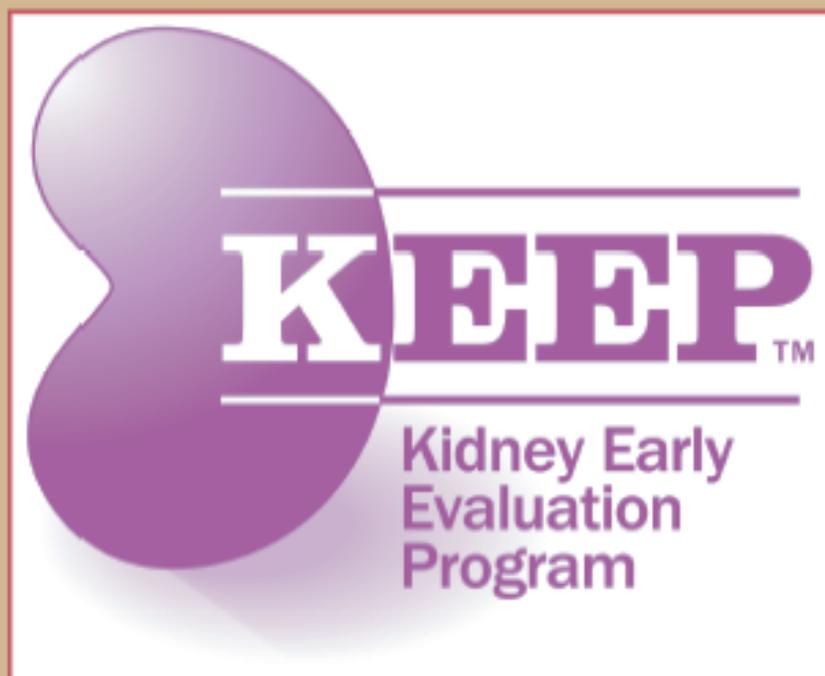


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**American Journal of
Kidney Diseases**



ANNUAL DATA REPORT

**NATIONAL KIDNEY FOUNDATION
KIDNEY EARLY EVALUATION PROGRAM™**



The Official Journal of the
National Kidney Foundation

W. B. Saunders

KEEP



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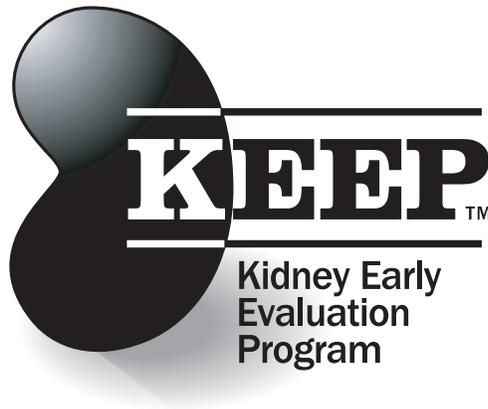
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Kidney Early Evaluation Program

The National Kidney Foundation gratefully acknowledges
the support of our primary sponsor



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Lifescan, Inc., and Ocean Spray Cranberries, Inc. for providing in-kind support.

Chronic kidney disease (CKD) has recently received increased attention as a public health problem. This awareness has been an outgrowth of the ever-increasing numbers of patients entering end-stage renal disease (ESRD) therapy—100,000 new cases in 2002—and the 400,000 prevalent patients now receiving treatment. At current growth rates, the number of treated ESRD patients is projected to reach 650,000 by 2010.

Identifying groups at risk for CKD has been a focus of the National Kidney Foundation's Kidney Disease Outcomes

KEEP

Quality Initiative (NKF K/DOQI), which suggests that eight million Americans have an estimate glomerular filtration rate (eGFR) less than 60 ml/min/1.73 m².

To identify people at risk for CKD, in 1997–1999 the NKF piloted the Kidney Early Evaluation Program (KEEP). Community-based and delivered by local NKF affiliates, the program has reached more than 11,000 people. This first KEEP data report summarizes the findings of this effort to reach and improve the health of people at risk for CKD.

The majority of enrollees were women, minorities, had higher education levels, were insured, and had a primary physician.

More than half of the participants had a history of hypertension, with a comparable amount still having a blood pressure greater or equal to than 140/90 mmHg. Almost a quarter reported having diabetes themselves, and 68 percent reported a family history of the disease. Although only 2–3 percent reported having CKD, 50 percent had evidence of

the disease through estimated glomerular filtration rates (eGFRs) or microalbuminuria.

Participants were more likely than those in the general population to be overweight or obese, and women and minorities the most likely. Those with self-reported CKD were more likely to be overweight or obese than those reporting a history of hypertension or diabetes.

Executive Summary

More than half of the participants had normal blood pressures, as defined by the Joint National Committee of Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). Twenty-nine percent had Stage 1 hypertension, 12 percent Stage 2, and 4 percent Stage 3.

Participants age 60 or older had three times the prevalence of elevated serum creatinine levels than their younger counterparts. For most demographic groups, the Modification of Diet in Renal Disease (MDRD) formula for measuring creatinine clearance resulted in a higher estimate of the number of people with CKD than did the Cockcroft-Gault formula. Estimates of the prevalence of CKD in KEEP participants range from 40 percent in those age 18–30 to 65 percent in those age 75 and above. Systolic blood pressure increased with more advanced stages of CKD, and the prevalence of elevated blood pressure was greater in anemic CKD participants than in those without anemia.

KEEP participants, particularly those with an eGFR <60 ml/min/1.73 m², were more likely to have anemia, as defined by the World Health Organization (WHO), than people in the general population. Diabetic participants with Stage 3 CKD (eGFR 30–<60) were three times more likely to have a hemoglobin less than 11 g/dl.

The KEEP program continues to grow, with more than 22,000 individuals enrolled through August, 2003. An increasing number of NKF affiliates are participating, broadening the geographic scope across the country.

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LIST OF ABBREVIATIONS

BMI	body mass index	MDRD	Modification of Diet in Renal Disease
BSA-CG	body surface area, Cockcroft-Gault method	MEC	mobile examination center
CARE	Computerized Assessment Risk Education	Nat Am	Native American
CDC	Centers for Disease Control & Prevention	NCHS	National Center for Health Statistics
CHAMPVA	Civilian Health and Medical Program of the Department of Veterans Affairs	NHANES III	Third National Health & Nutrition Examination Survey
CHAMPUS	Civilian Health and Medical Program of the United States	NKF	National Kidney Foundation
CKD	chronic kidney disease	NKF K/DOQI	National Kidney Foundation's Kidney Disease Outcomes Quality Initiative
CRP	C-reactive protein levels	NKF KEEP 2.0	National Kidney Foundation's Kidney Early Evaluation Program
DBP	diastolic blood pressure	Non-DM	non-diabetic
DM	diabetic or diabetes	Pac Isl	Pacific Islander
eGFR	estimated glomerular filtration rate	PD	peritoneal dialysis
ESRD	end-stage renal disease	RDBMS	Relational Database Management System
HTN	hypertension	SAF	Standard Analysis File
JNC-VI	National Joint Committee on Prevention, Detection, Evaluation, & Treatment of High Blood Pressure	SBP	systolic blood pressure
KDCC	KEEP Data Coordinating Center	WHO	World Health Organization
KEEP	Kidney Early Evaluation Program	VA	Veterans Administration

In this report we present data from the NKF's KEEP program, a national, community-based health initiative, implemented through NKF affiliates across the country.

More than 340,000 individuals were receiving renal replacement therapy in the United States at the end of 1999, a number projected to double by 2010. Almost half had a primary diagnosis of diabetes mellitus, and more than one-quarter a primary diagnosis of hypertension. Studies have demonstrated effective measures for preventing or at least delaying the progression of kidney disease, and

or more abnormal parameters; in 1998, 423 of 585 (72.3 percent); and in 1999, 392 of 488 (80.3 percent). During the pilot phase urine dipstick tests for microalbuminuria were conducted using Roche's Micral Test strips (Roche Diagnostic Corporation, Indianapolis, IN), and Bayer Diagnostics' Multistix 7 Microalbumin Strips for Urinalysis (Bayer Diagnostics, Tarrytown, NY) were used for blood and leukocyte measures. Plasma glucose testing with capillary blood was performed on LifeScan's One Touch Basic (LifeScan, Milpitas, CA), and serum creatinine testing was performed by Satellite Laboratory Services (Redwood City, California).

CHAPTER ONE

KEEP Program Introduction

decreasing morbidity and mortality. The objective of early diagnosis is to detect asymptomatic disease at a

time when inter-

KEEP pilot program

vention may favorably affect outcome. From 1997 to 1999, with support from Pfizer Inc. (New York, NY), the NKF piloted KEEP, a highly focused screening program adapted from Indiana's Computerized Assessment Risk Education (CARE), which began in 1991 and targeted first-order relatives of dialysis patients.

In 21 U.S. cities, KEEP targeted persons 18 years of age or older with hypertension or diabetes, and first-order relatives of patients with hypertension, diabetes, and kidney disease.

Data were collected on height, weight, blood pressure, age, family history, plasma glucose, and serum creatinine, and on the presence of microalbuminuria, pyuria, and hematuria. Of 889 persons screened in 1997, 635 (71.4 percent) had one

Of the 331 follow-up responses received, 203 people saw a physician within three months of the screening. The data showed not only that targeted screenings are an effective means of identifying persons at increased risk for kidney disease, but that they are effective in motivating persons with abnormal results to seek follow-up care.

KEEP program

Since the launch of the program's second phase in August 2000, with support from Ortho Biotech Products L.P. (Bridgewater, NJ), the NKF has reached 22,000 participants. The data in this report are based on 11,246 participants through October 2002.

KEEP screening programs were carried out by 35 NKF affiliates in 31 states who worked closely with local media—including newspapers, television, and radio stations—to provide community-wide awareness of kidney disease and to conduct recruitment for the KEEP screening programs.

The greatest strength is that it is a free service to the community yet offers extensive information. This is a much needed service. Participants were surprised to get the opportunity to speak with a doctor.

Terry Carney, General
Volunteer Coordinator,
Louisiana

Eligible participants were men or women at least 18 years old, with diabetes or hypertension, or with a first-order relative with diabetes, hypertension, or kidney disease. Because of the high prevalence of individuals meeting eligibility criteria, some affiliates concentrated their recruitment efforts in geographic areas with minority populations. Participants who did not meet the entry criteria but who had an elevated blood pressure measurement were allowed to continue.

Screening data were collected on sociodemographic characteristics and medical history; medication history data were not obtained. Systolic/diastolic blood pressures were measured, and blood and urine specimens were processed for determination of blood glucose, creatinine, hemoglobin, microalbuminuria, hematuria, and pyuria. In addition, eGFR, an indicator of kidney function, was calculated. Abnormal results were not considered diagnostic, but rather an indication of a high risk of health problems that merited further evaluation. Participants with abnormal results were counseled to contact their healthcare providers for follow-up evaluation, and were contacted later by study personnel to ensure this follow-up had occurred. Referrals to local clinics or physicians were provided for individuals without a physician or health insurance, and educational materials about kidney disease, hypertension, and diabetes were provided to all participants.

In September of 2001, microalbumin testing was conducted using Bayer Diagnostics' Clinitek Microalbumin Strips for Urinalysis. The Clinitek 50 Analyzer was utilized to interpret the results for both the Clinitek and Multistix 7 test strips. In 2002 an albumin measurement was added to the creatinine analysis. Blood glucose levels continued to be tested using glucose meters, and Satellite Laboratory Services of Redwood City, California conducted the serum creatinine and hemoglobin testing. Creatinine clearance was calculated using the Cockcroft-Gault formula, but has been recalculated using the MDRD formula for this data report.

The aims of KEEP include using health screenings to identify persons at increased risk for kidney disease, and encouraging at-risk persons to seek further evaluation with appropriate risk management from a health care provider.

KEEP administrative structure and oversight

KEEP is coordinated by five staff members at the national NKF office, and implemented by NKF affiliates across the U.S. The program is overseen by the NKF's KEEP Steering Committee, which has been chaired by John Flack, MD, MPH. This committee sets policies on the review and publication of KEEP data.

The KEEP Data Coordinating Center (KDCC), overseen by Allan Collins, MD, has developed the KEEP Information Management System to manage survey data in a Relational Database Management System (RDBMS) using the Microsoft Access software development tool. The KDCC also provides analytical services and generates Standard Analysis Files (SAFs) for NKF, manages data confidentiality, and is responsible for producing the KEEP annual report. Central to this

STEERING COMMITTEE

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National Kidney Foundation



years report are contributions from Drs. John Flack, Wendy Brown, Rosalind Peters, and Peter McCullough, Monica Gannon and Gigi Politoski, and participating NKF affiliates.

Database system, management, and quality control

To ensure the confidentiality of each participant, all participant-identifiable data elements are removed and replaced by an internally generated identification (ID) number. Separate standard analysis data sets, linked by the ID number, are maintained for the follow-up and further follow-up forms. Production of the standard analysis data set incorporates data validation and integrity checks to assure that all variables have valid data values based on pre-defined value ranges or data categories in the DATA FORMAT file. No participant record is dropped because of incomplete and/or invalid data.

Expansion of the KEEP program

To oversee the continued growth of KEEP, the NKF will appoint a Publication Subcommittee, responsible for reviewing collected information. The KEEP Steering Committee will report twice a year to an External Advisory Committee, which will be chaired by the President-Elect of the NKF, and will report to the President and Scientific Advisory Board of the NKF.

Demographics

Despite geographic variations in affiliate activity, the following statistics indicate that the KEEP targeting strategy was

effective in reaching a population at risk for developing kidney disease.

A total of 11,246 persons were eligible to participate in KEEP. The majority (56.3 percent; $n = 6,336$) were recruited from NKF affiliate divisions in the Atlantic region of the country, with a third of the participants from the South Atlantic area. The West Coast area had the fewest participants (9.6 percent; $n = 1,077$; Figures 1.1–4).

There was a skewed gender distribution, with twice as many women (67.3 percent; $n = 7,569$) as men (32.7 percent; $n = 3,677$) participating in the study. More than one-third of the participants (34.3 percent) were middle-aged adults between 46 and 60 years of age, with both a mean and median age of 52 years. Well more than half (58.8 percent) were between 46 and 75 years of age. The percentage of KEEP participants in this age range (58.8 percent) was more than 70 percent higher than the percentage of the general population in this range (33.8 percent), as reported in results of the National Health and Nutrition Examination Survey III (NHANES III, 1988–1994; Figures 1.5–6).

Close to half of KEEP participants were black (46.2 percent), and 36.8 percent were white. Native Americans comprised 5.7 percent of the population, 3.3 percent were Asian Americans, and 1.6 percent were Pacific Islanders. Ten percent identified themselves as being of Hispanic origin ($n = 1,133$). Compared to the NHANES III population, the KEEP cohort had almost four times as many black and “other race” participants, while its Hispanic composition was similar to that of the general population (Figure 1.7).

Overall, then, the KEEP population showed a skewed age distribution, with participants being older than people in the general population. This is consistent, however, with the age at which the comorbidities associated with kidney disease are most prevalent. The racial composition of KEEP participants reflects the program’s attempts to recruit African Americans, who are known to bear a disproportionate burden of both diabetes and hypertension, the top two causes of kidney disease. Native Americans also were heavily recruited, due to the large numbers who develop diabetes. The skewed gender distribution among KEEP participants may reflect the reluctance of men to engage in health seeking behaviors, and

indicate the need for increased emphasis on recruiting men into future KEEP programs.

Education

The majority of KEEP participants were well educated: 84 percent had at least a high school education, and 30.2 percent had a bachelor’s degree or higher. There were no significant differences in level of education by gender. Compared to the national data, KEEP participants were less likely to have completed high school but were 50 percent more likely to have a bachelor’s degree or higher. Black participants were more than three times as likely to have completed a college degree or higher than their counterparts in the general population, and Hispanic participants were more than two and a half times as likely to have a college education (Figures 1.8–12).

Health insurance

The great majority (84 percent) of KEEP participants reported having health insurance. The most commonly reported coverage was through Medicare (21.5 percent), consistent with the age distribution of the KEEP cohort, in which nearly one-third (31.6 percent) of participants were over 60 years of age. Compared to NHANES III data, slightly more KEEP participants (4.7 percent) were uninsured, with the difference noted among persons in the “other race” category. The level of insurance coverage for white and black participants was nearly identical to that based on NHANES III estimates. The geographic distribution of insurance coverage was similar between KEEP participants and the general population, and the youngest participants were the most likely to be uninsured (Figures 1.13–20).

Access to medical care

In addition to having insurance coverage, the majority of KEEP participants (88.8 percent) also reported having a private physician from whom to seek medical care. Most participants reported being seen by a family practice physician (59.3 percent male, 63.9 percent female), with 14–17 percent receiving care from internists. Although 264 participants reported a history of kidney disease, less than half of that number ($n = 107$) reported seeing a nephrologist for care, and approximately two percent of all participants reported visits to an endocrinologist (Figures 1.21–24).

