35%	34%	34%	35%	32%	33%
Fistula	69%	67%	67%	65%	63%	94%	93%	92%	90%	90%	59%	40%	34%	42%	41%	52%	52%	54%	52%	51%
Graft	6%	6%	6%	6%	7%	5%	6%	7%	9%	7%	17%	31%	36%	36%	24%	14%	14%	12%	16%	16%
Single pool Kt/V	1.5 ± 0.3	1.5 ± 0.3	1.5 ± 0.3	1.6 ± 0.3	1.6 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.5 ± 0.3	1.5 ± 0.3	1.5 ± 0.2	1.5 ± 0.3	1.5 ± 0.3	1.5 ± 0.3	1.5 ± 0.3	1.6 ± 0.3	1.6 ± 0.3	1.6 ± 0.3	1.6 ± 0.3	1.6 ± 0.3

Lab/biometric markers																				
Body mass index, kg/m^2	26.4 ± 5.3	26.3 ± 5.4	26.0 ± 5.5	25.9 ± 5.7	25.5 ± 5.7	22.2 ± 3.7	21.8 ± 3.7	21.4 ± 3.6	21.0 ± 3.5	20.8 ± 3.8	28.3 ± 6.6	28.8 ± 7.4	28.4 ± 6.6	29.5 ± 7.3	27.7 ± 7.6	27.9 ± 6.6	28.8 ± 7.0	28.6 ± 6.8	28.3 ± 7.4	28.3 ± 8.2
<18	3%	3%	4%	4%	5%	10%	13%	15%	19%	24%	3%	2%	2%	0%	7%	3%	2%	2%	3%	3%
18-24	42%	43%	44%	45%	49%	72%	71%	72%	70%	64%	34%	32%	32%	34%	35%	33%	30%	33%	39%	41%
25-29	34%	33%	32%	30%	28%	15%	13%	10%	9%	10%	21%	31%	29%	22%	20%	26%	32%	30%	21%	24%
30+	21%	21%	20%	21%	18%	4%	3%	3%	2%	2%	42%	36%	37%	44%	38%	37%	37%	36%	37%	32%
Serum albumin, g/dL	3.8 ± 0.5	3.8 ± 0.5	3.7 ± 0.5	3.7 ± 0.5	3.7 ± 0.5	3.8 ± 0.4	3.7 ± 0.4	3.7 ± 0.4	3.6 ± 0.4	3.6 ± 0.4	3.9 ± 0.4	3.9 ± 0.4	3.7 ± 0.5	3.8 ± 0.5	3.8 ± 0.4	3.8 ± 0.4	3.7 ± 0.4	3.7 ± 0.4	3.6 ± 0.4	3.6 ± 0.5
Hemoglobin, g/dL	11.5 ± 1.4	11.5 ± 1.4	11.5 ± 1.4	11.6 ± 1.4	11.5 ± 1.5	10.8 ± 1.2	10.7 ± 1.2	10.7 ± 1.3	10.7 ± 1.3	10.4 ± 1.4	11.5 ± 1.3	11.5 ± 1.3	11.6 ± 1.4	11.4 ± 1.3	11.4 ± 1.3	11.3 ± 1.3	11.5 ± 1.3	11.6 ± 1.3	11.4 ± 1.3	11.3 ± 1.4
Serum phosphorus, mg/dL	5.1 ± 1.6	5.0 ± 1.6	4.9 ± 1.6	4.8 ± 1.5	4.7 ± 1.6	5.6 ± 1.4	5.4 ± 1.4	5.3 ± 1.4	5.2 ± 1.4	5.1 ± 1.4	6.0 ± 1.8	5.3 ± 1.7	5.3 ± 1.7	5.3 ± 1.6	5.7 ± 1.7	5.6 ± 1.7	5.4 ± 1.7	5.3 ± 1.7	5.4 ± 1.7	5.3 ± 1.7
<3.5	12%	14%	16%	19%	21%	4%	6%	7%	8%	12%	3%	13%	10%	9%	8%	7%	10%	10%	9%	11%
