

**KEEP 2010**  
**Analytical Methods**

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## ANALYTICAL METHODS: THE KIDNEY EARLY EVALUATION PROGRAM (KEEP) 2000-2010

### Database Design and Study Participants

The Kidney Early Evaluation program (KEEP) is a free, community-based health screening program that targets populations at high risk for kidney disease. A pilot program conducted in 1997 screened almost 900 individuals and showed that targeted populations aged 18 years and older, with history of diabetes or hypertension, or with a first-order relative with diabetes, hypertension, or kidney disease, were highly likely to show evidence of kidney damage, microalbuminuria, and reduced kidney function. In August 2000, the National Kidney Foundation (NKF) officially launched KEEP nationwide. Now entering its tenth year, the program has screened more than 144,000 participants from 50 states and the District of Columbia. Data used for this 2010 KEEP Annual Data Report summary figures and reference tables were limited to data collected by December 31, 2009, with a total of 124,509 eligible participants after excluding those who did not meet KEEP inclusion criteria.

### General Criteria for Inclusion in KEEP Data Analysis

We report only eligible participants as previously defined.<sup>1</sup> Most analyses are descriptive. Due to missing responses by KEEP survey participants, we used the following inclusion criteria:

- In the overall analysis, we include all eligible participants.
- In analyses by any participant characteristic, we exclude participants with missing values for that characteristic. For example, when we report participant distribution by race or by self-reported disease, we exclude participants with missing values for race or self-reported disease. We report the specific exclusions under each figure.
- For all percent distribution analyses, denominators include only eligible participants without missing data for the specific characteristics.
- In the race/ethnicity categories, racial groups are white, African American, Native American, or other in most analyses, and participants with missing values for race were excluded. Ethnicity groups are Hispanic and non-Hispanic, and participants with missing values for ethnicity were treated as non-Hispanic.

- In the age category, participants are grouped as follows: 18 to 30, 31 to 45, 46 to 60, 61 to 75, and 75 to 110 years.
- Participants with missing values for biochemical measures such as blood pressure (BP), blood glucose, estimated glomerular filtration rate (eGFR), and hemoglobin, were excluded from calculations of the means of these measures.
- In any analyses involving multiple participant characteristics or biochemical measures, participants with any missing values for those characteristics or measures were excluded.

### Definitions

Chronic Kidney Disease (CKD) was defined as eGFR less than 60 mL/min/1.73 m<sup>2</sup> (1.00 mL/s/1.73 m<sup>2</sup>) or eGFR greater than or equal to 60 mL/min/1.73 m<sup>2</sup> and albumin-creatinine ratio (ACR) greater than or equal to 30 mg/g. GFR was estimated using two equations: the 4-variable Modification of Diet in Renal Disease Study equation (eGFR<sub>MDRD</sub>),<sup>2</sup> eGFR = 175 × standardized S<sub>cr</sub><sup>-1.154</sup> × age<sup>-0.203</sup> × 1.212 [if African American] × 0.742 [if female]; and the Chronic Kidney Disease Epidemiology Collaboration equation (eGFR<sub>CKD-EPI</sub>),<sup>3</sup> eGFR = 141 × min(Scr/κ, 1)<sup>α</sup> × max(Scr/κ, 1)<sup>-1.209</sup> × 0.993<sup>Age</sup> × 1.018 [if female] × 1.159 [if African American], where Scr is serum creatinine, κ is 0.7 for women and 0.9 for men, α is -0.329 for women and -0.411 for men, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. Serum creatinine values were calibrated to standardized serum creatinine at the Cleveland Clinic Research Laboratory.

### CKD Stages

- Stage 1: eGFR > 90 mL/min/1.73 m<sup>2</sup> (1.50 mL/s/1.73 m<sup>2</sup>) and ACR ≥ 30 mg/g.
- Stage 2: eGFR 60-89 mL/min/1.73 m<sup>2</sup> (1.00-1.48 mL/s/1.73 m<sup>2</sup>) and ACR ≥ 30 mg/g.
- Stage 3: eGFR 30-59 mL/min/1.73 m<sup>2</sup> (0.50-0.98 mL/s/1.73 m<sup>2</sup>).
- Stage 4: eGFR 15-29 mL/min/1.73 m<sup>2</sup> (0.25-0.48 mL/s/1.73 m<sup>2</sup>).
- Stage 5: eGFR < 15 mL/min/1.73 m<sup>2</sup> (0.25 mL/s/1.73 m<sup>2</sup>).

### History of Diabetes

- Self-reported diabetes.
- Retinopathy.

## Elevated Blood Sugar

- Fasting blood sugar  $\geq 126$  mg/dL (7.0 mmol/L), non-fasting blood sugar  $\geq 200$  mg/dL (11.1 mmol/L); or A1c  $\geq 7\%$  (if available).

## Diabetes

- Self-reported history of diabetes or retinopathy.
- Receiving medication for diabetes or receiving insulin.
- Elevated blood sugar defined by glucose  $\geq 126$  mg/dL (7.0 mmol/L) fasting or  $\geq 200$  mg/dL (11.1 mmol/L) non-fasting.
- A1c  $\geq 7\%$  (if available).