Figure 1.1 · rank order of NKF affiliates, by percent of participants in the KEEP study

KEEP: n=11,246

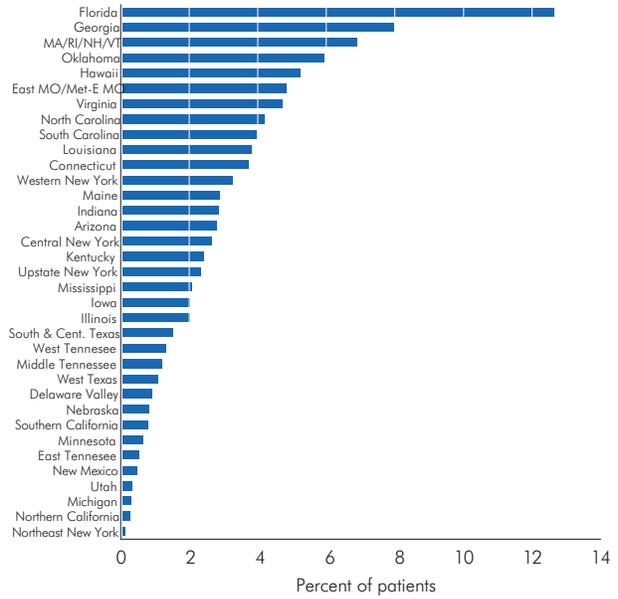


Figure 1.2 · percent distribution of KEEP participants, by U.S. Census division

KEEP: n=11,246 (values in parentheses represent the means of the quartiles)

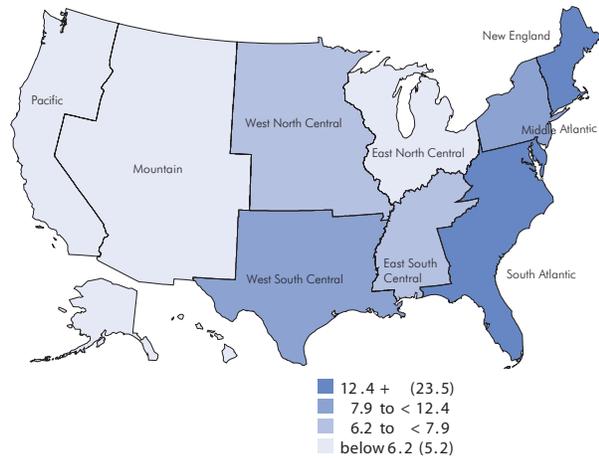


Figure 1.3 · percent distribution of KEEP participants, by state

KEEP: n=11,246 (values in parentheses represent the means of the quintiles)

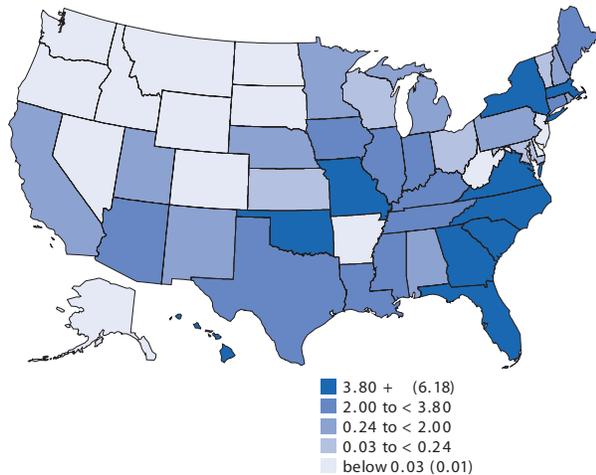


Figure 1.4 · rank order of participants, by U.S. census division

KEEP: n=11,246

Divisions
 SA: South Atlantic
 NE: New England
 WSC: West South Central
 MA: Middle Atlantic
 ESC: East South Central
 WNC: West North Central
 ENC: East North Central
 PAC: Pacific
 MTN: Mountain

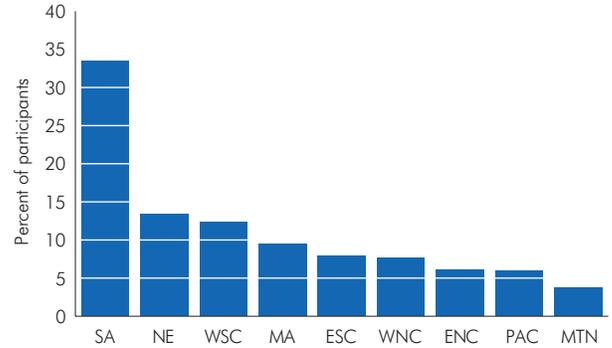


Figure 1.5 · percent distribution of KEEP & NHANES III participants, by U.S. census region

KEEP: n=11,246, NHANES III: n=19,618

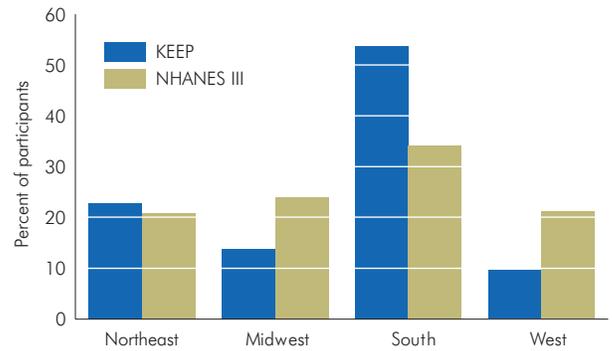


Figure 1.6 · percent distribution of KEEP & NHANES III participants, by age & gender

KEEP: n=11,246, NHANES III: n=19,618

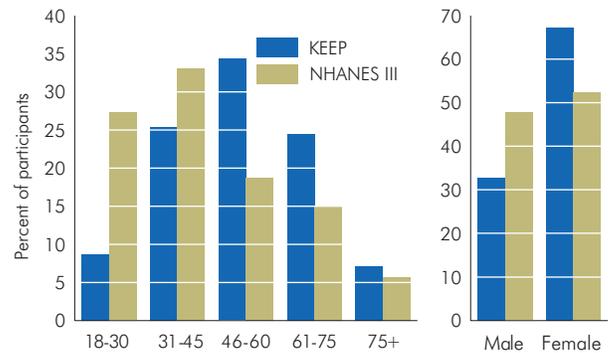
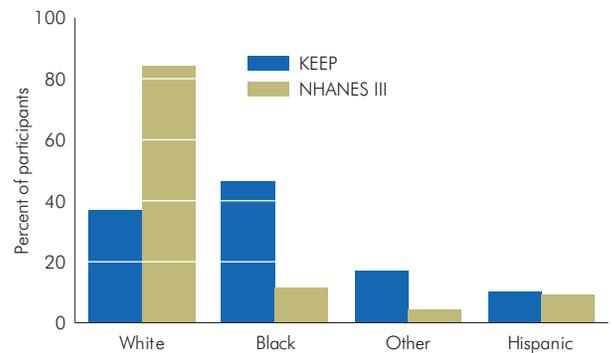


Figure 1.7 · percent distribution of KEEP & NHANES III participants, by race/ethnicity

KEEP: n=10,907, NHANES III: n=19,618; excludes participants with unknown or missing race; race & Hispanic ethnicity are not mutually exclusive



EDUCATION

Figure 1.8 · percent distribution of KEEP & NHANES III participants, by educational status

KEEP: n=11,097, NHANES III: n=19,401; excludes participants with missing educational status

Educational status

GSL: Grade school or less
 SHS: Some high school
 HSG: High school graduate
 SC: Some college
 CG: College graduate
 PG: Post-graduate

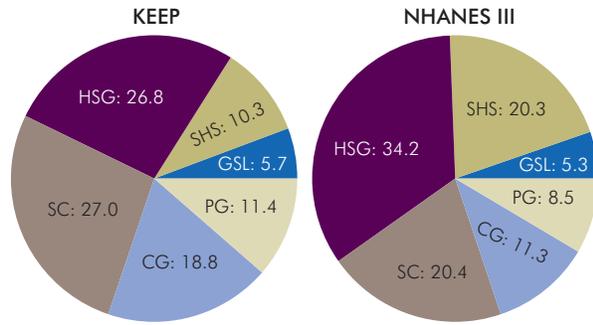


Figure 1.9 · percent distribution of KEEP & NHANES III participants, by age & educational status

KEEP: n=11,097, NHANES III: 19,401

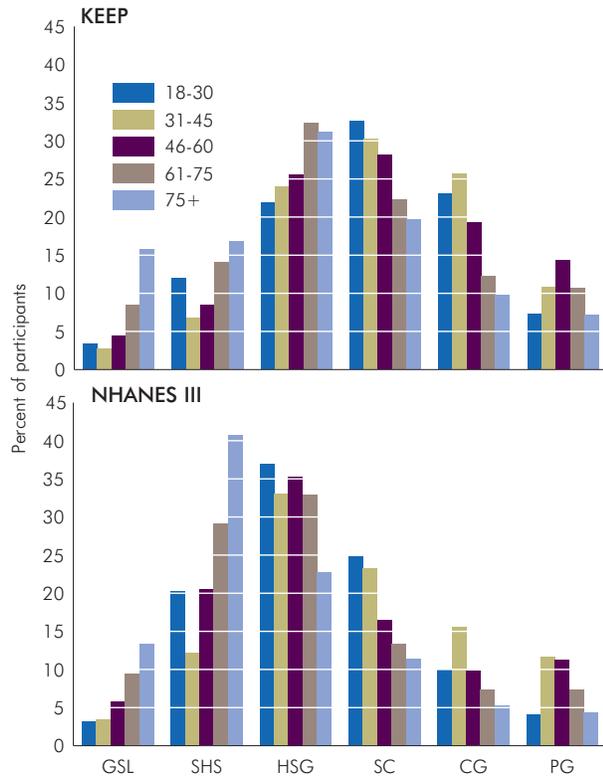


Figure 1.10 · percent distribution of KEEP & NHANES III participants, by gender & educational status

KEEP: n=11,097, NHANES III: n=19,401

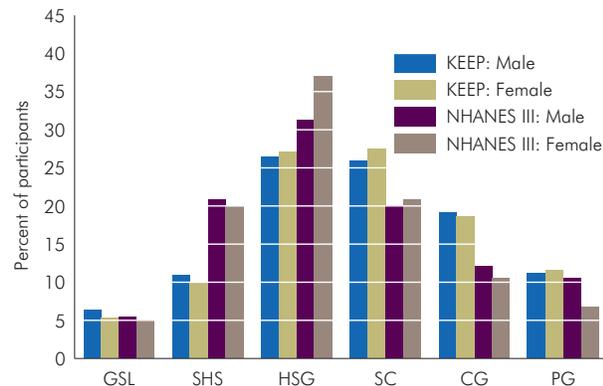


Figure 1.11 · percent distribution of KEEP & NHANES III participants, by race & educational status

KEEP: n=10,790, NHANES III: n=19,401; excludes participants with missing race or missing educational status; race & Hispanic ethnicity are not mutually exclusive

Educational status
 GSL: Grade school or less
 SHS: Some high school
 HSG: High school graduate
 SC: Some college
 CG: College graduate
 PG: Post-graduate

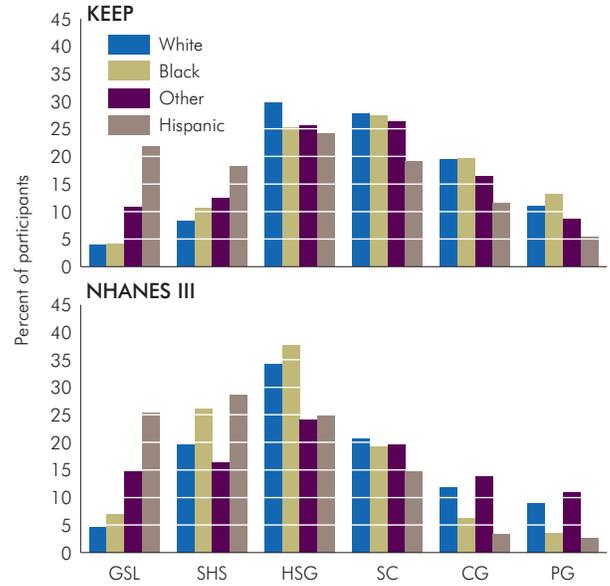
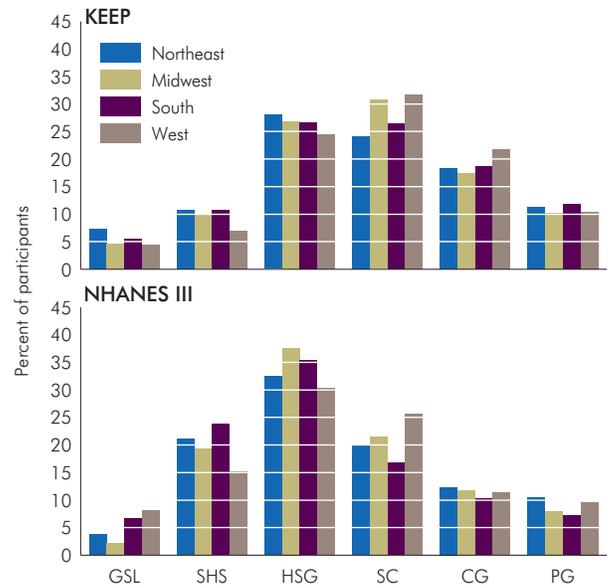


Figure 1.12 · percent distribution of KEEP & NHANES III participants, by U.S census region & educational status

KEEP: n=11,097, NHANES III: n=19,401; excludes participants with missing educational status



**INSURANCE
 COVERAGE**

Figure 1.13 · percent distribution of KEEP & NHANES III participants with insurance, by age

KEEP: n= 10,768, NHANES III: n=18,770; excludes missing or unknown insurance status

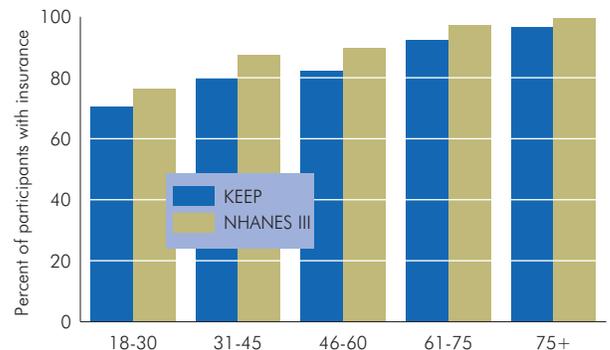


Figure 1.14 · percent distribution of KEEP & NHANES III participants with insurance, by race/ethnicity

KEEP: n=10,445, NHANES III: n=18,770; excludes participants with unknown or missing race or insurance status; race & Hispanic ethnicity are not mutually exclusive

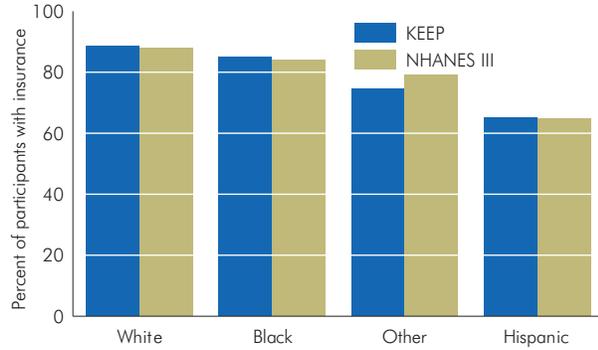


Figure 1.15 · percent distribution of KEEP & NHANES III participants with insurance, by region

KEEP: n=10,768, NHANES III: n=18,770; excludes participants with unknown or missing insurance status

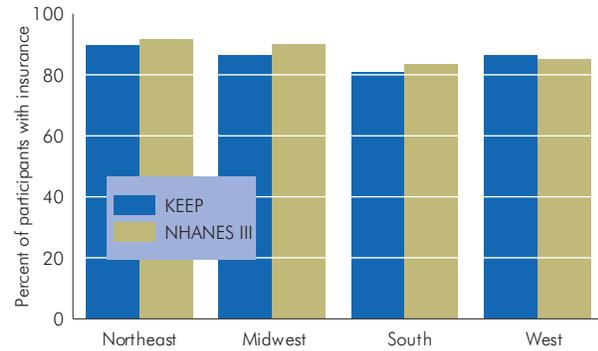


Figure 1.16 · percent distribution of KEEP participants, by type of insurance

KEEP: n=11,246

Insurance coverage
 M/care: Medicare
 M & M: Medicare & Medicaid
 M w/oth: Medicare with other insurance
 Non-M/care: Non-Medicare
 Unk/M: Unknown or missing

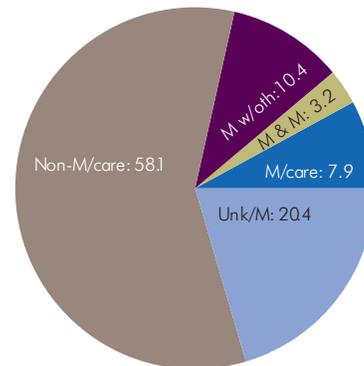


Figure 1.17 · percent distribution of KEEP participants, by age & type of insurance