3.5-4.4	24%	26%	27%	26%	27%	16%	19%	19%	21%	19%	17%	18%	24%	24%	18%	18%	22%	23%	23%	24%
4.5-5.4	27%	26%	26%	26%	26%	28%	30%	30%	32%	33%	22%	27%	26%	30%	15%	27%	27%	29%	26%	27%
5.5-6.4	18%	18%	16%	16%	13%	28%	25%	26%	24%	20%	27%	19%	17%	16%	25%	24%	19%	18%	17%	16%
6.5+	18%	16%	15%	13%	13%	24%	20%	18%	15%	16%	31%	22%	24%	21%	34%	24%	22%	20%	25%	22%
Serum calcium, mg/dL	9.0 ± 0.8	9.0 ± 0.7	9.0 ± 0.7	9.0 ± 0.7	8.9 ± 0.8	9.0 ± 0.8	8.8 ± 0.8	8.8 ± 0.8	8.7 ± 0.7	8.8 ± 0.9	9.2 ± 0.7	9.1 ± 0.7	9.1 ± 0.8	8.9 ± 0.7	8.8 ± 0.7	9.0 ± 0.8	9.0 ± 0.7	8.9 ± 0.7	8.9 ± 0.7	8.7 ± 0.8
<8.4	17%	18%	17%	18%	24%	20%	25%	26%	30%	33%	9%	14%	16%	22%	27%	20%	16%	17%	20%	31%
8.4-9.4	59%	59%	60%	59%	55%	58%	57%	56%	55%	47%	58%	56%	54%	56%	55%	55%	62%	64%	62%	49%
9.5+	24%	23%	24%	23%	21%	23%	18%	18%	15%	21%	33%	31%	30%	21%	18%	25%	22%	19%	18%	20%
CRP, mg/L	4.5 [2.0,9.0]	5.0 [2.6,11.0]	5.6 [3.0,12.0]	6.0 [3.0,13.0]	7.0 [4.0,15.7]	1.0 [0.5,2.0]	1.0 [0.5,3.1]	1.3 [0.7,3.6]	1.4 [0.7,4.5]	2.2 [0.5,6.7]	-	-	-	-	-	-	-	-	-	-
<1	7%	6%	5%	5%	3%	42%	36%	33%	32%	32%	-	-	-	-	-	-	-	-	-	-
1-2.9	26%	22%	18%	15%	14%	39%	35%	35%	32%	22%	-	-	-	-	-	-	-	-	-	-
3-9.9	44%	45%	47%	46%	44%	15%	20%	22%	24%	30%	-	-	-	-	-	-	-	-	-	-
10+	23%	28%	30%	34%	39%	4%	9%	10%	12%	16%	-	-	-	-	-	-	-	-	-	-
Medication																				
Calcium-based phosphate binder	48%	43%	40%	38%	36%	67%	60%	55%	52%	45%	58%	42%	45%	32%	52%	54%	49%	48%	46%	35%
Non-calcium-based phosphate binder	50%	54%	54%	55%	54%	57%	51%	51%	50%	48%	46%	52%	56%	48%	57%	41%	44%	44%	51%	56%
Cinacalcet	10%	13%	17%	20%	29%	13%	16%	16%	18%	22%	19%	21%	30%	27%	46%	10%	12%	14%	18%	29%
Vitamin D	53%	54%	54%	55%	57%	72%	71%	70%	68%	65%	91%	81%	85%	82%	81%	61%	65%	66%	64%	68%

Mean ± standard deviation, median [IQR], or prevalence (%) shown.