## Elevated Measured BP

- Diabetes or CKD (eGFRCKD-EPI): systolic BP  $\geq 130$  mmHg or diastolic BP  $\geq 80$  mmHg.
- No diabetes or CKD (eGFRCKD-EPI): systolic BP  $\geq 140$  mmHg or diastolic BP  $\geq 90$  mmHg.

## Hypertension

- Self-reported history of high BP.
- Receiving medication for high BP.
- Elevated BP (JNC 7)<sup>4</sup> defined by systolic BP  $\geq 130$  mmHg or diastolic BP  $\geq 80$  mmHg for persons with history of diabetes or CKD (eGFRCKD-EPI) and systolic BP  $\geq 140$  mmHg or diastolic BP  $\geq 90$  mmHg for persons with no history of diabetes or CKD (eGFRCKD-EPI).

## Elevated Cholesterol

- Cholesterol level  $> 200$  mg/dL (5.17 mmol/L).

## High Cholesterol

- Self-reported high cholesterol.
- Receiving medication for high cholesterol.
- Elevated cholesterol level defined by cholesterol  $> 200$  mg/dL (5.17 mmol/L).

## Body Mass Index Groups

- Underweight: body mass index (BMI)  $< 18.5$  kg/m<sup>2</sup>.
- Normal: BMI 18.5-24.9 kg/m<sup>2</sup>.
- Overweight: BMI 25-29.9 kg/m<sup>2</sup>.
- Obese: BMI 30-39.9 kg/m<sup>2</sup>.
- Extremely obese: BMI  $\geq 40$  kg/m<sup>2</sup>.

## Microalbuminuria

- Clinitek ACR  $\geq 30$  mg/g

## WHO Anemia

- Men: hemoglobin  $< 13$  g/dL (130 g/L).
- Women: hemoglobin  $< 12$  g/dL (120 g/L).

## KDOQI Anemia

- Men: hemoglobin  $< 13.5$  g/dL (135 g/L).
- Women: hemoglobin  $< 12$  g/dL (120 g/L).

## Mean BP

- Diastolic BP + (systolic BP – diastolic BP)/3.

## Risk Factors for Cardiovascular Disease

- BMI  $\geq 30$  kg/m<sup>2</sup>.
- Self-reported diabetes or retinopathy.
- History of smoking.
- WHO anemia.
- Elevated BP (JNC 7).<sup>4</sup>

## Cardiovascular Disease

- Self-reported heart attack.
- Heart bypass surgery.
- Heart angioplasty.
- Stroke.
- Heart failure.
- Abnormal heart rhythm.
- Peripheral vascular disease (only for KEEP version 2).

## Glycemic Control

- Fasting blood sugar  $< 126$  mg/dL (7.0 mmol/L), non-fasting blood sugar  $< 200$  mg/dL (11.1 mmol/L), and A1c  $< 7\%$ .

## BP Control

- History of diabetes or CKD (eGFRCKD-EPI): systolic BP  $< 130$  mmHg and diastolic BP  $< 80$  mmHg.
- No history of diabetes or CKD (eGFRCKD-EPI): systolic BP  $< 140$  mmHg and diastolic BP  $< 90$  mmHg

## Cholesterol Control

- Cholesterol level  $\leq 200$  mg/dL (5.17 mmol/L).

## Ascertainment of Mortality and End-Stage Renal Disease

KEEP obtains informed consent from individual participants to use Social Security number, first name, last name, and birth date in potential linkages for future research studies. All-cause mortality data were ascertained by linking the KEEP study cohort to the first-quarter 2010 Social Security Administration Death Master File. End-stage renal disease (ESRD) data were obtained from a patient linking request of the KEEP study cohort to the United States Renal Data System (USRDS). All KEEP study participants were followed through December 31, 2009, for mortality and through September 2009 for ESRD endpoints, censored at death date.

## Abnormal Mineral Metabolism Values

Values were determined for calcium and phosphorus using the Architect c8000 (Abbott Laboratories, Abbott Park, Illinois), with Arsenazo-III dye for calcium and ammonium molybdate for phosphorus. The intact-parathyroid hormone (PTH) assay was performed using Immulite 2000 (Siemens Medical Solutions Diagnostics, Los Angeles, California), a two-site chemiluminescent enzyme-labeled immunometric assay. All laboratory tests were performed at Consolidated Laboratory Services (CLS; Van Nuys, California), and, after May 2008, at Quest Diagnostics (Madison, New Jersey). Quest used Immulite 2000 to analyze PTH and Olympus Au 5400 (Olympus Optical, Tokyo, Japan) to analyze calcium and phosphorus.