KEEP: n=11,246

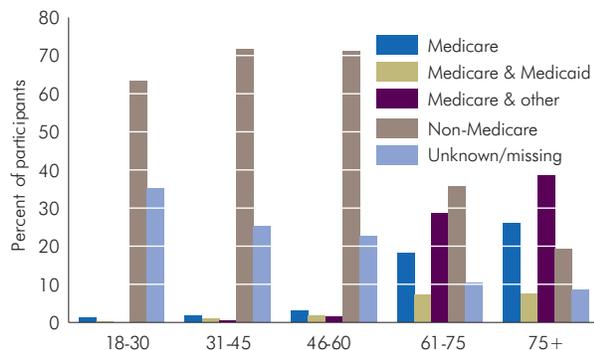


Figure 1.18 · percent distribution of KEEP participants, by gender & type of insurance

KEEP: n = 1,246

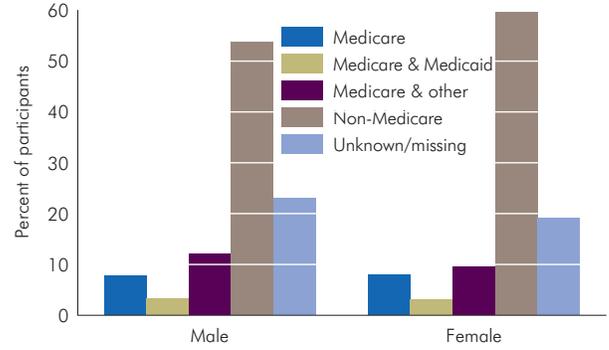


Figure 1.19 · percent distribution of KEEP participants, by race/ethnicity & type of insurance

KEEP: n=10,907, excludes participants with unknown or missing race; race & Hispanic ethnicity are not mutually exclusive

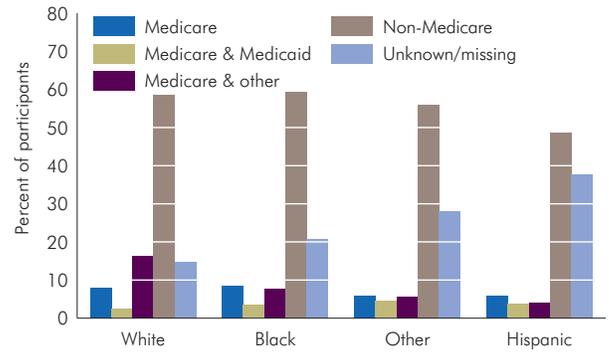
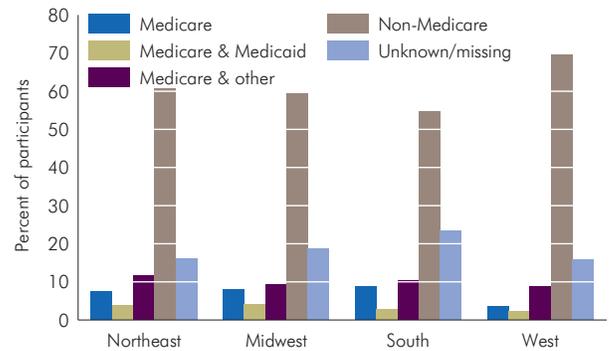


Figure 1.20 · percent distribution of KEEP participants, by U.S. census region & type of insurance

KEEP: n = 1,246



ACCESS TO MEDICAL CARE

Figure 1.21 · percent distribution of KEEP participants, by gender, primary physician & specialty physician

participants can have access to more than one physician specialty

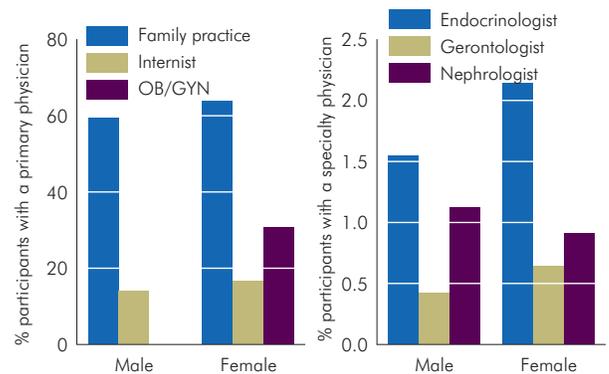


Figure 1.22 · percent distribution of KEEP participants with a physician, by age & gender

KEEP: n=10,933, excludes participants who did not answer this question

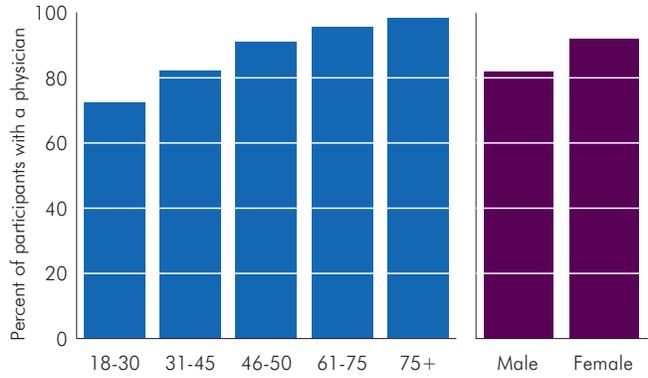


Figure 1.23 · percent distribution of KEEP participants with a physician, by race/ethnicity

KEEP: n=10,606, excludes participants who did not answer this question & those with missing race; race & Hispanic ethnicity are not mutually exclusive

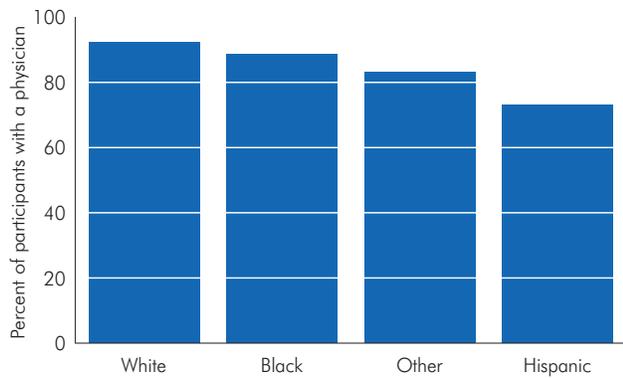
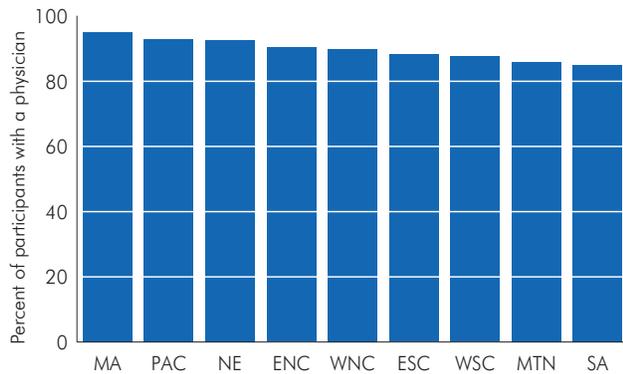


Figure 1.24 · rank order of participants with a physician, by U.S. census division

KEEP: n=10,933, excludes participants who did not answer this question

Divisions
 MA: Middle Atlantic
 PAC: Pacific
 NE: North East
 ENC: East North Central
 WNC: West North Central
 ESC: East South Central
 WSC: West South Central
 MTN: Mountain
 SA: South Atlantic



CHAPTER



SUMMARY

Figure 1.1 • The Florida and Georgia KEEP affiliates had the greatest proportion of study participants.

Figure 1.2 • The majority of KEEP participants resided in affiliate divisions along the Atlantic region of the country, with a third residing in the South Atlantic division.

Figure 1.5 • The South Atlantic Division had the greatest proportion of participants in both the KEEP and NHANES III studies; the West Coast had the fewest KEEP participants at 9.6 percent.

Figure 1.6 • KEEP participants tended to be older than their NHANES III counterparts, and there were more females than males in each study population.

Figure 1.7 • The proportion of white participants in the NHANES III population was more than twice that of whites in the KEEP population.

Figure 1.8 • The proportion of KEEP and NHANES III participants who were at least high school graduates was 84 and 74.4 percent, respectively.

Figure 1.10 • The educational status of participants was similar for males and females in both the KEEP and NHANES III populations.

Figure 1.11 • The proportion of KEEP participants with a college degree was similar for whites and blacks, while in the NHANES III population, whites and individuals of “other” races were the most likely to have a college degree.

Figure 1.13 • The proportion of both KEEP and NHANES III participants with insurance increased with increasing age.

Figure 1.16 • Over 58 percent of KEEP participants had an insurance carrier other than Medicare.

Figure 1.19 • Whites and blacks represented the highest proportions of KEEP participants with a non-Medicare insurance carrier.

Figure 1.21 • Over 59 percent of males and 64 percent of females in the KEEP population had a family practice practitioner as their primary physician.

Figure 1.24 • The Middle Atlantic division had the greatest proportion of KEEP participants with a physician (95.1 percent) while the lowest proportion occurred in the South Atlantic division (85.1 percent).

Introduction

The KEEP screening programs were undertaken by NKF to identify people at risk for, or in the early stages of, kidney disease. Early identification is vital if prompt treatment is to be instituted to reverse, halt, or at least slow the progression of kidney disease, which has become a national epidemic. The KEEP program specifically targeted high-risk groups, including persons with diabetes or hypertension, or with family members who have diabetes, hypertension, or kidney disease. The data presented show that the targeting efforts have been successful. As a result, the KEEP cohort

mass index (BMI). Obesity was strongly correlated with hypertension and diabetes, and even more compelling is the rate of obesity among persons with evidence of chronic kidney disease or damage. While only 2.3 percent of participants reported a history of CKD, almost half were found to have laboratory evidence of kidney disease or damage.

The prevalence of both diabetes and hypertension doubled between the 18–30 and 31–45 year-old age categories, suggesting that more attention should be given to young people to prevent two of the most common precursors of CKD.

CHAPTER TWO

Participant Characteristics

has a skewed distribution in relation to the age and race of its participants, with more older and black subjects being recruited. In

addition, KEEP was comprised of a sample of volunteer subjects, which resulted in an uneven gender distribution and oversampling of highly educated persons.

Despite the KEEP population being comprised of highly educated, well-insured participants with access to medical care, there were a number of significant health problems noted. More than half of all participants reported a history of hypertension, and almost that many had measured blood pressures greater than 140/90 mmHg. Close to half of the persons reporting a history of diabetes did not have adequate blood pressure control, as their pressures also were greater than 140/90 mmHg—a level considerably higher than target blood pressure levels of <130/80 mmHg.

Obesity was a very significant problem, with three-quarters of participants being above normal weight based on body

The KEEP data reveal the benefits of targeted screening programs, underscore the lack of control of key risk factors for kidney disease, and identify the need for more intensive prevention efforts to confront the escalating rate of end-stage renal disease in this country.

Prevalence of risk factors for kidney disease

This chapter presents summary statistics regarding the disease history of persons participating in the KEEP program from its inception in August 2000 until October 2002.

Almost a quarter (24.3 percent) of KEEP participants reported a history of diabetes; half (51.5 percent) reported a history of hypertension, and 16 percent (n = 1,824) reported a combined history of both hypertension and diabetes.

Diabetes

The prevalence of diabetes in the KEEP population doubled between the 18–30 and 31–45 year-old age

If it had not been for the screening, I would have been unaware of my medical problems.

Alice McAllister,
Florida;
October 2002

categories (6.5 percent to 13.8 percent), and almost doubled again between the 31–45 and 46–60 year-old groups (13.8 to 25.3 percent) and while the proportions of diabetics in the NHANES III population are noticeably lower the percent increases between age categories are similar. By race, KEEP individuals of other races (which includes Native Americans) had the highest rate of diabetes at 30 percent. The prevalence of self-reported diabetes in the KEEP cohort was more than four and a half times higher than in the general population, reflecting the targeting strategy of the KEEP program (Figures 2.1–2).

There also was a significant rise in the number of diabetics within each classification stage defined by JNC VI. Diabetic participants were 30 percent more likely to have elevated pressures than non-diabetics (56.4 percent compared to 42.8 percent). Compared to non-diabetic participants, diabetics were 21 percent more likely to have a systolic blood pressure (SBP) or diastolic blood pressure (DBP) classified as Stage 1 (140–159 SBP; 90–99 DBP); 45 percent more likely to be classified as Stage 2 (160–179 SBP; 100–109 DBP); and 76 percent more likely to be classified as Stage 3 (≥ 180 SBP; ≥ 110 DBP; Figure 2.3).

The number of KEEP diabetics with elevated pressures also was significantly greater than the NHANES III estimates. Compared to diabetics in the NHANES III cohort, diabetic KEEP participants were 40 percent more likely to have Stage 1 blood pressures; 60 percent more likely to have Stage 2 pressures; and more than one and a half times more likely to have Stage 3 pressures. Even among non-diabetic participants, KEEP subjects were more likely to have elevated blood pressures compared to the non-diabetics sampled in NHANES III (Figure 2.3).

Within the KEEP cohort, black diabetic participants had the highest prevalence of increased blood pressures, and were almost 7.7 percent more likely to have elevated pressures than white participants (Figure 2.4).

Hypertension

The prevalence of self-reported hypertension in the KEEP cohort was significantly higher than expected based on rates in the general population. More than 40 percent of KEEP participants of “other” races, and more than half of all men, women, whites, and blacks, reported a history of hypertension. It should be noted, however, that hypertension was one of the eligibility criteria.

As expected, the prevalence of both self-reported and measured high blood pressure increased with advancing age. The rate of elevated pressures doubled between the first and second age categories (18–30 and 31–45 years), with the rate of increase declining with each older age group (Figure 2.6).

The prevalence of elevated blood pressures ($\geq 140/90$ mmHg), as measured during the screening visits, ranged from 36 to 50 percent among all racial and ethnic groups and among both genders. Hispanic participants were least

likely to have elevated blood pressures, while black subjects had the highest prevalence in each of the JNC VI hypertension stages. The prevalence of elevated blood pressure in the KEEP study versus the general population was almost 132 percent higher for blacks, and 151 percent higher for whites (Figures 2.8–9).

Evaluation of measured blood pressures as compared to self-reported history of hypertension suggests that only a small percentage of participants with a positive history had their blood pressure controlled to within normal limits. Blacks had the smallest difference between the prevalence of self-reported hypertension (54.5 percent) and the prevalence of measured high blood pressure (50.4 percent), suggesting less effective blood pressure control compared to other demographic groups (Figures 2.10–11).

Obesity

Obesity is a major risk factor for both diabetes and hypertension, the primary precursors of CKD, as well as an independent risk factor for CKD itself. Based on calculated BMI, the majority (78.4 percent) of KEEP participants were overweight (BMI 25.0–29.9) or obese (BMI >30.0), with 8.6 percent ($n = 957$) classified as extremely obese (BMI > 40) (Figure 2.12).

Blacks and Native Americans were most likely to be extremely obese, both at a rate almost 50 percent higher than in white participants. Women were two and a half times more likely to be extremely obese than men. Compared to the general population, KEEP participants were almost twice as likely to be obese, and three times more likely to be extremely obese. The gender difference in extreme obesity noted among KEEP participants is similar to that in the NHANES III data (Figures 2.13–15).

Within KEEP, there was a strong relationship between BMI and both diabetes and hypertension. Extremely obese participants were 70 percent more likely to have a history of hypertension, and 200 percent more likely to have a history of diabetes, than their normal-weight counterparts. Among extremely obese participants the prevalence of hypertension was two and a half times more common than the prevalence of diabetes (Figures 2.16–17).

Smoking

Smoking is a lifestyle behavior associated with complications of both diabetes and hypertension, and in this study is also associated with kidney disease. Almost half of KEEP participants had a smoking history: 14.0 percent ($n = 1,475/10,536$) were current smokers, and 31.3 percent ($n = 3,302/10,536$) used to smoke (Figure 2.18). Of the current smokers, 23.6 percent had diabetes, 45 percent had hypertension, and 46 percent showed evidence of chronic kidney disease (Figures 2.20–22).

CKD

Although only 2.3 percent ($n = 264$) of KEEP participants reported a history of kidney disease, nearly half (47.4 per-

cent) of those with laboratory data were found to have evidence of kidney disease or damage. A determination of CKD was based on either a calculated eGFR of <60 ml/min/1.73m², or an eGFR ≥ 60 ml/min/1.73 m² accompanied by evidence of microalbuminuria (Figure 2.23).

The NKF has developed a classification system for determining the stage of kidney disease. Based on these guidelines, KEEP participants fell into the following CKD categories (based on the total number of participants with lab values available, n =10,651). According to K/DOQI, persons with eGFRs greater than 90 ml/min/1.73 m² may be “at risk,” depending on other health conditions (e.g. diabetes or hypertension) or lifestyle behaviors. Persons are considered to be in Stage 1 if eGFR ≥ 90 ml/min/1.73m² but there is evidence of kidney damage based on the presence of microalbuminuria; Stage 2 if there is evidence of kidney damage (microalbuminuria) plus mild decrease in kidney function (eGFR 60–89 ml/min/1.73 m²); Stage 3 if eGFR is between 30–59 ml/min/1.73 m²; Stage 4 if eGFR is between 15–29 ml/min/1.73 m²; and Stage 5 if eGFR <15 ml/min/1.73 m² or the person is on dialysis.