**CRP was restricted to facilities routinely measuring CRP, US and Russia were excluded because CRP not commonly measured. ADPKD = adult polycystic kidney disease; ALP = alkaline phosphatase; HIV = human immunodeficiency virus; PTH = parathyroid hormone.*

B

Characteristics	Europe					Japan					US Black					US non-Black				
	<1 (n = 1685)	1-3.9 (n = 6372)	4-5.9 (n = 2484)	6-8.9 (n = 1816)	9+ (n = 1904)	<1 (n = 1482)	1-3.9 (n = 4022)	4-5.9 (n = 762)	6-8.9 (n = 370)	9+ (n = 192)	<1 (n = 38)	1-3.9 (n = 271)	4-5.9 (n = 138)	6-8.9 (n = 87)	9+ (n = 136)	<1 (n = 188)	1-3.9 (n = 1182)	4-5.9 (n = 419)	6-8.9 (n = 259)	9+ (n = 226)
Demographics																				
Age, y	66 ± 15	68 ± 14	66 ± 15	65 ± 15	61 ± 16	66 ± 12	65 ± 12	64 ± 12	61 ± 12	59 ± 12	57 ± 15	61 ± 14	63 ± 14	58 ± 15	55 ± 13	63 ± 15	67 ± 14	64 ± 15	64 ± 15	56 ± 17
Sex (% male)	57%	62%	65%	62%	57%	63%	66%	62%	61%	54%	53%	52%	47%	46%	58%	51%	55%	59%	50%	54%
Race (% Black)	2%	2%	3%	3%	5%	0%	0%	0.00%	0%	0%	100%	100%	100%	100%	100%	0%	0%	0%	0%	0%
Vintage, y	1.9 [0.7,5.6]	2.0 [0.8,4.8]	2.2 [0.8,5.3]	2.8 [1.0,6.3]	3.6 [1.2,7.5]	4.2 [1.4,10.4]	4.1 [1.1,9.3]	4.6 [1.1,10.4]	6.5 [1.2,12.0]	8.4 [3.2,13.3]	4.2 [1.3,7.9]	2.2 [0.9,5.0]	2.9 [1.0,5.9]	2.7 [1.0,4.9]	3.7 [1.8,6.6]	1.3 [0.6,3.8]	1.6 [0.6,3.5]	1.8 [0.8,4.1]	2.3 [0.9,4.6]	2.8 [1.1,5.2]
Comorbidity history																				
Diabetes	35%	39%	39%	34%	30%	44%	43%	40%	33%	24%	49%	59%	59%	57%	53%	56%	63%	63%	63%	48%
Hypertension	84%	87%	88%	87%	86%	81%	83%	79%	74%	76%	86%	95%	96%	94%	92%	91%	91%	91%	92%	88%
Coronary artery disease	40%	38%	38%	35%	35%	31%	31%	31%	29%	34%	46%	52%	42%	46%	49%	52%	60%	58%	53%	41%
Heart failure	27%	25%	23%	19%	23%	22%	19%	19%	15%	19%	26%	39%	45%	40%	32%	37%	42%	41%	42%	33%
Cerebrovascular disease	17%	17%	16%	15%	15%	15%	17%	13%	12%	13%	19%	18%	12%	18%	10%	19%	20%	16%	15%	9%
Peripheral vascular disease	29%	30%	30%	27%	27%	16%	16%	17%	14%	8%	19%	30%	25%	22%	21%	34%	37%	34%	33%	25%