- Elevated PTH: > 70 pg/mL for CKD (eGFR<sub>MDRD</sub>) stage 3, > 110 pg/mL for stage 4, and > 300 pg/mL for stage 5 (values in ng/L are equivalent).
- Abnormal phosphorus: < 2.7 mg/dL (0.87 mmol/L) or > 4.6 mg/dL (1.49 mmol/L), stage 3 and 4; < 3.5 mg/dL (1.13 mmol/L) or > 5.5 mg/dL (1.78 mmol/L) stage 5.
- Abnormal calcium: < 8.4 mg/dL (2.10 mmol/L) or > 10.2 mg/dL (2.54 mmol/L).

## Laboratory Analysis

Data collected at KEEP screening events include height, weight, blood pressure, age, family history, and plasma glucose. Urine was checked for ACR and for presence of pyuria, hematuria, and microalbuminuria. Venous blood specimens were collected and sent to a central laboratory, where hemoglobin, serum creatinine, cholesterol, hemoglobin A1c, intact PTH, calcium, and phosphorus testing was conducted.

Clinitek Microalbumin Reagent Strips (Siemens Healthcare Diagnostics Inc., Tarrytown, New York) for urinalysis were used to obtain microalbumin and ACR results. Siemens' Multistix PRO Reagent Strip for Urinalysis was used for blood and leukocyte measures. Urinalysis testing was performed using Siemens' Clinitek 50 Analyzer.

Plasma glucose testing on venous blood specimens was performed using SureStep Pro test strips and SureStep consumer meters (LifeScan, Milpitas, California).

Through October 2005, hemoglobin and serum creatinine testing was performed by Satellite Laboratory Services (Redwood City, California), hemoglobin using the Sysmex SE2100 (Sysmex America Inc., Mundelein Illinois), and creatinine using the Olympus 5431 (Olympus Optical, Tokyo, Japan).

Between November 2005 and May 2008, laboratory testing was performed by Consolidated Laboratory Services, Van Nuys, California. Hemoglobin testing was conducted using whole blood on the Abbott Cell-Dyn 3200 (Abbott Laboratories, Abbott Park, Illinois), and PTH testing was conducted on plasma using Siemens Immulite 2000 (Siemens Healthcare Diagnostics, Deerfield, Illinois). The Abbott Architect c8000 (Abbott Laboratories, Abbott Park, Illinois) was used to conduct serum creatinine, calcium, phosphorus, and cholesterol tests.

Beginning June 2008, Quest Diagnostics (Madison, New Jersey) became the third laboratory vendor for KEEP. Quest used Olympus Au 5400 (Olympus Optical, Tokyo, Japan) to analyze serum creatinine, total cholesterol, triglycerides, high-density lipoprotein cholesterol direct, low-density lipoprotein cholesterol direct, calcium, and phosphorus. Hemoglobin and hemoglobin A1c were analyzed using the Beckman Coulter LH750 (Beckman Coulter International, Switzerland) and Roche Integra (Roche Diagnostics-USA, Indianapolis, Indiana) respectively, and Siemens Immulite 2000 was used for analyzing intact PTH.

## Reference Tables

Tables 1 to 18.1 present total counts of eligible KEEP participants and show prevalence of CKD (eGFR<sub>MDRD</sub> and eGFR<sub>CKD-EPI</sub>), diabetes, hypertension, high cholesterol, obesity, microalbuminuria, anemia, risk factors for cardiovascular disease, and self-reported kidney disease or stones, overall and by age, sex, race/ethnicity,

region, smoking status, education, insurance status, and whether a participant has a physician.

Tables 19 to 21.1 report counts of eligible KEEP participants with elevated PTH, abnormal calcium, and abnormal phosphorus overall and by age, sex, race/ethnicity, region, smoking status, education, insurance status, and whether a participant has a physician.

Table 22 reports counts of eligible KEEP participants by NKF affiliate.

Tables 22.1 to 22.12 present total counts, prevalence, and odds ratios for KEEP participants with eGFR less than 60 mL/min/1.73 m<sup>2</sup> (eGFR<sub>MDRD</sub> and eGFR<sub>CKD-EPI</sub>), microalbuminuria, CKD, diabetes, hypertension, diabetes and hypertension, obesity, glycemic control, BP control, WHO anemia, and KDOQI anemia. To calculate odds ratios, we used a set of logistic regressions with all affiliates as independent variables and Florida as the reference.

Tables 22.13 to 22.15 report total counts, prevalence, and odds ratios for KEEP participants with elevated PTH, abnormal calcium, and abnormal phosphorus by division or region. To calculate odds ratios, we used a set of logistic regressions with all divisions as independent variables and South Atlantic as the reference, or with all regions as independent variables and South as the reference.

## References

1. Jurkovitz CT, Qiu Y, Wang C et al. The Kidney Early Evaluation Program (KEEP): program design and demographic characteristics of the population. *Am J Kidney Dis.* 2008;51(Suppl 2):S3-S12.
2. Stevens LA, Stoycheff N. Standardization of serum creatinine and estimated glomerular filtration rate in the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis.* 2008;51(Suppl 2):S77-S82.
3. Levey AS, Stevens LA, Schmid CH et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604-612.
4. Chobanian AV, Bakris GL, Black HR et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA.* 2003;289:2560-2572.