Of all KEEP participants with evidence of CKD, 67.4 percent were female, almost half were black (47.9 percent) and over a third were white. Within racial and ethnic groups, the distribution of CKD was similar among most KEEP groups,

ranging from 44.2 percent among white participants to 50.0 percent for blacks, with Hispanics having a prevalence of 46.3 percent (Figure 2.24–25).

The majority of participants found to have CKD were located in the South (52.8 percent), followed by the Northeast (23.1 percent), which reflects the regional distribution of the KEEP population. Within regions there was a fairly even distribution of CKD prevalence, with only a slight increase in the western region compared to the rest of the country; rates ranged from 46.6 to 50.0 percent. The regional distribution of CKD reflected the regional distribution of key risk factors for the disease (Figure 2.26).

There were racial and ethnic differences noted in the Stages of CKD. Blacks were twice as likely to be identified in Stage 1 compared to whites, while whites had the highest prevalence of subjects identified in Stage 3 (Figure 2.27).

Family history and risk factors

The proportions of patients and associated risk factors were distributed evenly within each U.S census region. Participants in the South were 2–4 times more likely to have either CKD or a risk factor for CKD (diabetes, hypertension, obesity, or a history of smoking); a family history of diabetes, hypertension, or CKD was not directly associated with the eventual development of these conditions (Figures 2.28–31).

HISTORY OF
DIABETES

Figure 2.1 · percent distribution of KEEP & NHANES III participants with self-reported diabetes, by age & gender

KEEP: n=11,062, total reported diabetics = 2,690, NHANES III: n=19,593; excludes participants without a reported diabetic status

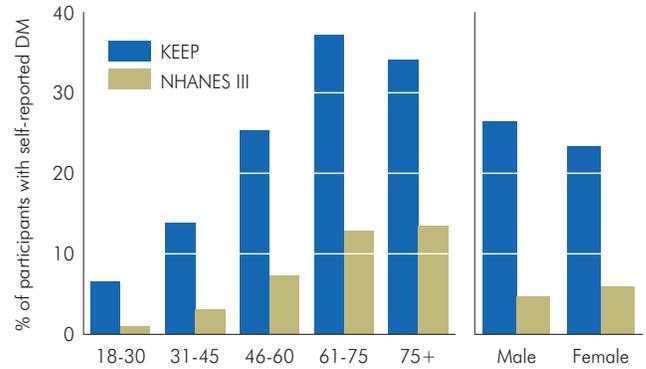


Figure 2.2 · percent distribution of KEEP & NHANES III participants with self-reported diabetes, by race/ethnicity

KEEP: n=11,062, total reported diabetics = 2,690, NHANES III: n=19,593; excludes participants with missing diabetic status; race & Hispanic ethnicity are not mutually exclusive

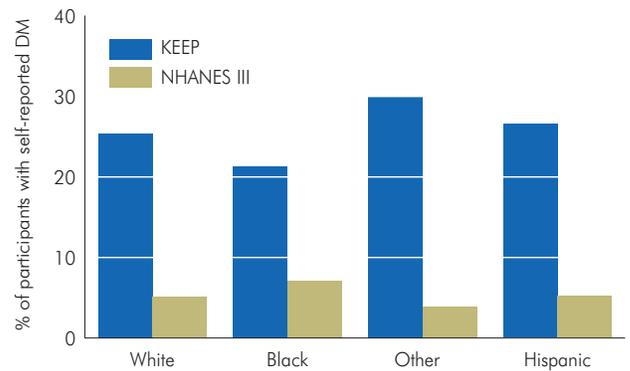


Figure 2.3 · percent distribution of KEEP & NHANES III participants by measured blood pressure & self-reported diabetes status

KEEP: n=10,883, NHANES III: n=19,216; excludes participants with missing diabetic status or blood pressure values; hypertension status based on JNC VI definition

JNC VI hypertension
 Stage I: systolic 140–159 or diastolic 90–99
 Stage II: systolic 160–179 or diastolic 100–109
 Stage III: systolic ≥180 or diastolic ≥110

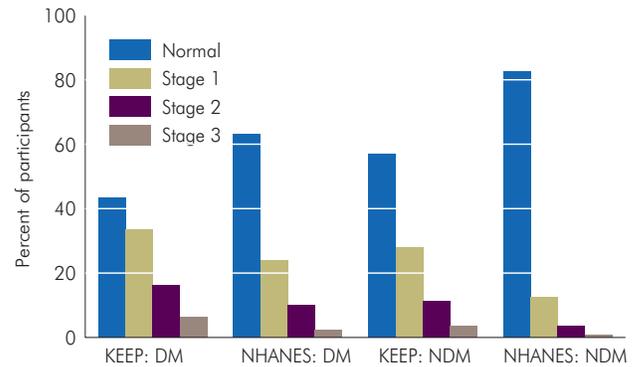
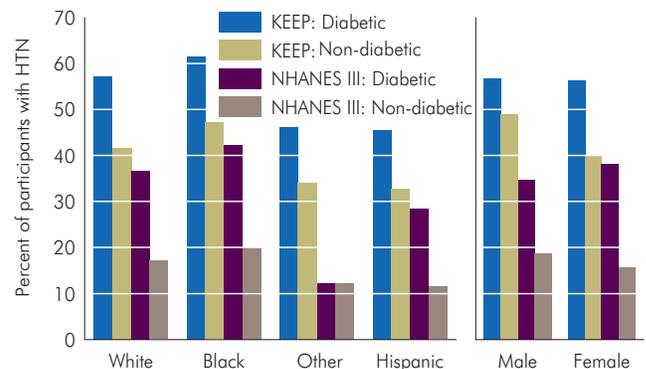


Figure 2.4 · percent distribution of KEEP & NHANES III participants with an elevated blood pressure (≥140/90), by race/ethnicity, gender, & self-reported diabetic status

KEEP: race, n=10,557, gender n=10,883, NHANES III: n=19,216; excludes participants with missing race, blood pressure values, or diabetic status; race & Hispanic ethnicity are not mutually exclusive



HISTORY OF HYPERTENSION

Figure 2.5 · percent distribution of KEEP & NHANES III participants with self-reported diabetes, by measured blood pressure

KEEP: n=10,833 total, 2,659 with self-reported diabetes; NHANES III: n=19,216; excludes participants with missing blood pressure values or diabetic status; hypertension based on JNC VI definition

JNC VI hypertension

Stage I: systolic 140–159 or diastolic 90–99
 Stage II: systolic 160–179 or diastolic 100–109
 Stage III: systolic ≥180 or diastolic ≥110

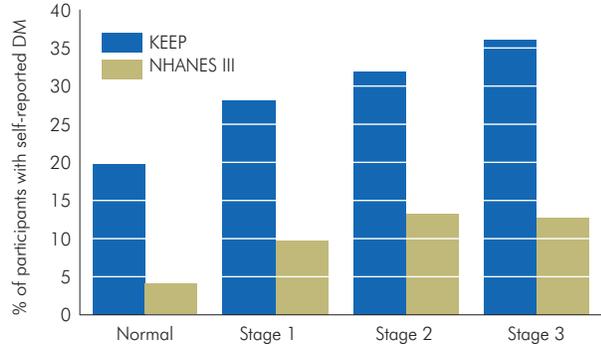


Figure 2.6 · percent distribution of KEEP & NHANES III participants with self-reported hypertension, by age & gender

KEEP: n=11,131 total, 5,732 with hypertension; NHANES III n=19,426; excludes participants with missing hypertension status

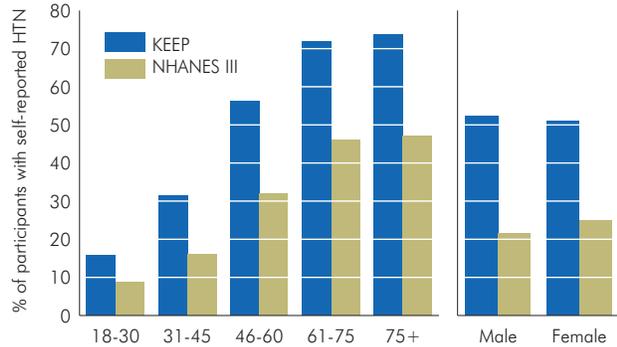


Figure 2.7 · percent distribution of KEEP & NHANES III participants with self-reported hypertension, by race/ethnicity

KEEP: n=10,802 total, 5,576 with self-reported hypertension; NHANES III: 19,426; excludes participants with missing race or hypertension status; race & Hispanic ethnicity are not mutually exclusive

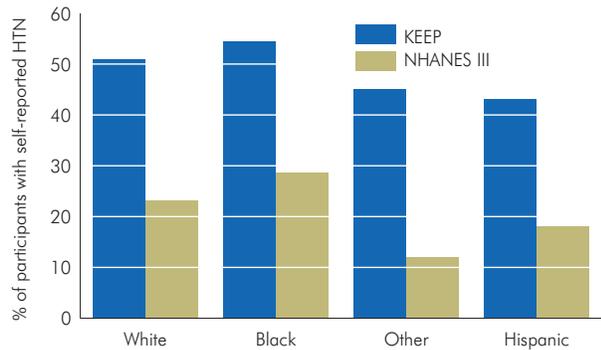


Figure 2.8 · percent distribution of KEEP participants with measured blood pressure, by gender

Keep: n=11,064; excludes participants with missing blood pressure values; hypertension based on JNV VI definition

JNC VI hypertension

Stage I: systolic 140–159 or diastolic 90–99
 Stage II: systolic 160–179 or diastolic 100–109
 Stage III: systolic ≥180 or diastolic ≥110

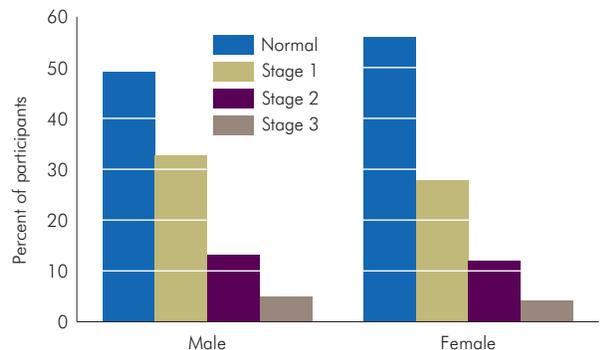


Figure 2.9 · percent distribution of KEEP & NHANES III participants with measured blood pressure, by race/ethnicity

KEEP: n= 10,557, NHANES III: n=19,239; excludes participants with missing blood pressure values or unknown or missing race; race & Hispanic ethnicity are not mutually exclusive; hypertension based on JNC VI definition

JNC VI hypertension
 Stage I: systolic 140–159 or diastolic 90–99
 Stage II: systolic 160–179 or diastolic 100–109
 Stage III: systolic ≥180 or diastolic ≥110

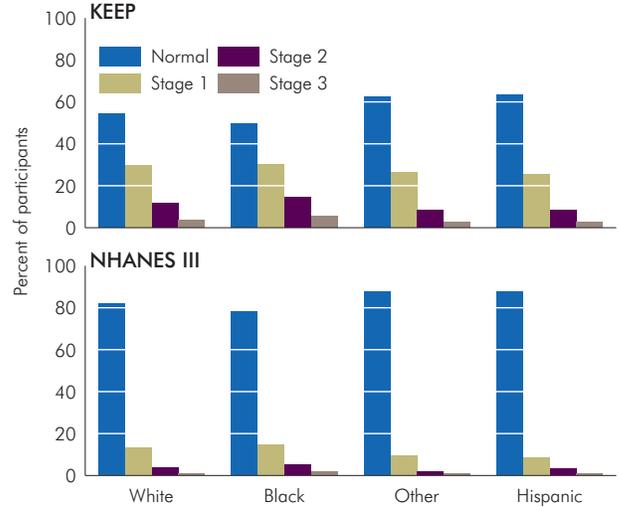


Figure 2.10 · percent distribution of KEEP participants with self-reported hypertension compared to measured blood pressure (≥140/90), by gender

KEEP: total for reported hypertension, n=11,131, total for measured blood pressure, n=11,064

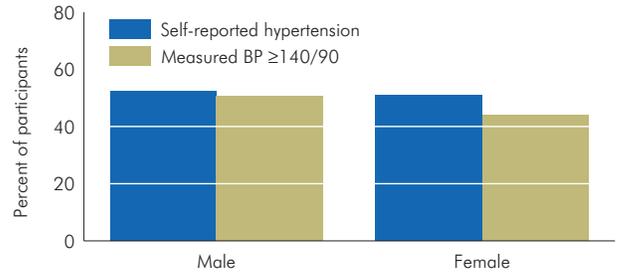
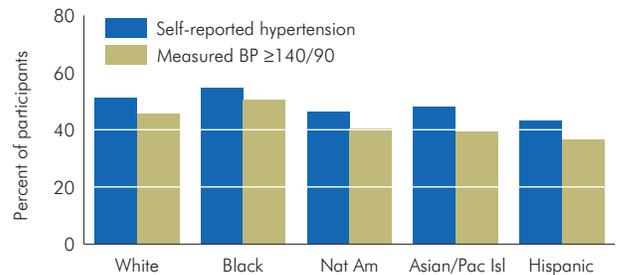


Figure 2.11 · percent distribution of KEEP participants with self-reported hypertension compared to measured blood pressure (≥140/90), by race/ethnicity

KEEP: n=11,131, total for reported hypertension, n=11,064, total for measured blood pressure; race & Hispanic ethnicity are not mutually exclusive



HISTORY OF OBESITY

Figure 2.12 · percent distribution of KEEP & NHANES III participants, by BMI

KEEP: n=11,122, NHANES III: n=17,689; excludes participants with missing BMI values

BMI
 BMI < 18.5: UW: Underweight
 BMI 18.5–24.9: N: Normal
 BMI 25–29.9: OW: Overweight
 BMI 30–39.9: O: Obese
 BMI ≥40: EO: Extremely obese

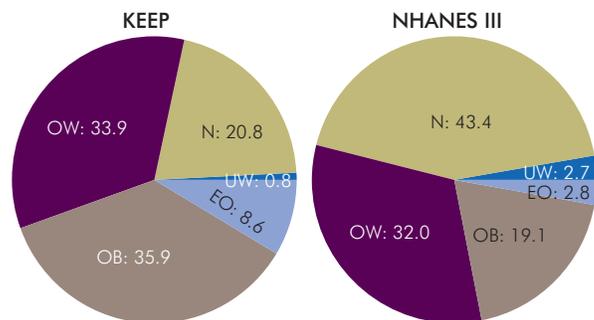


Figure 2.13 · percent distribution of KEEP & NHANES III participants, by gender & BMI

KEEP: n=11,122, NHANES III: n=17,689; excludes participants with missing BMI

BMI
 BMI < 18.5: Underweight
 BMI 18.5–24.9: Normal
 BMI 25–29.9: Overweight
 BMI 30–39.9: Obese
 BMI ≥40: Extremely obese

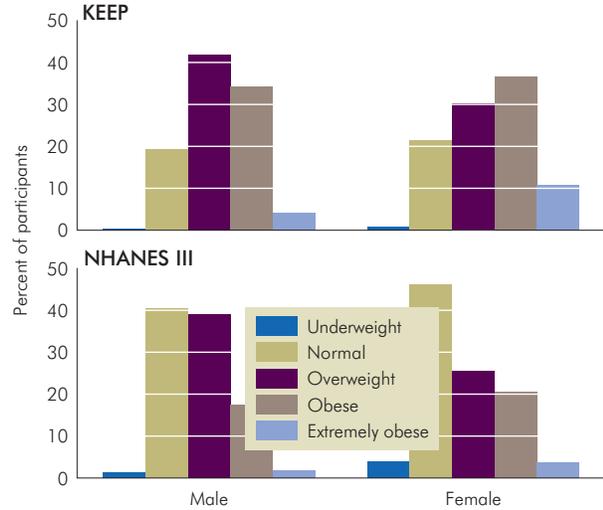


Figure 2.14 · percent distribution of KEEP & NHANES III participants, by race/ethnicity & BMI

KEEP: race, n=10,797, NHANES III: n=17,689; excludes participants with missing BMI value or race; race & Hispanic ethnicity are not mutually exclusive

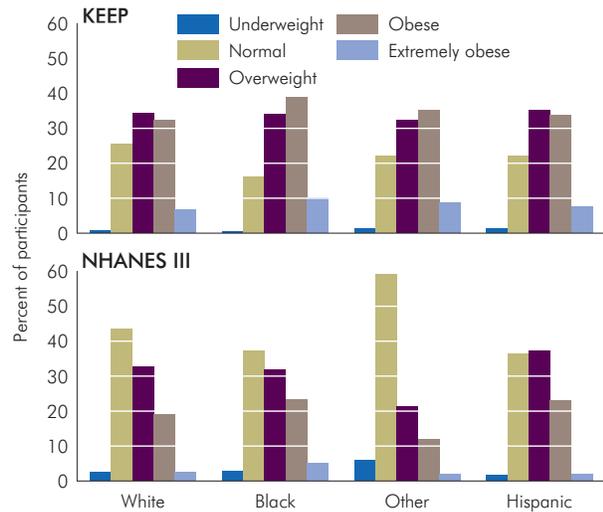


Figure 2.15 · distribution of KEEP & NHANES III participants, by U.S. census region & BMI