Other cardiovascular disease	36%	36%	32%	30%	32%	27%	26%	26%	23%	26%	11%	26%	26%	26%	20%	34%	35%	32%	32%	23%
Gastrointestinal bleeding	4%	5%	4%	4%	4%	4%	4%	4%	5%	2%	6%	6%	4%	5%	4%	4%	7%	7%	4%	3%
Lung disease	12%	15%	13%	14%	12%	4%	3%	4%	4%	4%	16%	13%	12%	13%	11%	23%	22%	20%	21%	15%
Neurologic disease	15%	12%	11%	12%	10%	9%	8%	7%	5%	3%	8%	18%	7%	13%	10%	18%	12%	10%	9%	10%
Psychiatric disorder	16%	16%	14%	12%	17%	4%	3%	4%	4%	3%	22%	25%	15%	17%	23%	34%	25%	25%	30%	26%
Cancer	19%	17%	16%	16%	15%	13%	11%	12%	9%	7%	11%	9%	9%	9%	7%	13%	16%	15%	13%	11%
Recurrent cellulitis / gangrene	10%	10%	9%	9%	8%	4%	4%	4%	3%	2%	11%	9%	7%	5%	10%	11%	13%	15%	12%	8%
HIV	0.50%	0.50%	0.60%	0.60%	0.90%	0.80%	0.50%	0.30%	0.70%	0%	5%	6%	7%	4%	8%	2%	0.80%	0%	0%	1%
ADPKD	6%	6%	7%	7%	6%	3%	4%	5%	4%	9%	0%	0%	0.80%	0%	2%	6%	3%	5%	4%	3%
Dialysis treatments																				
Vascular access type																				
Catheter	30%	27%	25%	24%	27%	2.00%	1%	1%	0%	2%	41%	23%	26%	36%	27%	41%	35%	31%	29%	34%
Fistula	65%	67%	69%	69%	66%	91%	93%	93%	93%	95%	30%	44%	45%	40%	44%	38%	51%	56%	57%	54%
Graft	6%	6%	6%	7%	6%	8%	6%	6%	7%	3%	30%	33%	30%	24%	29%	20%	14%	13%	14%	12%
Single pool Kt/V	1.5 ± 0.3	1.5 ± 0.3	1.5 ± 0.3	1.5 ± 0.3	1.5 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.4 ± 0.3	1.5 ± 0.3	1.6 ± 0.2	1.5 ± 0.3	1.5 ± 0.3	1.5 ± 0.3	1.6 ± 0.3	1.6 ± 0.3	1.6 ± 0.3	1.6 ± 0.3	1.5 ± 0.3
Lab/biometric markers																				
Body mass index, kg/m^2	25.2 ± 5.5	25.9 ± 5.2	26.7 ± 5.6	26.6 ± 5.7	26.3 ± 5.8	21.2 ± 3.5	21.7 ± 3.6	21.9 ± 3.6	22.2 ± 4.0	22.2 ± 4.3	28.5 ± 8.6	28.3 ± 6.9	28.8 ± 6.6	29.4 ± 7.6	28.9 ± 7.3	27.6 ± 7.5	28.3 ± 7.0	28.4 ± 6.7	29.8 ± 7.4	28.7 ± 7.5
<18	6%	4%	3%	3%	4%	17%	14%	12%	11%	12%	6%	2%	1%	3%	2%	5%	2%	2%	0%	3%
18-24	48%	45%	41%	41%	43%	71%	71%	71%	71%	68%	34%	33%	35%	29%	32%	36%	35%	32%	29%	32%
25-29	28%	33%	33%	33%	32%	9%	12%	14%	14%	12%	17%	31%	20%	26%	25%	28%	27%	31%	28%	27%
30+	18%	19%	24%	24%	22%	2%	3%	3%	4%	8%	43%	33%	45%	42%	40%	31%	36%	35%	43%	38%

