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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 showed that targeted populations aged 18 years and older, with a 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 eleventh year, the program has screened approximately 170,000 participants from 50 states and the District of Colombia. Data used for this 2011 KEEP Annual Data Report summary figures and reference tables were limited to data collected by December 31, 2010, with a total of 138,605 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.1 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.
- When calculating the means of biochemical measures such as blood pressure (BP), blood glucose, estimated glomerular filtration rate (eGFR), and hemoglobin, participants with missing values for these measures were excluded.
- 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^2 (1.00 mL/s/1.73 m^2) or eGFR greater than or equal to 60 mL/min/1.73 m^2 and albumin-creatinine ratio (ACR) greater than or equal to 30 mg/g. GFR was estimated using the 4-variable Modification of Diet in Renal Disease (MDRD) Study equation ($eGFR_{MDRD}$),[2] $eGFR = 175 \times \text{standardized } S_{cr}^{-1.154} \times age^{-0.203} \times 1.212$ [if African American] $\times$ 0.742 [women], and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation ($eGFR_{CKD\text{-}EPI}$),[3] $eGFR = 141 \times \min(Scr/\kappa\ 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female] x 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^2 (1.50 mL/s/1.73 m^2) and ACR ≥ 30 mg/g.
- Stage 2: eGFR 60-89 mL/min/1.73 m^2 (1.00-1.48 mL/s/1.73 m^2) and ACR ≥ 30 mg/g.
- Stage 3: eGFR 30-59 mL/min/1.73 m^2 (0.50-0.98 mL/s/1.73 m^2).
- Stage 4: eGFR 15-29 mL/min/1.73 m^2 (0.25-0.48 mL/s/1.73 m^2).
- Stage 5: eGFR < 15 mL/min/1.73 m^2 (0.25 mL/s/1.73 m^2).

History of Diabetes

- Self-reported diabetes.
- Retinopathy.

Elevated Blood Sugar

- Fasting blood sugar ≥ 126 mg/dL, non-fasting blood sugar ≥ 200 mg/dL.

Diabetes

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

Elevated Measured BP

- Diabetes or CKD (CKD-EPI): systolic BP ≥ 130 mmHg or diastolic BP ≥ 80 mmHg.
- No diabetes or CKD (CKD-EPI): systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg.

Hypertension

- Self-reported history of high BP.
- Receiving medication for high BP.
- Elevated BP (JNC 7)[4] defined by systolic BP ≥ 130 mmHg or diastolic BP ≥ 80 mmHg for persons with history of diabetes or CKD (CKD-EPI) and systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg for persons without history of diabetes or CKD (CKD-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^2.
- Normal: BMI 18.5-24.9 kg/m^2.
- Overweight: BMI 25-29.9 kg/m^2.
- Obese: BMI 30-39.9 kg/m^2.
- Extremely obese: BMI ≥ 40 kg/m^2.

Microalbuminuria

- Clinitek ACR ≥ 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 ≥ 30 kg/m^2.
- Self-reported diabetes or retinopathy.
- History of smoking.
- WHO anemia.
- Elevated BP (JNC 7).

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 (CKD-EPI): systolic BP < 130 mmHg and diastolic BP < 80 mmHg.
- Otherwise systolic BP < 140 mmHg and diastolic BP < 90 mmHg

Cholesterol Control

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

Mineral Metabolism Values

- Elevated PTH: > 70 pg/mL for CKD 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).

Ascertainment of Mortality and End-Stage Renal Disease

KEEP obtains informed consent from individual KEEP 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 2011 Social Security Administration Death Master File. Data on dialysis was obtained through linking the KEEP study cohort to the United States Renal Data System. All KEEP study participants were followed up through December 31, 2010 for mortality. All participants were followed up through September, 2010 for dialysis outcomes and censored at death date.

Laboratory Analysis

Data collected at KEEP screening events included height, weight, blood pressure, waist circumference, age, family history, and plasma glucose. Urine was checked for presence of pyuria, hematuria, microalbuminuria, and albumin-to-creatinine ratio. Venous blood specimens were collected and sent to a central laboratory, where hemoglobin, serum creatinine and cholesterol testing was conducted. Hemoglobin A1c, intact PTH, calcium, and phosphorus testing was also conducted on certain participants.

Clinitek Microalbumin Reagent Strips (Siemens Healthcare Diagnostics Inc., Tarrytown, New York) for urinalysis were used to obtain microalbumin and albumin-to-creatinine ratio results. Siemens' Mul¬tistix 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 meters (LifeScan, Milpitas, California).

Through October 2005, hemoglobin and serum creatinine testing was performed by Satellite Laboratory Ser¬vices (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 to 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, Ab¬bott Park, Illinois), and intact PTH testing was conducted on plasma using Siemens Immulite 2000 (Siemens Healthcare Diagnostics, Deerfield, Illinois) a two-site chemiluminescent enzyme-labeled immunometric assay. The Abbott Architect c8000 (Abbott Laboratories, Abbott Park, Illinois) was used to conduct serum creatinine, calcium, phosphorus, and cholesterol tests (with Arsenazo-III dye for calcium and ammonium molybdate for phosphorus).

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, HDL direct, LDL direct, calcium, and phosphorus. Hemoglobin and hemoglobin A1c were analyzed using 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 present total counts of eligible KEEP participants and show prevalence of CKD, 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, a participant has a physician.

Table 22 reports counts of eligible KEEP participants by NKF affiliate. smoking status, education, insurance status, and whether

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^2, microalbuminuria, CKD, diabetes, hypertension, diabetes and hypertension, obesity, glycemic control, BP control, WHO anemia, and KDOQI anemia. To calculate the odds ratio, we used a set of logistic regressions with all Affiliates as independent variables and Florida as the reference. (The references to NKF Affiliate offices in this report also include the NKF's Division offices.)

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 census division or region. To calculate the odds ratio, we used a set of logistic regressions with all divisions as independent variables and South Atlantic as the reference, or with all census regions as independent variables and South as the reference.

References

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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.