KEEP: n=11,122, NHANES III: n=17,689; excludes participants with missing BMI value

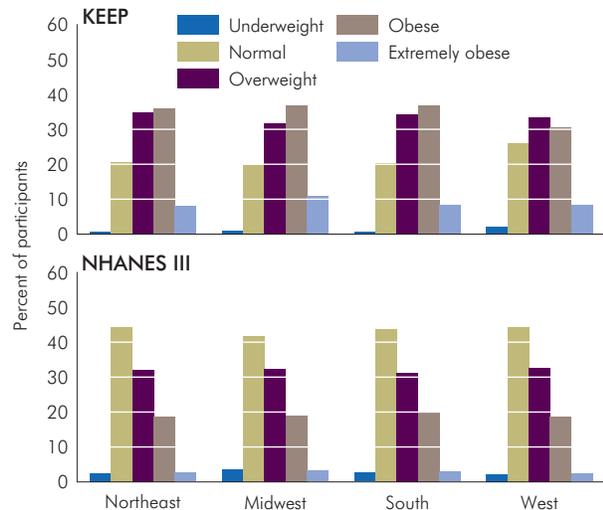


Figure 2.16 · percent distribution of KEEP participants with self-reported diabetes or hypertension, by BMI

KEEP: for diabetes, n=10,942 total, 2,657 with self-reported diabetes; for hypertension, n=11,011 total, 5,673 with self-reported hypertension; excludes participants with missing or unknown diabetic status

BMI
 BMI < 18.5: Underweight
 BMI 18.5–24.9: Normal
 BMI 25–29.9: Overweight
 BMI 30–39.9: Obese
 BMI ≥40: Extremely obese

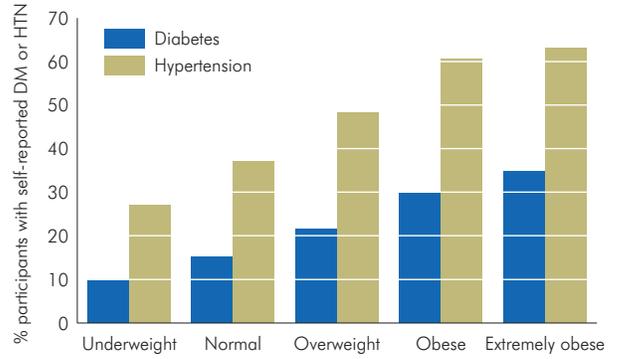
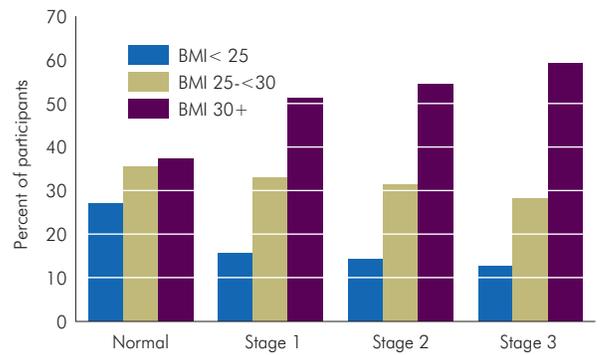


Figure 2.17 · percent distribution of KEEP participants, by measured blood pressure & BMI

KEEP: n=10,946; excludes participants with missing blood pressure values or BMI; hypertension based on JNC VI definition; excludes participants with missing or unknown hypertension status

JNC VI hypertension
 Stage I: systolic 140–159 or diastolic 90–99
 Stage II: systolic 160–179 or diastolic 100–109
 Stage III: systolic ≥180 or diastolic ≥110



HISTORY OF SMOKING

Figure 2.18 · percent distribution of KEEP participants, by smoking status

KEEP: n=10,536; excludes participants with missing smoking status

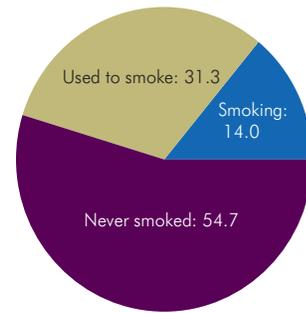


Figure 2.19 · percent distribution of KEEP participants, by race/ethnicity & smoking status

KEEP: n=10,536; race & Hispanic ethnicity are not mutually exclusive

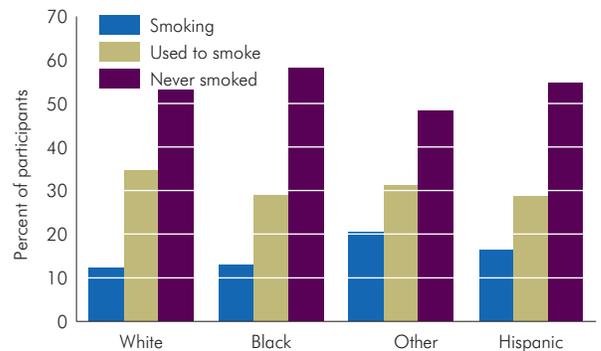


Figure 2.20 · percent distribution of KEEP participants with self-reported diabetes, by smoking pattern

KEEP: n=10,367 total, 2,513 with self-reported diabetes; excludes participants with missing smoking status or diabetic status

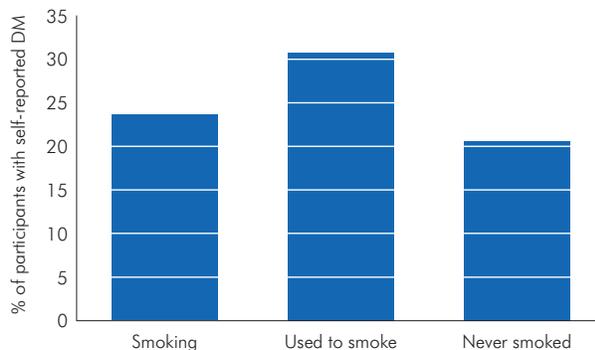


Figure 2.21 · percent distribution of KEEP participants with self-reported hypertension, by smoking pattern

KEEP: n=10,437 total, 5,369 with self-reported hypertension; excludes participants with missing smoking status or hypertension status

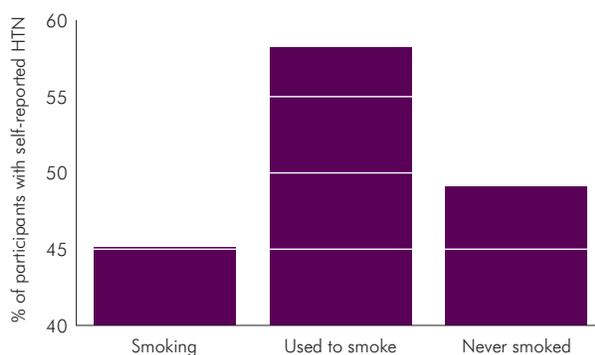
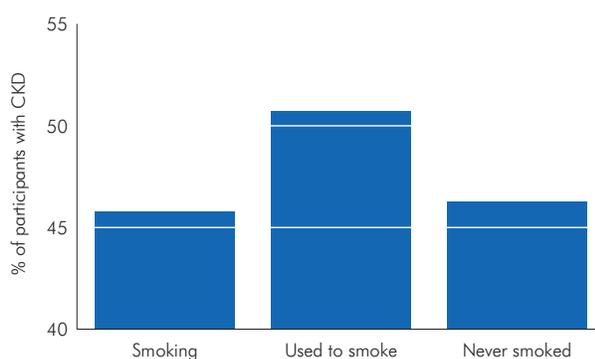


Figure 2.22 · percent distribution of KEEP participants with CKD, by smoking pattern

KEEP: n=10,002; excludes participants with missing smoking status or CKD status

CKD definition
 If calculated creatinine clearance by K/DOQI
 MDRD < 60 ml/min/1.73 m² or;
 If calculated creatinine clearance by K/DOQI
 MDRD ≥ 60 ml/min/1.73 m² and
 microalbuminuria +



HISTORY OF CKD

Figure 2.23 · percent distribution of KEEP participants, by stage of CKD

KEEP: n=10,651; excludes participants with missing creatinine clearance values

CKD stages
 Stage 1: CCR ≥ 90, microalbuminuria = +
 Stage 2: CCR 60–89, microalbuminuria = +
 Stage 3: CCR 30–59
 Stage 4: CCR 15–29
 Stage 5: CCR < 15 or patient on dialysis

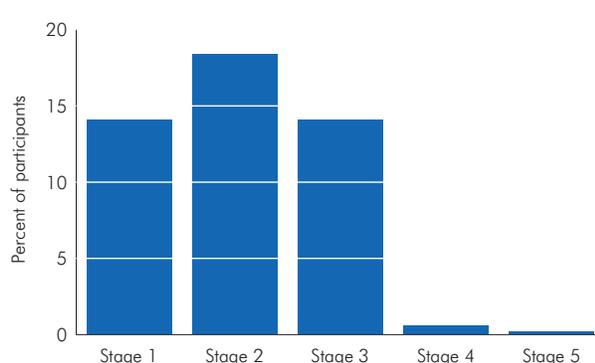


Figure 2.24 · percent distribution of KEEP participants with evidence of CKD, overall & within gender

KEEP: n=10,651 (male, 3,519, female 7,132), participants with CKD, n=5,051

CKD definition
 If calculated creatinine clearance by K/DOQI MDRD < 60 ml/min/1.73 m² or;
 If calculated creatinine clearance by K/DOQI MDRD ≥ 60 ml/min/1.73 m² and microalbuminuria +

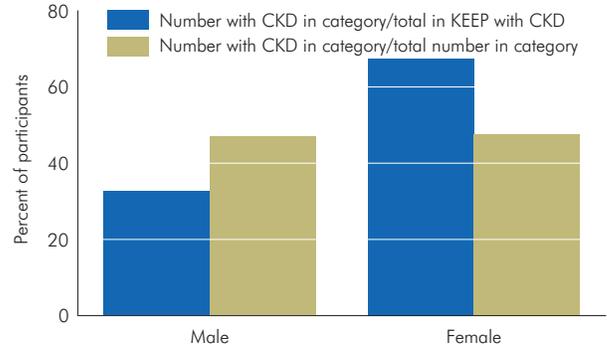


Figure 2.25 · percent distribution of KEEP participants with evidence of CKD, overall & within race/ethnicity

KEEP: race, n=10,343; participants with CKD, n=4,897; race & Hispanic ethnicity are not mutually exclusive

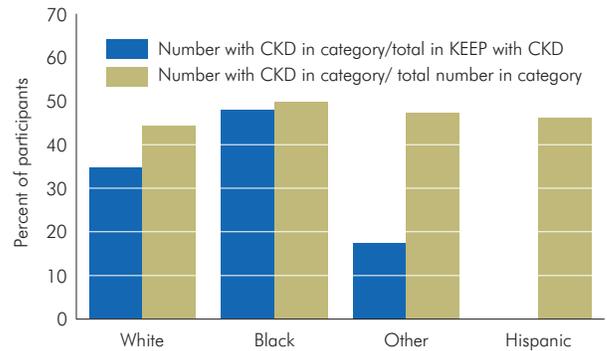


Figure 2.26 · percent distribution of KEEP participants with evidence of CKD, overall & within U.S. census region

KEEP: n=10,651; participants with CKD, n=5,051

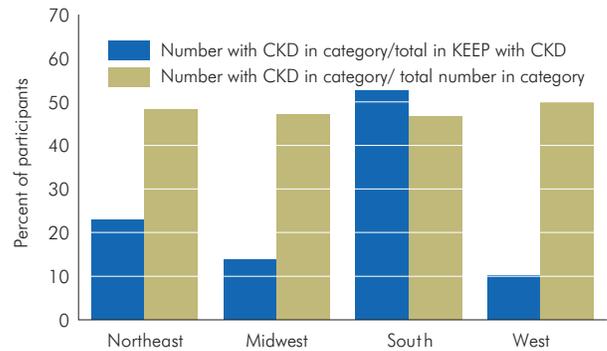
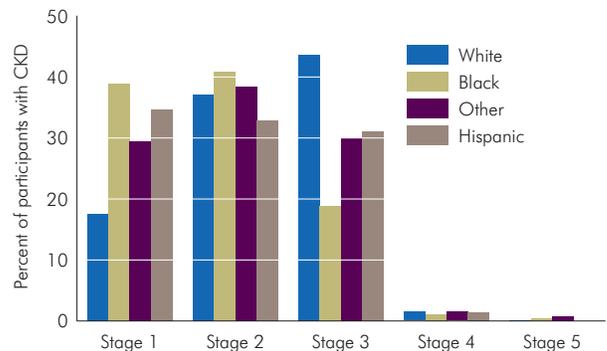


Figure 2.27 · percent distribution of KEEP participants with evidence of CKD, by CKD stage & race/ethnicity

KEEP: participants with CKD, n=4,897; excludes participants with missing race; race & Hispanic ethnicity are not mutually exclusive

CKD stages
 Stage 1: CCR ≥ 90, microalbuminuria = +
 Stage 2: CCR 60–89, microalbuminuria = +
 Stage 3: CCR 30–59
 Stage 4: CCR 15–29
 Stage 5: CCR < 15 or patient on dialysis



FAMILY HISTORY & COMORBIDITY

Figure 2.28 · distribution of KEEP participants, by U.S. census region & risk factor

KEEP: CKD, n=5,051; self-reported diabetes, n=2,690; hypertension, n=5,732; obesity, n=4,953; currently smoking, n=1,475

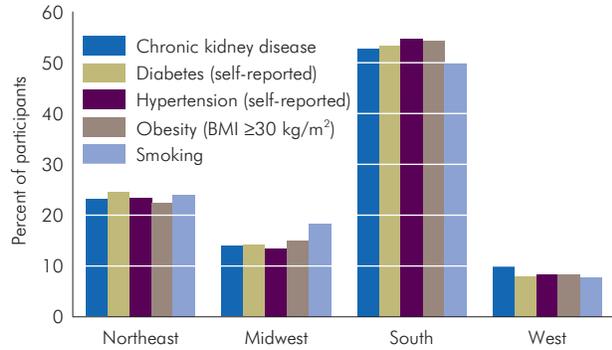


Figure 2.29 · percent distribution of KEEP participants with a family history of diabetes, hypertension, or kidney disease, by participant's self-reported diabetic status

KEEP: diabetics, n=2,690, non-diabetics, n=8,372; excludes participants with missing self-reported diabetic status

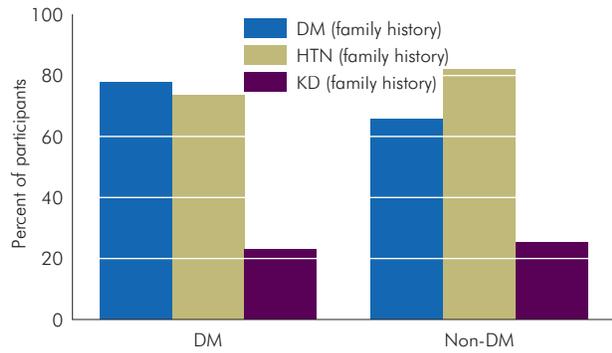


Figure 2.30 · percent distribution of KEEP participants with a family history of diabetes, hypertension, or kidney disease, by participant's measured blood pressure

KEEP: normal, n=5,953; stage 1, n=3,250; stage 2, n=1,374; stage 3, n=487; hypertension status based on JNC VI definition; excludes participants with missing blood pressure values

JNC VI hypertension
 Stage I: systolic 140–159 or diastolic 90–99
 Stage II: systolic 160–179 or diastolic 100–109
 Stage III: systolic ≥180 or diastolic ≥110

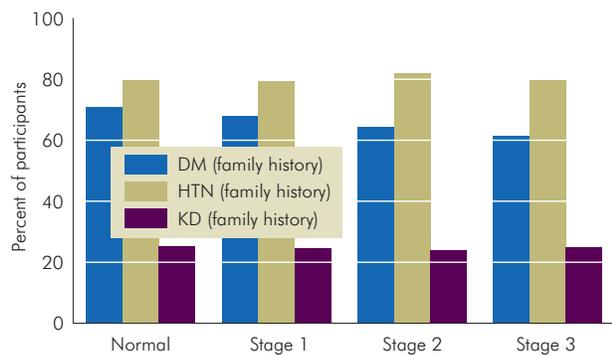
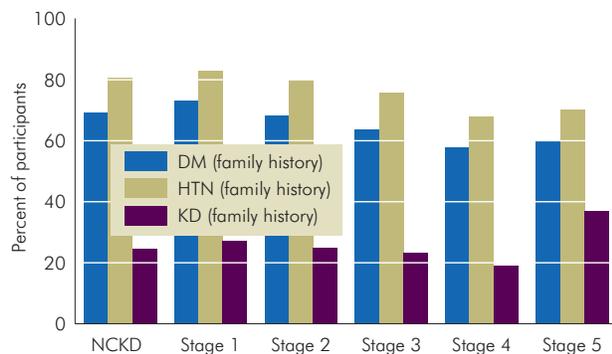


Figure 2.31 · percent distribution of KEEP participants with a family history of diabetes, hypertension, or kidney disease, by participant's CKD status

KEEP: non-CKD, n=5,600; stage 1, n=1,502; stage 2, n=1,965; stage 3, n=1,499; stage 4, n=65; stage 5, n=20

CKD stages
 Stage 1: CCR ≥ 90, microalbuminuria = +
 Stage 2: CCR 60–89, microalbuminuria = +
 Stage 3: CCR 30–59
 Stage 4: CCR 15–29
 Stage 5: CCR <15 or patient on dialysis



CHAPTER

SUMMARY

Figure 2.1 • The proportions of KEEP and NHANES III participants with self-reported diabetes increased with increasing age up to age 75; there were more diabetic males than females in the KEEP population.