Serum albumin, g/dL	3.7 ± 0.5	3.7 ± 0.5	3.8 ± 0.5	3.8 ± 0.5	3.8 ± 0.5	3.7 ± 0.4	3.7 ± 0.4	3.7 ± 0.4	3.8 ± 0.3	3.8 ± 0.4	3.7 ± 0.5	3.8 ± 0.5	3.9 ± 0.4	3.8 ± 0.4	3.8 ± 0.4	3.6 ± 0.5	3.7 ± 0.4	3.7 ± 0.4	3.7 ± 0.4	3.8 ± 0.5
Hemoglobin, g/dL	11.4 ± 1.4	11.5 ± 1.4	11.6 ± 1.4	11.5 ± 1.4	11.5 ± 1.5	10.6 ± 1.3	10.7 ± 1.2	10.7 ± 1.3	10.7 ± 1.3	10.7 ± 1.3	11.3 ± 1.4	11.6 ± 1.4	11.5 ± 1.3	11.4 ± 1.4	11.4 ± 1.3	11.5 ± 1.4	11.5 ± 1.3	11.5 ± 1.3	11.3 ± 1.3	11.4 ± 1.5
Serum phosphorus, mg/dL	4.8 ± 1.6	4.8 ± 1.5	5.0 ± 1.5	5.3 ± 1.5	5.6 ± 1.7	5.2 ± 1.4	5.3 ± 1.4	5.8 ± 1.5	5.9 ± 1.4	6.2 ± 1.6	4.8 ± 1.9	5.0 ± 1.4	5.5 ± 1.6	5.8 ± 1.8	6.3 ± 1.8	4.9 ± 1.7	5.0 ± 1.5	5.5 ± 1.6	5.9 ± 1.7	6.8 ± 1.9
<3.5	20%	18%	14%	10%	9%	9%	6%	3%	2%	2%	26%	11%	10%	7%	3%	18%	13%	5%	3%	1%
3.5-4.4	28%	29%	26%	21%	18%	22%	20%	13%	11%	9%	24%	27%	15%	16%	13%	27%	25%	23%	13%	9%
4.5-5.4	23%	26%	27%	29%	25%	30%	31%	27%	28%	23%	24%	29%	24%	26%	19%	23%	29%	29%	25%	19%
5.5-6.4	16%	15%	18%	19%	20%	24%	25%	29%	31%	29%	11%	17%	31%	18%	19%	14%	18%	19%	27%	17%
6.5+	13%	12%	15%	20%	28%	15%	18%	27%	28%	38%	16%	15%	20%	32%	47%	19%	14%	24%	31%	54%
Serum calcium, mg/dL	9.1 ± 0.8	9.0 ± 0.7	8.9 ± 0.7	8.9 ± 0.8	9.0 ± 0.8	9.0 ± 0.8	8.8 ± 0.7	8.8 ± 0.8	8.9 ± 0.8	9.0 ± 0.9	9.1 ± 1.2	9.1 ± 0.7	9.1 ± 0.8	9.0 ± 0.8	9.0 ± 0.8	9.1 ± 0.9	9.0 ± 0.7	8.9 ± 0.7	8.8 ± 0.7	8.8 ± 0.8
<8.4	15%	16%	19%	23%	22%	19%	26%	31%	26%	23%	16%	13%	13%	15%	26%	18%	15%	20%	25%	30%
8.4-9.4	52%	62%	61%	55%	53%	55%	58%	51%	54%	47%	38%	63%	57%	56%	45%	48%	65%	61%	58%	50%
9.5+	33%	22%	21%	22%	24%	26%	16%	18%	20%	30%	46%	24%	30%	29%	29%	34%	20%	19%	17%	20%
CRP, mg/L	5.8 [3.0,12.0]	5.2 [2.7,11.5]	5.0 [2.7,10.9]	5.0 [2.8,10.6]	5.0 [3.0,10.8]	1.2 [0.7,4.0]	1.0 [0.5,3.0]	1.2 [0.6,3.5]	1.2 [0.5,3.0]	1.1 [0.5,3.2]	-	-	-	-	-	-	-	-	-	-
<1	5%	6%	6%	5%	4%	33%	37%	35%	38%	39%	-	-	-	-	-	-	-	-	-	-
1-2.9	19%	21%	21%	22%	19%	35%	36%	35%	36%	32%	-	-	-	-	-	-	-	-	-	-
3-9.9	43%	44%	46%	45%	49%	22%	19%	20%	21%	21%	-	-	-	-	-	-	-	-	-	-
10+	33%	30%	28%	28%	28%	10%	8%	10%	5%	7%	-	-	-	-	-	-	-	-	-	-
Medication																				
Calcium-based phosphate binder	50%	44%	40%	39%	36%	68%	56%	54%	54%	55%	47%	50%	40%	35%	45%	55%	46%	50%	43%	53%
Non-calcium-based phosphate binder	42%	50%	55%	62%	64%	48%	52%	54%	57%	63%	45%	43%	54%	63%	61%	36%	41%	50%	56%	59%
Cinacalcet	5%	11%	17%	22%	34%	11%	16%	18%	21%	28%	18%	16%	22%	38%	44%	4%	10%	16%	26%	36%
Vitamin D	45%	49%	60%	63%	64%	67%	71%	72%	77%	76%	58%	80%	95%	91%	85%	39%	61%	76%	77%	71%

