

# Trends in Mineral Metabolism: Kidney Early Evaluation Program (KEEP) and the National Health and Nutrition Examination Survey (NHANES) 1999-2004

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on behalf of the Kidney Early Evaluation Program Investigators

**Background:** Chronic kidney disease (CKD) is associated with mineral metabolism dysregulation, cardiovascular disease, and premature mortality. No study specifically examined mineral metabolism trends in a generalizable sample of patients at increased CKD risk.

**Methods:** This cross-sectional analysis from November 1, 2005, to December 31, 2006, of calcium, phosphorus, and parathyroid hormone (PTH) includes 2,646 individuals with estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m<sup>2</sup> in the National Kidney Foundation Kidney Early Evaluation Program (KEEP), a community-based health-screening program targeting individuals 18 years and older with diabetes, hypertension, or family history of kidney disease, diabetes, or hypertension. A parallel analysis of National Health and Nutrition Examination Survey (NHANES) 1999-2004 data was performed.

**Results:** In KEEP, as eGFR decreased from 55 to less than 60 mL/min/1.73 m<sup>2</sup> to less than 30 mL/min/1.73 m<sup>2</sup>, calcium level decreased ( $9.55 \pm 0.47$  to  $9.34 \pm 0.62$  mg/dL;  $P < 0.001$ ), phosphorus level increased ( $3.70 \pm 0.59$  to  $4.15 \pm 0.80$  mg/dL;  $P < 0.001$ ), and PTH level increased ( $66.3 \pm 36.3$  to  $164 \pm 109$  pg/mL; mean,  $80.8 \pm 57.0$  pg/mL;  $P < 0.001$ ). NHANES 1999-2004 showed similar trends, with PTH values not as high. Individuals within opinion-based Kidney Disease Outcomes Quality Initiatives targets from the highest to the lowest eGFR group were as follows: calcium, 93.0% to 92.3% (KEEP) and 97.4% to 89.6% (NHANES); phosphorus, 90.4% to 90.3% (KEEP) and 91.6% to 87.1% (NHANES); and PTH, 46.1% to 31.2% (KEEP) and 56.4% to 36.1% (NHANES).

**Conclusions:** In a community-based CKD screening population, increased PTH level occurs early in patients with stage 3, typically with normal calcium and phosphorus levels. These findings support the importance of including PTH with calcium and phosphorus monitoring for individuals with eGFR less than 60 mL/min/1.73 m<sup>2</sup>.

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**INDEX WORDS:** Calcium; chronic kidney disease; Kidney Early Evaluation Program (KEEP); mineral metabolism; National Health and Nutrition Examination Survey (NHANES); parathyroid hormone (PTH); phosphorus.

Chronic kidney disease (CKD) is associated with several complications, including mineral metabolism dysregulation, increased cardiovascular disease (CVD) morbidity, and premature mortality. Mineral metabolism abnormalities in dialysis patients present with persistently increased parathyroid hormone (PTH) levels, typi-

cally accompanied by hyperphosphatemia. More than half the patients with chronic kidney failure or end-stage renal disease treated with hemodialysis or peritoneal dialysis in several large observational studies showed hyperphosphatemia, a finding associated with increased mortality.<sup>1-6</sup> Observational and prospective data also show an

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**Table 1. Characteristics of KEEP and NHANES Populations by Estimated Glomerular Filtration Rate**

	Estimated Glomerular Filtration Rate (mL/min/1.73 m <sup>2</sup> )					
	KEEP			NHANES 1999-2004*		
	55-<60	45-<55	<45	55-<60	45-<55	<45
No. of participants	768	1,082	796	430	571	437
Age (y)						
18-45	25.8	49.5	24.7	50.0	24.0	26.0
46-60	50.3	34.2	15.5	52.1	36.6	11.3
61-75	28.4	40.3	31.3	32.3	39.7	28.1
≥75	13.8	45.9	40.3	24.2	41.4	34.4
Sex						
Men	31.1	40.3	28.6	37.5	36.6	25.9
Women	28.1	41.2	30.7	32.4	40.0	27.6
Race						
White	29.2	41.3	29.5	35.6	39.1	25.3
African American	29.6	39.9	30.5	25.8	35.0	39.2
Other	26.9	40.2	32.9	29.3	37.8	32.9
Body mass index (kg/m <sup>2</sup> )						
≥30	29.8	38.5	31.7	35.0	37.7	27.3
<30	28.3	43.0	28.7	35.2	39.5	25.3
Smoking status						
Current smoker	28.2	43.6	28.2	49.4	25.9	24.7
Nonsmoker	28.8	40.8	30.4	32.1	40.6	27.3
Education						
<High school	22.7	39.8	37.5	26.9	42.3	30.8
≥High school	30.5	41.1	28.4	37.5	37.1	25.4
Diabetes†						
Yes	22.7	41.0	36.3	26.8	35.3	38
No	33.9	40.8	25.3	36.1	39.4	24.5
Hypertension‡						
Yes	28.0	41.0	31.0	31.6	39.7	28.7
No	39.7	40.1	20.3	51.0	32.0	17.1
Anemia§						
Yes	15.4	34.6	50.0	17.6	27.2	55.2
No	33.2	42.8	24.0	37.0	40.5	22.6
Cardiovascular disease						
Yes	23.2	38.9	37.9	23.1	35.4	41.5
No	33.0	42.2	24.8	40.0	40.4	19.6
Albumin-creatinine ratio (mg/g)						
<30	32.7	42.6	24.7	40.3	40.7	18.9
30-300	19.8	38.0	42.2	25.6	40.3	34.1
>300	10.0	23.1	66.9	17.2	22.1	60.7

Note: Categorical values are expressed in percent.

Abbreviations: KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition Examination Survey.

\*In NHANES, for analyses related to smoking status and self-reported cardiovascular disease, the study population is limited to participants 20 years and older.

†KEEP definition: self-reported or measured (glucose ≥ 126 mg/dL [≥7.0 mmol/L] fasting or ≥ 200 mg/dL [11.1 mmol/L] nonfasting); NHANES definition: self-reported.

‡Self-reported or measured (systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 80 mm Hg if patient has diabetes or chronic kidney disease, otherwise systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg).

§As defined by the World Health Organization (hemoglobin < 13 g/dL [<130 g/L] for men and < 12 g/dL [<120 g/L] for women).

association between phosphorus level greater than 3.5 mg/dL and mortality in patients with CKD.<sup>7,8</sup> The direct or indirect mechanism by which greater serum phosphorus values and mor-

tality are linked is not fully understood. Mineral metabolism dysregulation is a novel cardiovascular risk marker in patients with CKD because of associations with arterial stiffness,<sup>9</sup> vascular cal-

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