Figure 2.2 • The greatest proportion of KEEP participants with self-reported diabetes occurred in individuals of “other” races, which includes Native Americans.

Figure 2.3 • Of KEEP participants with both a reported history of diabetes and a measured blood pressure, 56.4 percent had a measured blood pressure greater than 140/90 mmHg.

Figure 2.4 • By race, the greatest proportion of KEEP participants with elevated blood pressure occurred in black diabetics, who were nearly 7.7 percent more likely to have elevated blood pressure when compared to whites, while in the NHANES III population, black diabetics were 15.6 percent more likely than whites to have elevated blood pressure.

Figures 2.6–7 • By gender and race, more than half of the men, women, whites, and blacks in the KEEP population reported a history of hypertension, compared to 20–25 percent in the NHANES III population.

Figure 2.8–9 • The proportion of KEEP participants with a measured blood pressure of greater than 140/90 mmHg ranged from 36 to 51 percent in all racial and ethnic groups, as well as in men and women.

Figure 2.11 • Blacks participants had the least difference between the prevalence of self-reported hypertension (54.5 percent) and the prevalence of measured elevated blood pressure, suggesting that they may be undertreated.

Figure 2.12 • Based on body mass index, 78.4 percent of KEEP participants were overweight to extremely obese, compared to 53.9 percent in the NHANES III population.

Figure 2.17 • The proportion of KEEP participants with body mass indices greater than or equal to 30 kg/m² increased with increased severity of hypertension.

Figure 2.18 • Close to half of all KEEP participants had a history of smoking.

Figure 2.20 • Nearly 31 percent of KEEP participants with self-reported diabetes used to smoke, 24 percent currently smoked, and 21 percent had never smoked.

Figure 2.21 • Of the KEEP participants with self-reported hypertension, 58 percent used to smoke, 45 percent currently smoked, and 49 percent had never smoked.

Figure 2.22 • The proportion of KEEP participants with CKD who used to smoke was 51 percent.

Figure 2.23 • Nearly half (47.4 percent) of all KEEP participants were considered “high risk” for developing kidney disease.

Figure 2.26 • The majority of KEEP participants with CKD resided in the South (52.8 percent) followed by the Northeast (23.1 percent).

Figure 2.28 • The proportions of patients and their associated risk factors were distributed evenly within each region; participants in the South were two to four times more likely to have either CKD or a risk factor for CKD compared to participants residing in the Northeast, Midwest, or West regions.

According to surveys conducted by the Centers for Disease Control and Prevention (CDC), rates of obesity are increasing in the adult U.S. population. Information gathered from the CDC's Behavioral Risk Factor Surveillance System indicates that the prevalence of obesity in adults increased from 12 percent in 1991, to 19.8 percent in 2000, and to 20.9 percent in 2001, a 74 percent increase over the ten-year period (Mokdad et al, JAMA 2003). Past and current studies have revealed that obesity is highly associated with diabetes and hypertension, and is a major risk factor for the development of chronic kidney disease (CKD).

In both self-reported diabetics and non-diabetics the tendency to be overweight increased with age, while the highest rates of obesity occurred in diabetics age 18–30, indicating a potential for increased risk of CKD in the younger population. Diabetic females had the highest prevalence of obesity, and, when comparing rates of obesity among races, black diabetic participants were the most likely to be obese (Figures 3.4–6)

Obesity & Body Mass Index

CHAPTER THREE

Participants with self-reported hypertension had higher rates of obesity for all age, race, and ethnic categories, and both genders (Figures 3.7–9).

The KEEP screening programs were developed to identify people at risk for CKD. Data from these studies show that obesity

is a highly significant problem, with three-quarters of KEEP participants being above normal weight based on their body mass index (BMI).

In the KEEP participants, BMI increased with age, and the highest prevalence of obesity occurred in participants age 46–75. The majority of participants had a medium body size, and females were more likely to be obese or extremely obese than males. By race, blacks and individuals of “other races” were more prone to obesity, while Hispanics had the greatest proportion of participants with a normal BMI (Figures 3.1–3).

By gender, males with self-reported kidney disease were more likely to be overweight, while females had higher rates of obesity regardless of their kidney disease status. Hispanic participants with self-reported kidney disease accounted for the greatest proportion of participants who were overweight, while all those not reporting the disease had a slightly higher tendency for obesity than those with kidney disease (Figures 3.10–12).

With this rising prevalence of obesity in the U.S. population comes an increased burden of cost on our already stressed healthcare infrastructure. Preventive programs focused on reducing the incidence of obesity in the U.S population will not only reduce these costs, but will also directly decrease the number of individuals suffering from related diseases such as diabetes and hypertension.

[I learned] the importance of watching for signs of diabetes & kidney disease. I appreciated the opportunity to participate in this program...because of my family history.

Dorothy Vedder, Florida;
March 2002

BODY SIZE & BMI

Figure 3.1 · percent distribution of KEEP participants, by age, body size, & BMI

KEEP: body size, n=10,963; BMI, n=11,122; excludes participants with missing body size or BMI value

BMI
 BMI < 18.5: Underweight
 BMI 18.5–24.9: Normal
 BMI 25–29.9: Overweight
 BMI 30–39.9: Obese
 BMI ≥40: Extremely obese

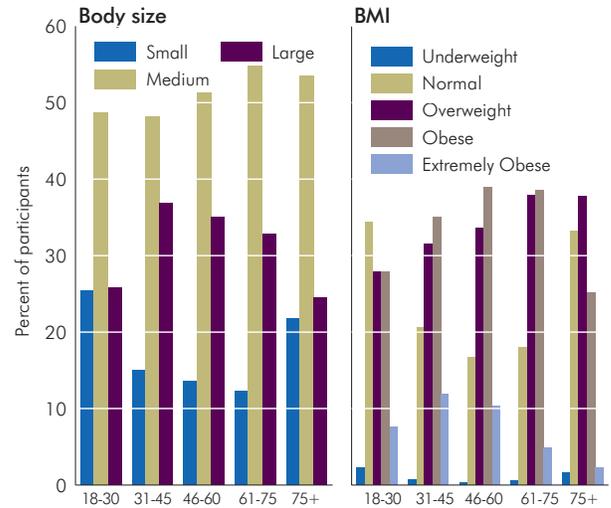


Figure 3.2 · percent distribution of KEEP participants, by gender, body size, & BMI

KEEP: body size, n=10,963; BMI, n=11,122; excludes participants with missing body size or BMI value

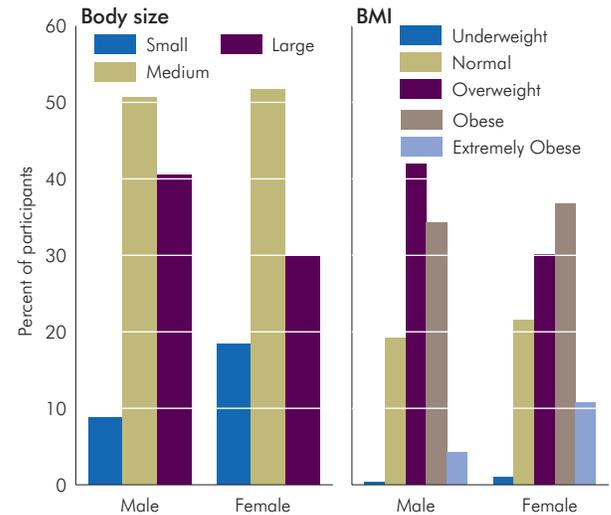


Figure 3.3 · percent distribution of KEEP participants, by race/ethnicity, body size, & BMI

KEEP: body size, n=10,666; BMI, n=10,790; excludes participants with missing body size, BMI value, race, or ethnicity; race & Hispanic ethnicity are not mutually exclusive

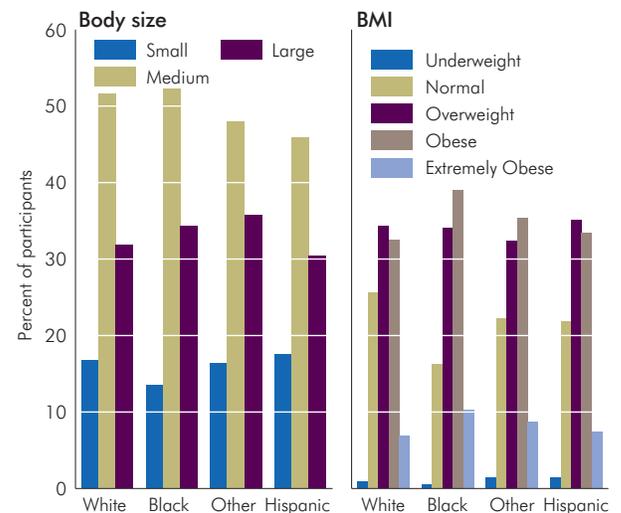


Figure 3.4 · percent distribution of KEEP participants, by age, self-reported diabetic status, & BMI

KEEP: self-reported diabetics, n=2,657; self-reported non-diabetics, n=8,285; excludes participants with missing BMI value or diabetic status

BMI
 BMI <18.5: Underweight
 BMI 18.5–24.9: Normal
 BMI 25–29.9: Overweight
 BMI 30–39.9: Obese
 BMI ≥40: Extremely obese

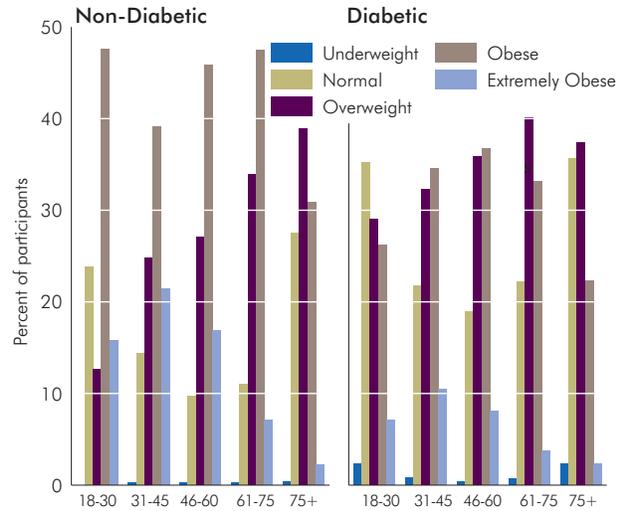


Figure 3.5 · percent distribution of KEEP participants, by gender, self-reported diabetic status, & BMI

KEEP: self-reported diabetics, n=2,657; self-reported non-diabetics, n=8,285; excludes participants with missing BMI value or diabetic status

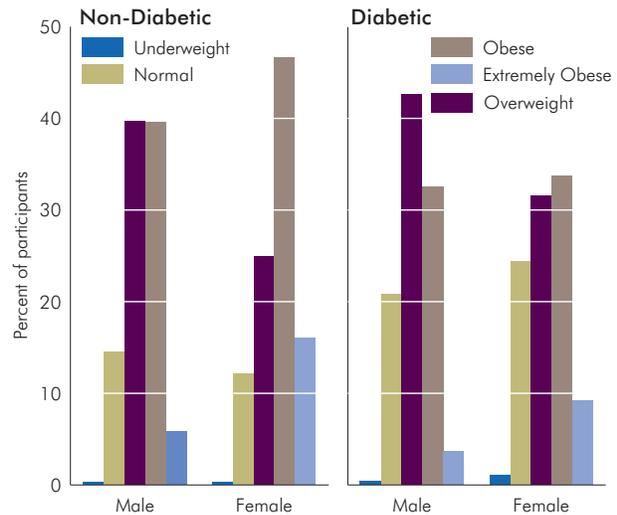


Figure 3.6 · percent distribution of KEEP participants, by race/ethnicity, self-reported diabetic status, & BMI

KEEP: self-reported diabetics, n=2,575; self-reported non-diabetics, n=8,044; excludes participants with missing race, ethnicity, BMI value, or diabetic status; race & Hispanic ethnicity are not mutually exclusive

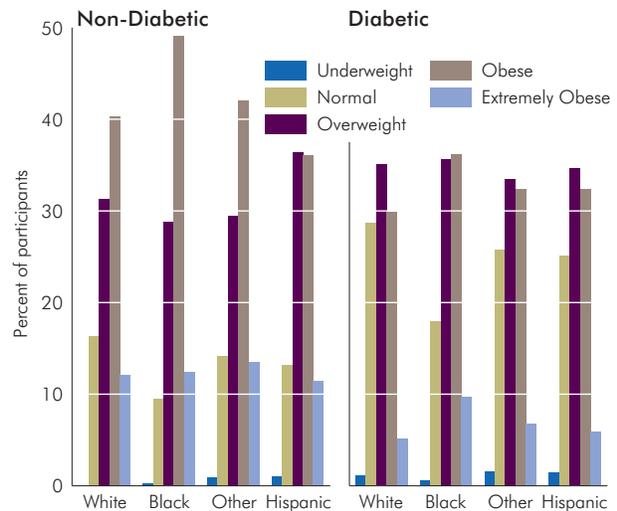


Figure 3.7 · percent distribution of KEEP participants, by age, self-reported hypertension status, & BMI

KEEP: self-reported hypertension; n=5,673; no self-reported hypertension, n=5,338; excludes participants with missing BMI value, or hypertension status

BMI
 BMI <18.5: Underweight
 BMI 18.5–24.9: Normal
 BMI 25–29.9: Overweight
 BMI 30–39.9: Obese
 BMI ≥40: Extremely obese

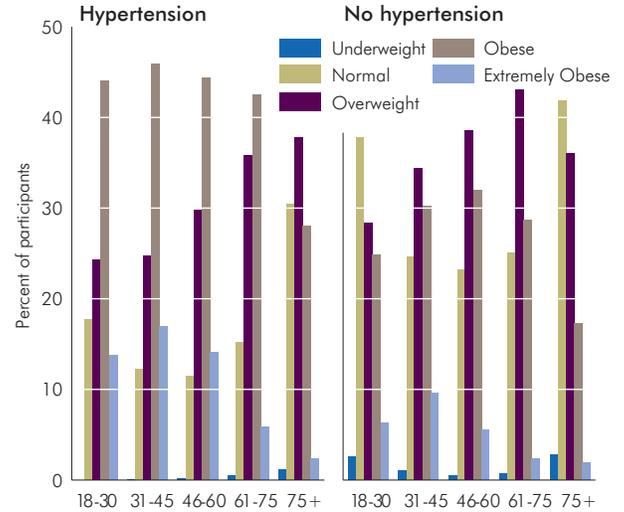


Figure 3.8 · percent distribution of KEEP participants, by gender, self-reported hypertension status, & BMI

KEEP: self-reported hypertension; n=5,673; no self-reported hypertension, n=5,338; excludes participants with missing BMI value, or hypertension status

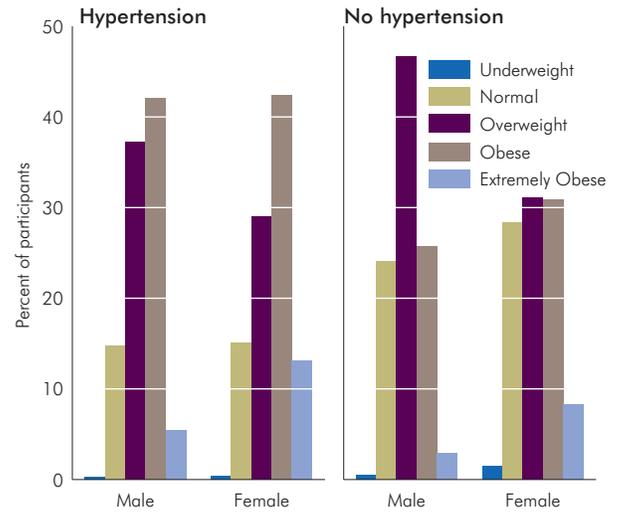
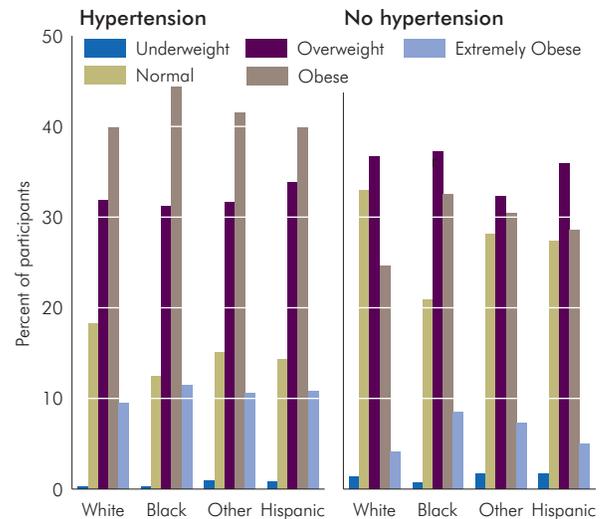