Mean ± standard deviation, median [IQR], or prevalence (%) shown.

**CRP was restricted to facilities routinely measuring CRP, US and Russia were excluded because CRP not commonly measured. ADPKD = adult polycystic kidney disease; ALP = alkaline phosphatase; HIV = human immunodeficiency virus; PTH = parathyroid hormone.*

Supplementary Table S2

Adjusted associations (HR, 95% CI) between (A) normalized PTH, (B) normalized ALP, and time-to-event clinical outcomes, by level of adjustment

A

outcome	Normalized PTH	model 1	model 2	model 3	model 4	model 5
all-cause mortality						
	<1	1.20(1.08,1.34)	1.21(1.09,1.35)	1.19(1.07,1.32)	1.07(0.96,1.18)	1.08(0.97,1.19)
	1-3.9	1.11(1.02,1.20)	1.05(0.97,1.14)	1.03(0.94,1.11)	0.97(0.90,1.06)	0.98(0.90,1.06)
	4-5.9	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	6-8.9	0.95(0.85,1.06)	1.02(0.91,1.13)	1.02(0.91,1.13)	1.05(0.94,1.17)	1.05(0.94,1.17)
	9+	1.00(0.91,1.11)	1.26(1.13,1.39)	1.26(1.13,1.40)	1.26(1.13,1.40)	1.25(1.13,1.39)
CV mortality						
	<1	1.15(0.97,1.37)	1.15(0.97,1.37)	1.15(0.97,1.36)	1.06(0.90,1.26)	1.08(0.91,1.28)
	1-3.9	1.06(0.92,1.21)	1.01(0.88,1.15)	0.98(0.86,1.12)	0.95(0.84,1.09)	0.96(0.84,1.09)
	4-5.9	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	6-8.9	0.94(0.79,1.13)	1.01(0.84,1.22)	1.02(0.85,1.23)	1.05(0.88,1.26)	1.05(0.87,1.26)
	9+	1.08(0.92,1.28)	1.33(1.12,1.58)	1.35(1.14,1.60)	1.35(1.14,1.60)	1.34(1.13,1.59)
Non-CV mortality						
	<1	1.23(1.09,1.40)	1.25(1.10,1.41)	1.21(1.07,1.38)	1.07(0.95,1.21)	1.08(0.95,1.22)
	1-3.9	1.14(1.04,1.25)	1.08(0.98,1.19)	1.05(0.95,1.16)	0.99(0.89,1.09)	0.99(0.89,1.09)
	4-5.9	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	6-8.9	0.95(0.84,1.09)	1.02(0.89,1.16)	1.01(0.89,1.16)	1.05(0.92,1.20)	1.05(0.92,1.20)
	9+	0.96(0.85,1.09)	1.22(1.07,1.38)	1.21(1.06,1.38)	1.21(1.06,1.38)	1.21(1.06,1.38)
Any fracture						

	<1	0.88(0.69,1.13)	0.85(0.67,1.09)	0.83(0.65,1.06)	0.78(0.61,1.00)	0.78(0.61,0.99)
	1-3.9	1.09(0.91,1.30)	1.02(0.85,1.23)	1.01(0.84,1.21)	0.98(0.81,1.17)	0.97(0.81,1.17)
	4-5.9	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	6-8.9	1.02(0.81,1.27)	1.07(0.85,1.34)	1.07(0.85,1.35)	1.10(0.87,1.38)	1.11(0.88,1.39)
	9+	0.88(0.69,1.12)	1.04(0.81,1.33)	1.05(0.82,1.35)	1.07(0.84,1.38)	1.08(0.85,1.39)
Hip fracture						
	<1	0.60(0.38,0.95)	0.60(0.38,0.95)	0.58(0.37,0.92)	0.52(0.33,0.83)	0.52(0.32,0.82)
	1-3.9	1.14(0.86,1.50)	1.07(0.81,1.41)	1.06(0.80,1.40)	0.99(0.75,1.31)	0.98(0.74,1.30)
	4-5.9	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	6-8.9	1.07(0.75,1.53)	1.13(0.80,1.62)	1.14(0.79,1.63)	1.14(0.79,1.64)	1.15(0.80,1.66)
	9+	0.82(0.56,1.20)	1.04(0.71,1.53)	1.05(0.71,1.54)	1.06(0.72,1.57)	1.07(0.72,1.58)

Model 1: unadjusted [stratified by DOPPS phase and country]
Model 2: + demographics: age, sex, Black race, dialysis vintage
Model 3: + 13 DOPPS 'standard' comorbid conditions
Model 4: + single pool Kt/V, body mass index, serum albumin, serum creatinine, hemoglobin
Model 5: + MBD treatments (calcium-based phosphate binder, non-calcium-based phosphate binder, active vitamin D, calcimimetics) and markers (serum phosphate, serum calcium)
ALP = alkaline phosphatase; CV = cardiovascular; PTH = parathyroid hormone.

B

outcome	Normalized ALP	model 1	model 2	model 3	model 4	model 5
all-cause mortality						
	<0.5	0.70(0.64,0.77)	0.73(0.66,0.80)	0.77(0.70,0.84)	0.81(0.74,0.89)	0.81(0.74,0.89)
	0.5-0.74	0.87(0.81,0.93)	0.86(0.80,0.92)	0.88(0.82,0.94)	0.90(0.84,0.96)	0.90(0.84,0.96)
	0.75-0.99	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	1-1.49	1.11(1.02,1.20)	1.13(1.04,1.23)	1.08(1.00,1.18)	1.05(0.97,1.15)	1.05(0.97,1.15)
	1.5+	1.33(1.20,1.47)	1.56(1.40,1.72)	1.42(1.28,1.57)	1.35(1.22,1.50)	1.35(1.22,1.50)
CV mortality						
	<0.5	0.76(0.66,0.89)	0.78(0.67,0.91)	0.82(0.70,0.96)	0.86(0.73,1.00)	0.86(0.74,1.00)
	0.5-0.74	0.88(0.78,1.00)	0.87(0.76,0.98)	0.89(0.78,1.01)	0.90(0.80,1.03)	0.91(0.80,1.03)
	0.75-0.99	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	1-1.49	1.09(0.94,1.26)	1.11(0.96,1.29)	1.05(0.91,1.21)	1.03(0.89,1.19)	1.03(0.89,1.19)
	1.5+	1.35(1.14,1.59)	1.56(1.33,1.84)	1.42(1.20,1.68)	1.38(1.17,1.63)	1.37(1.16,1.61)
Non-CV mortality						
	<0.5	0.67(0.60,0.75)	0.70(0.63,0.79)	0.74(0.66,0.83)	0.78(0.70,0.88)	0.78(0.70,0.88)
	0.5-0.74	0.86(0.79,0.93)	0.85(0.78,0.93)	0.87(0.80,0.95)	0.89(0.82,0.97)	0.89(0.82,0.97)
	0.75-0.99	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	1-1.49	1.11(1.01,1.23)	1.15(1.04,1.27)	1.10(1.00,1.22)	1.07(0.96,1.18)	1.07(0.96,1.18)
	1.5+	1.31(1.16,1.49)	1.55(1.37,1.76)	1.41(1.25,1.61)	1.34(1.18,1.53)	1.35(1.18,1.54)
Any fracture						
	<0.5	0.65(0.51,0.82)	0.72(0.57,0.91)	0.74(0.58,0.94)	0.77(0.60,0.97)	0.76(0.60,0.97)
	0.5-0.74	0.96(0.80,1.14)	0.99(0.83,1.18)	0.99(0.83,1.19)	1.00(0.84,1.20)	1.00(0.84,1.20)
	0.75-0.99	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	1-1.49	1.35(1.11,1.64)	1.34(1.10,1.62)	1.30(1.07,1.58)	1.27(1.05,1.55)	1.28(1.05,1.56)
	1.5+	1.38(1.08,1.75)	1.48(1.16,1.89)	1.39(1.09,1.78)	1.35(1.06,1.74)	1.36(1.06,1.75)
Hip fracture						
	<0.5	0.57(0.39,0.83)	0.63(0.43,0.92)	0.64(0.44,0.94)	0.65(0.44,0.95)	0.65(0.44,0.95)
	0.5-0.74	0.90(0.69,1.19)	0.92(0.70,1.21)	0.92(0.70,1.22)	0.93(0.71,1.23)	0.94(0.71,1.24)
	0.75-0.99	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)