Figure 3.9 · percent distribution of KEEP participants, by race/ethnicity, self-reported hypertension status, & BMI

KEEP: self-reported hypertension; n= 5,520; no self-reported hypertension, n=5,169; excludes participants with missing BMI value, race, ethnicity, or hypertension status; race & Hispanic ethnicity are not mutually exclusive



BMI & KIDNEY DISEASE

Figure 3.10 · percent distribution of KEEP participants, by age, self-reported kidney disease, & BMI

KEEP: self-reported kidney disease, n=262; no self-reported kidney disease, n=10,860; excludes participants with missing BMI value

BMI	
BMI < 18.5:	Underweight
BMI 18.5–24.9:	Normal
BMI 25–29.9:	Overweight
BMI 30–39.9:	Obese
BMI ≥40:	Extremely obese

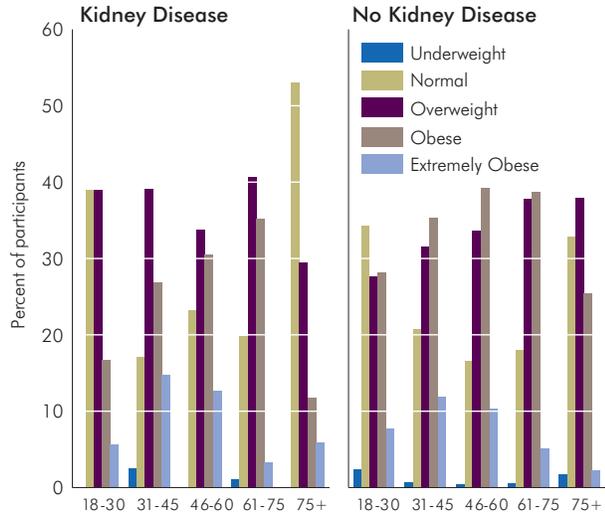


Figure 3.11 · percent distribution of KEEP participants, by gender, self-reported kidney disease, & BMI

KEEP: self-reported kidney disease; n=262, no self-reported kidney disease, n=10,860; excludes participants with missing BMI value

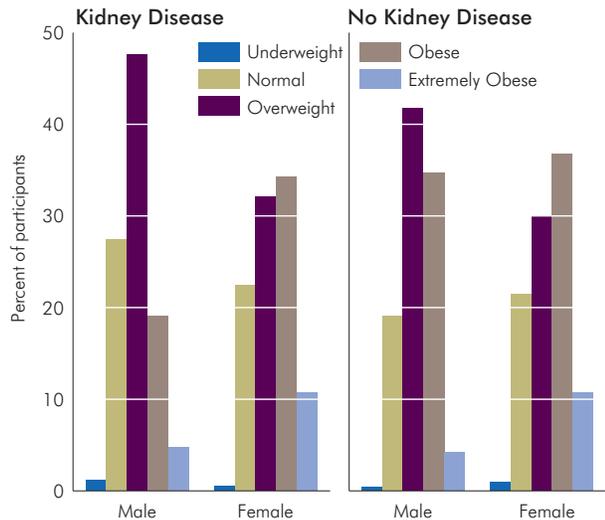
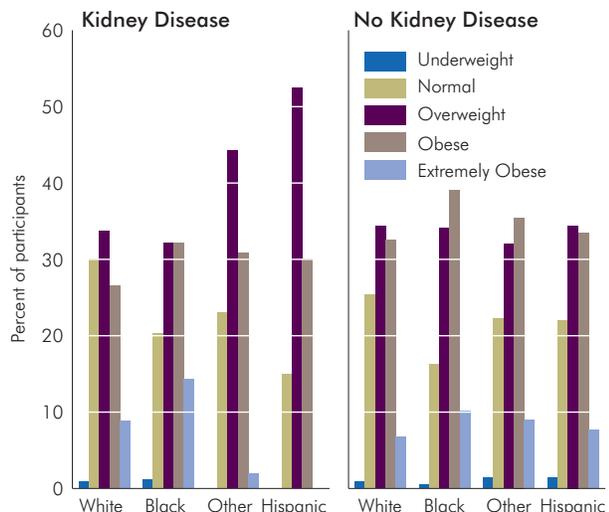


Figure 3.12 · percent distribution of KEEP participants, by race/ethnicity, self-reported kidney disease, & BMI

KEEP: self-reported kidney disease; n=249, no self-reported kidney disease, n=10,541; excludes participants with missing BMI value, or missing or unknown race or ethnicity; race & Hispanic ethnicity are not mutually exclusive



CHAPTER SUMMARY

Figure 3.1 • Medium body size was the most prominent in all KEEP participants, while, depending on age, 63–83 percent of the participants were overweight to extremely obese.

Figure 3.2 • The proportion of KEEP participants who were overweight was highest in males; obesity, however, was slightly more prominent in females.

Figure 3.3 • Whites had the highest proportion of participants with normal body mass indices, and overweight patients were equally distributed over all racial and ethnic categories.

Figure 3.4 • The greatest proportion of obese patients was diabetic, while non-diabetics age 18–30 and those age 75 and older represented the greatest proportion of patients with a normal BMI.

Figure 3.5 • The proportion of KEEP participants with a normal body mass index was higher in non-diabetics compared to diabetics.

Figure 3.6 • By race and ethnicity, the greatest proportion of obese participants was black and diabetic.

Figure 3.7 • The greatest proportion of obese participants occurred in those with hypertension and age 75 or younger; rates for overweight patients increased with increasing age up to 75 years in participants with or without hypertension.

Figure 3.8 • Male and female participants with hypertension were more likely to be obese than their non-hypertensive counterparts; non-hypertensive male participants were the most likely to be overweight.

Figure 3.9 • Rates of obesity are higher, in all racial and ethnic categories, for participants with hypertension than for non-hypertensive participants.

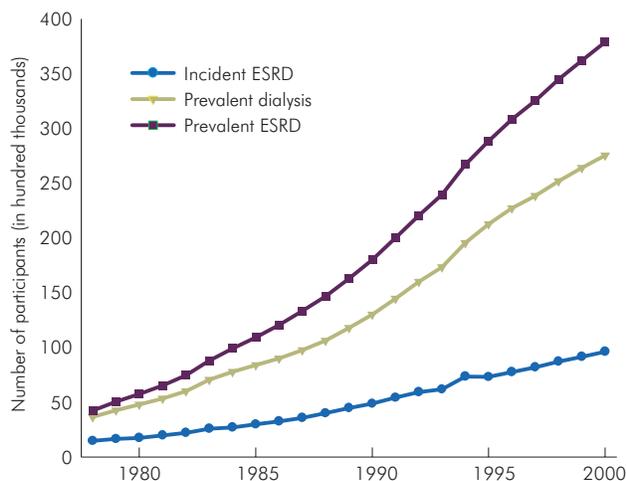
Figure 3.10 • KEEP participants age 75 and older with CKD represented the greatest proportion of patients with a normal body mass index.

Figure 3.11 • The greatest proportion of overweight participants was male with CKD, while females had the highest rates of obesity, regardless of CKD status.

Figure 3.12 • Hispanics and individuals of “other races” with CKD represented the greatest proportion of participants who were overweight.

Figure 4.1 • End-stage renal disease: trends in patient counts

USRDS 2002 Annual Data Report



Trends of ESRD requiring renal replacement therapy indicate a nonlinear acceleration in incidence and prevalence. CKD, not requiring renal replacement therapy, accounts for a much larger pool of U.S. patients, and is expected to show similar trends in incidence and prevalence. Because ESRD patients must be selected, and because of the competing mortality of cardiovascular disease (CVD), the epidemiology of ESRD and CKD are not directly superimposable.

Because obesity is a central, upstream determinant of hypertension and type II diabetes, the obesity epidemic

CHAPTER FOUR

Major Risk Factors for Chronic Kidney Disease

studies suggest that rates of conventional CVD risk factors, including elevated low-density lipoprotein cholesterol and tobacco use, decline in frequency.

in the United States is expected to create a secondary epidemic of diabetic nephropathy. Hyper-

tension alone can be a determinant of non-diabetic kidney disease, and is a common comorbidity of those with forms of primary kidney disease such as polycystic kidney disease and forms of non-diabetic glomerulopathies. Other CVD risk factors are known to cluster with obesity, diabetes, and hypertension, including dyslipidemia (reduced high-density lipoprotein cholesterol, elevated triglycerides, and elevated lipoprotein), sedentary lifestyle, and to a lesser degree, active smoking. As patients advance from CKD to ESRD,

In aggregate, these data support the notion that the diabetes epidemic is creating a secondary epidemic of diabetic CKD, and possibly nondiabetic CKD. There is a relatively tight clustering of obesity, DM, and HTN to support this conclusion. In addition, participants had very high rates of DM in their family members, which may have prompted them to become study members. Fortunately, rates of smoking in this population were lower than that of the general population, and again, likely reflect selection bias for those who are concerned about their health. Lastly, anemia is a common finding in those with eGFR <60 ml/min/1.73 m², especially among those with DM, potentially representing a risk factor for the development of adverse cardiac remodeling, future CVD, and progressive loss of kidney function.

This program is tremendous. Your emphasis on people & your follow-up is highly appreciated.

Richard Casper, Florida;
June 2002

HYPERTENSION

Figure 4.2 · percent distribution of KEEP participants, by measured blood pressure

KEEP: n=11,064; excludes participants with missing blood pressure values; hypertension based on JNC VI definition

JNC VI hypertension
 Stage I: systolic 140–159 or diastolic 90–99
 Stage II: systolic 160–179 or diastolic 100–109
 Stage III: systolic ≥180 or diastolic ≥110

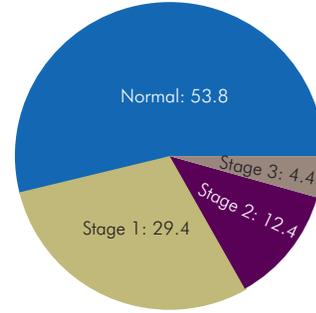


Figure 4.3 · percent distribution of KEEP participants with self-reported hypertension, by age & gender

KEEP: n=11,131 total, 5,722 with self-reported hypertension; excludes participants with missing hypertension status

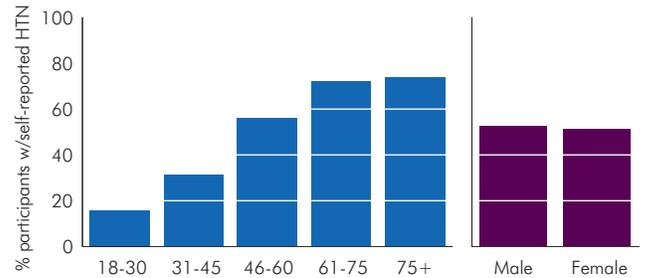


Figure 4.4 · percent distribution of KEEP participants reporting family members with hypertension, by age & gender

KEEP: n=10,942 total, 8,755 with self-reported hypertension; excludes participants with missing family history of hypertension

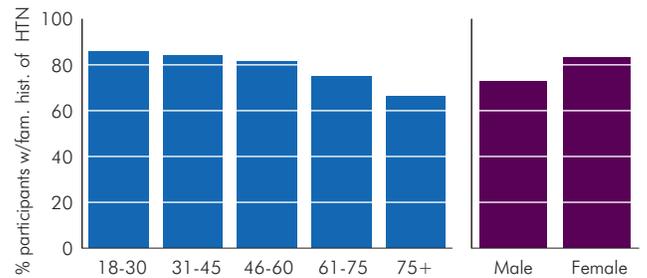
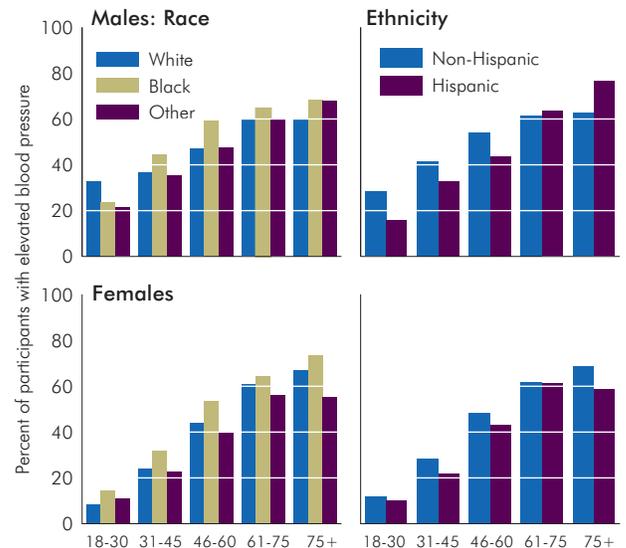


Figure 4.5 · percent distribution of KEEP participants with elevated blood pressure (≥140/90 mmHg), by age, gender, race, & ethnicity

KEEP: n=10,729; excludes participants with missing hypertension values or missing or unknown race; hypertension based on JNC VI definition



DIABETES

Figure 4.6 · percent distribution of KEEP participants with self-reported diabetes, by age & gender

KEEP: n=11,062 total, 2,690 with self-reported diabetes; excludes participants with missing diabetes status

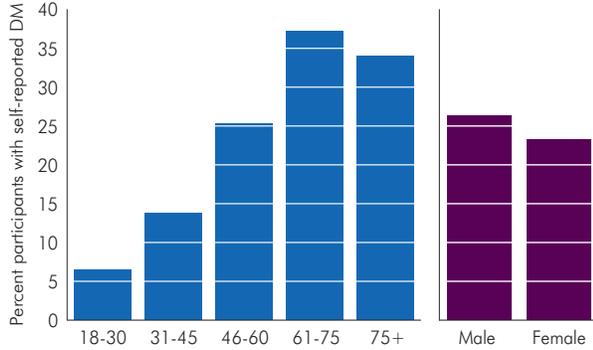


Figure 4.7 · percent distribution of KEEP participants with a family history of diabetes, by age & gender

KEEP: n=10,876 total, 7,469 with a reported family history of diabetes; excludes participants with missing family history of diabetes

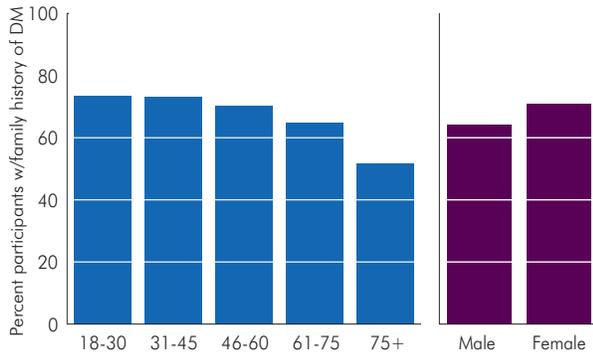


Figure 4.8 · percent distribution of KEEP participants with self-reported diabetes, by age, race, & ethnicity

KEEP: n=10,732 total, 2,607 with self-reported diabetes; excludes participants with missing diabetic status, or missing or unknown race

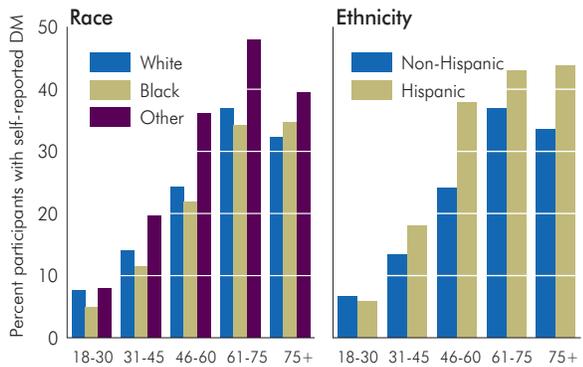
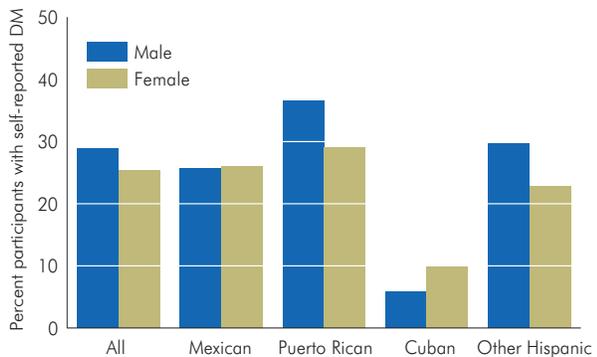