1-1.49	1.33(0.98,1.80)	1.37(1.02,1.84)	1.33(0.99,1.79)	1.29(0.95,1.74)	1.29(0.95,1.75)
1.5+	1.37(0.95,1.98)	1.60(1.11,2.32)	1.52(1.05,2.21)	1.45(1.00,2.11)	1.46(1.00,2.13)

Model 1: unadjusted [stratified by DOPPS phase and country]
Model 2: + demographics: age, sex, Black race, dialysis vintage
Model 3: + 13 DOPPS 'standard' comorbid conditions
Model 4: + single pool Kt/V, body mass index, serum albumin, serum creatinine, hemoglobin
Model 5: + MBD treatments (calcium-based phosphate binder, non-calcium-based phosphate binder, active vitamin D, calcimimetics) and markers (serum phosphate, serum calcium)
ALP = alkaline phosphatase; CV = cardiovascular; PTH = parathyroid hormone.

Supplementary Table S3

Akaike Information Criteria for adjusted Cox models including normalized PTH vs. normalized ALP

Outcome	**AIC for PTH**	**AIC for ALP**
All cause mortality	63787.291	63639.740
CV mortality	23035.357	22992.370
Non-CV mortality	40998.315	40896.212
Any fracture	11571.600	11526.407
Hip fracture	4544.006	4530.547

AIC = Akaike Information Criteria; ALP = alkaline phosphatase; CV = cardiovascular; PTH = parathyroid hormone. 'AIC for PTH' represents the AIC for the adjusted Cox regression model with normalized PTH as the exposure variable and 'AIC for ALP' represents the AIC for the adjusted Cox regression model with normalized ALP as the exposure variable; lower AIC is indicative of a better model fit, and thus reflects a better set of predictors for the outcome. A lower AIC for all 5 outcomes in this table demonstrates that normalized ALP was a better predictor than normalized PTH for every outcome.

Supplementary Table S4

Sample size in each cell of the analysis (Figure 2) of the combined associations between normalized ALP, normalized PTH, and time-to-even clinical outcomes

normalized	normalized ALP					
PTH	<0.5	0.5-0.74	0.75-0.99	1.0-1.49	1.5+	Total
<1	1182	1621	755	445	171	4174
1-3.9	3285	5558	3090	1932	755	14620
4-5.9	891	1863	1153	868	338	5113
6-8.9	537	1236	909	716	325	3723
9+	363	944	851	1047	866	4071
Total	6258	11222	6758	5008	2455	31701

ALP = alkaline phosphatase; PTH = parathyroid hormone.

Modified STROBE Statement—checklist of items that should be included in reports of observational studies (Cohort/Cross-sectional and case-control studies)

	Item No	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement).	5-7
Bias	9	Describe any efforts to address potential sources of bias	5-7
Study size	10	Explain how the study size was arrived at (if applicable)	5-7

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-7
		(*b*) Describe any methods used to examine subgroups and interactions	5-7
		(*c*) Explain how missing data were addressed	5-7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	5-7
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	8
		(c) **Use of a flow diagram**	5, 6, and Supplementary Figure S1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 8, Table 1, and Supplementary Table S1
		(b) Indicate number of participants with missing data for each variable of interest	5-8, and Supplementary Figure S1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	8-9
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	8-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which	Figure 1

		confounders were adjusted for and why they were included	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.