Figure 4.9 · percent distribution of Hispanic KEEP participants with self-reported diabetes, by gender

KEEP: all Hispanics, n=1,115 total, 297 with self-reported diabetes; excludes participants with missing diabetic status



OBESITY

Figure 4.10 · percent distribution of KEEP participants with self-reported diabetes, by BMI & gender

KEEP: self-reported diabetes, n=2,657

BMI
 BMI < 18.5: Underweight
 BMI 18.5–24.9: Normal
 BMI 25–29.9: Overweight
 BMI 30–39.9: Obese
 BMI ≥40: Extremely obese

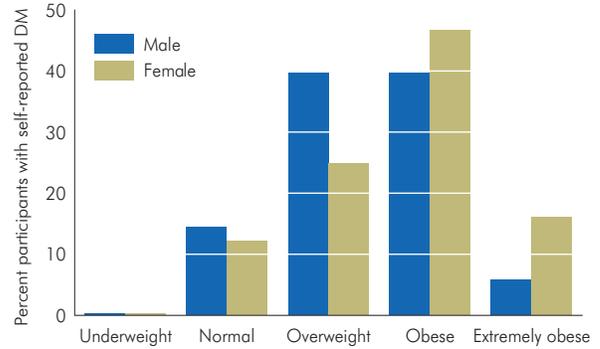


Figure 4.11 · percent distribution of KEEP participants, by age, gender, & BMI

KEEP: n=11,122; excludes participants with missing BMI values

BMI
 BMI < 18.5: Underweight
 BMI 18.5–24.9: Normal
 BMI 25–29.9: Overweight
 BMI 30–39.9: Obese
 BMI ≥40: Extremely obese

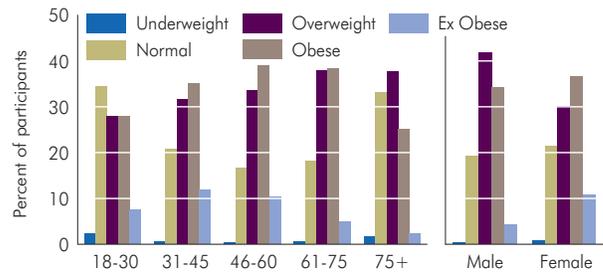


Figure 4.12 · percent distribution of KEEP participants, by age, race, ethnicity, & BMI

KEEP: n=10,790; excludes participants with missing race or BMI values

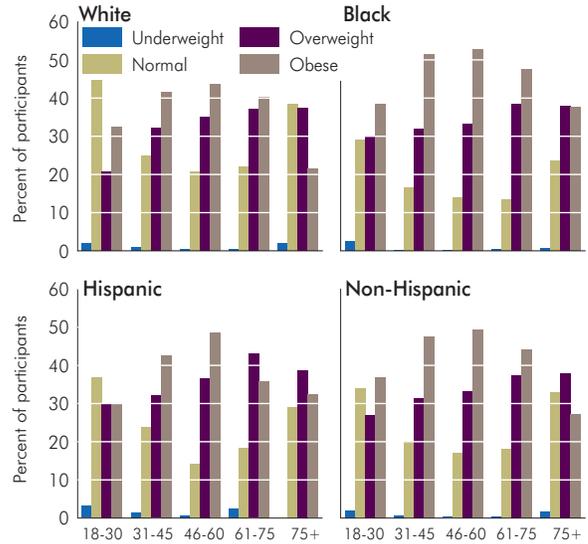


Figure 4.13 · percent distribution of Hispanic KEEP participants with obesity (≥ 25 kg/m²), by gender

KEEP: n=886; excludes participants with missing Hispanic ethnicity or BMI values

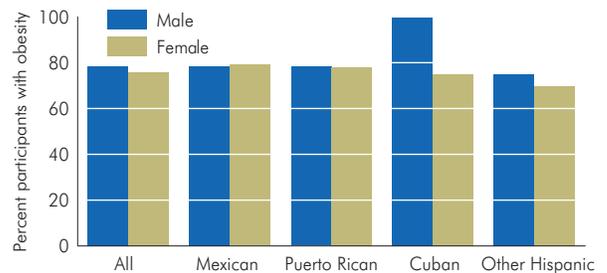
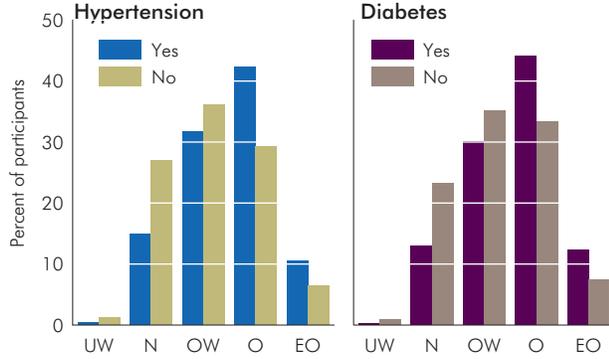


Figure 4.14 · percent distribution of KEEP participants, by BMI, self-reported hypertension, & diabetic status

KEEP: diabetes, n=10,942; hypertension, n=11,011; excludes participants with missing diabetic status or hypertension status

BMI	
BMI < 18.5:	Underweight
BMI 18.5–24.9:	Normal
BMI 25–29.9:	Overweight
BMI 30–39.9:	Obese
BMI ≥40:	Extremely obese



SMOKING

Figure 4.15 · percent distribution of KEEP participants, by age, gender, & smoking status

KEEP: n=10,536; excludes participants with missing smoking status

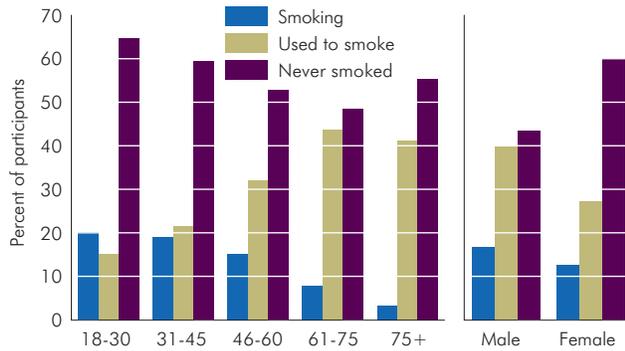


Figure 4.16 · percent distribution of KEEP participants, by age, race, & smoking status

KEEP: n=10,233; excludes participants with missing race or smoking status

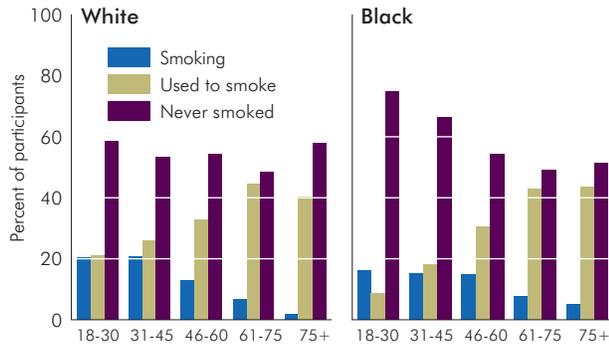
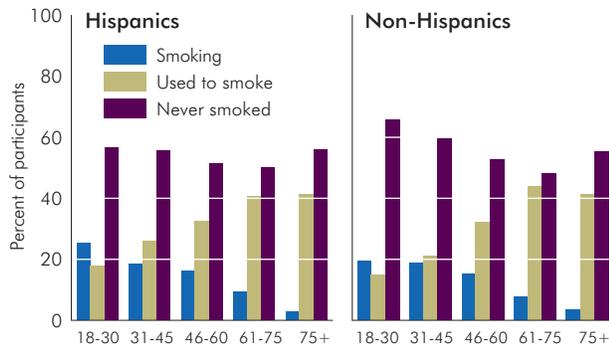


Figure 4.17 · percent distribution of KEEP participants, by age, Hispanic ethnicity, & smoking status

KEEP: n=10,233; excludes participants with missing race/ethnicity or smoking status



ANEMIA

Figure 4.18 · percent distribution of KEEP participants with anemia, by age & gender

KEEP: n=10,136; excludes participants with missing hemoglobin values or race; anemia defined by NKF-K/DOQI: males: Hgb <12 g/dl; females age >50: Hgb <12 g/dl; females age ≤50: Hgb <11

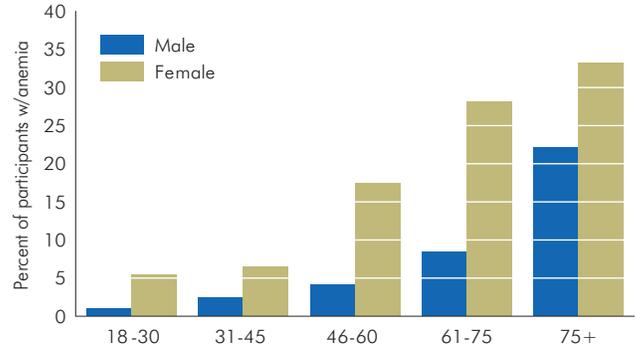


Figure 4.19 · percent distribution of KEEP participants with anemia, by age, race, & ethnicity

KEEP: n=10,136; excludes participants with missing hemoglobin values or race or ethnicity; anemia defined by NKF-K/DOQI: see above

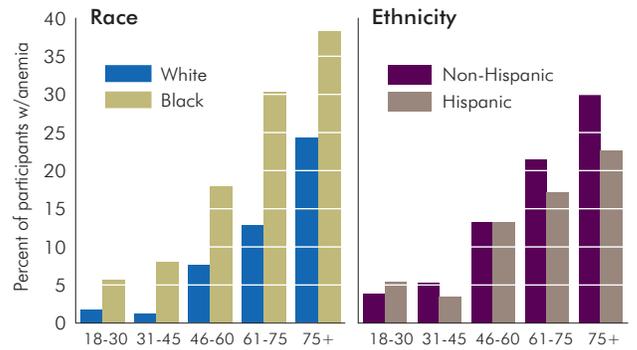
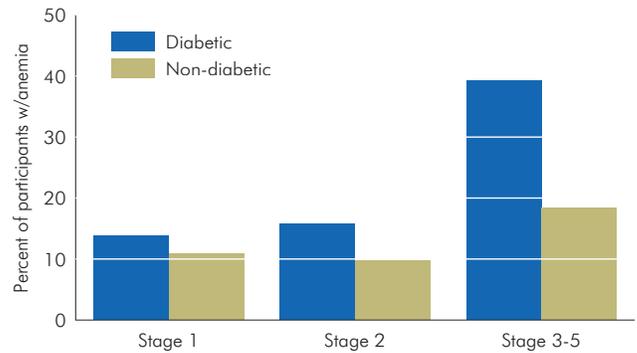


Figure 4.20 · percent distribution of KEEP participants with anemia, by CKD & self-reported diabetic status

KEEP: n=9,935; anemia defined by NKF-K/DOQI: see above; CKD status defined by calculated creatinine clearance (CCR) using the MDRD formula

CKD stages
 Stage 1: CCR ≥ 90, microalbuminuria = +
 Stage 2: CCR 60–89, microalbuminuria = +
 Stage 3: CCR 30–59
 Stage 4: CCR 15–29
 Stage 5: CCR < 15 or patient on dialysis



MULTIPLE RISK FACTORS

Figure 4.21 · percent distribution of KEEP & NHANES III participants, by number of risk factors

KEEP: n=10,053; NHANES III: n=16,652. Anemia as defined by WHO, hypertension according to JNC VI definition (Stages 1, 2, and 3).

Major risk factors
 Anemia (WHO definition)
 Diabetes (self-reported)
 Hypertension (measured)
 Obesity (BMI ≥ 25 kg/m²)
 Smoking or used to smoke

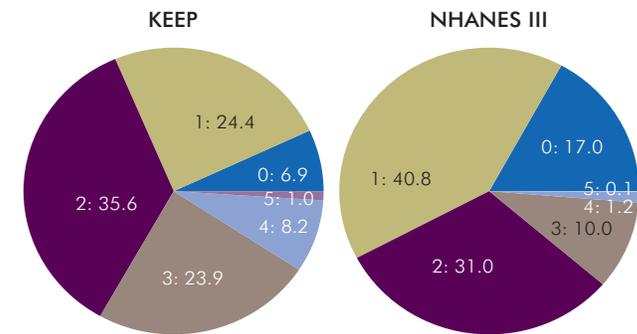


Figure 4.22 · percent distribution of KEEP participants with elevated blood pressure ($\geq 140/90$ mmHg), by BMI & self-reported diabetic status

KEEP: $n=10,769$; excludes participants with missing BMI value or blood pressure value; hypertension based on JNC VI definition

BMI index

- BMI <18.5: Underweight
- BMI 18.5–24.9: Normal
- BMI 25–29.9: Overweight
- BMI 30–39.9: Obese
- BMI ≥ 40 : Extremely Obese

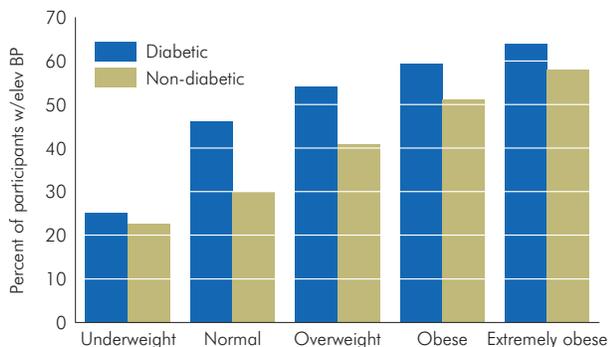


Figure 4.23 · percent distribution of KEEP participants with elevated blood pressure ($\geq 140/90$ mmHg), by BMI & smoking status

KEEP: $n=10,268$; excludes participants with missing BMI value, blood pressure value, or smoking status; hypertension based on JNC VI definition

JNC VI hypertension

- Stage I: systolic 140–159 or diastolic 90–99
- Stage II: systolic 160–179 or diastolic 100–109
- Stage III: systolic ≥ 180 or diastolic ≥ 110

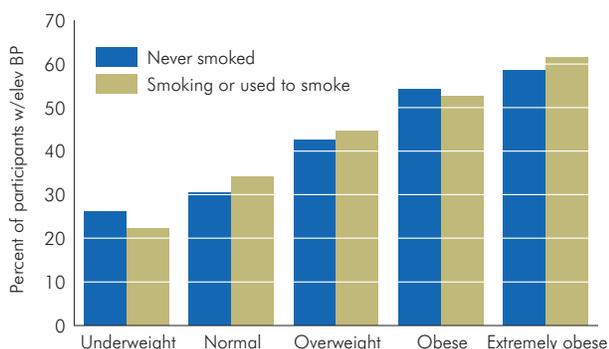


Figure 4.24 · percent distribution of KEEP participants with elevated blood pressure ($\geq 140/90$ mmHg), by BMI & anemia status

KEEP: $n=10,216$; excludes participants with missing BMI value, blood pressure value, or hemoglobin; hypertension based on JNC VI definition; anemia defined as Hgb <11 g/dl

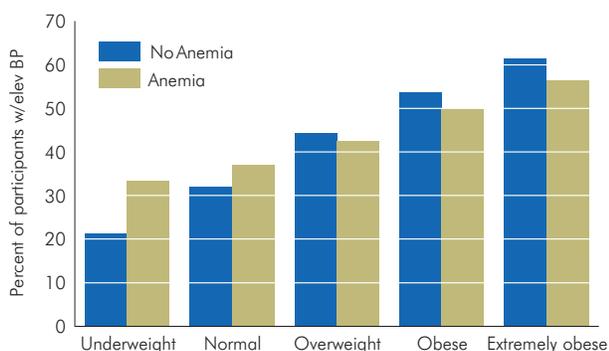
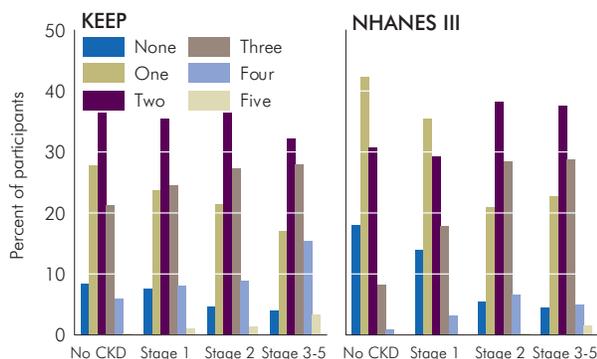


Figure 4.25 · percent distribution of KEEP & NHANES III participants, by number of risk factors & CKD status

KEEP: $n=10,008$; NHANES III: $n=15,594$; excludes participants with missing CKD status or risk factor description; CKD status defined by calculated creatinine clearance (CCR) using the MDRD formula; see figure 4.21 for risk factors

CKD stages

- Stage 1: CCR ≥ 90 , microalbuminuria = +
- Stage 2: CCR 60–89, microalbuminuria = +
- Stage 3: CCR 30–59
- Stage 4: CCR 15–29
- Stage 5: CCR <15 or patient on dialysis



CHAPTER SUMMARY

Figure 4.2 • Over 50 percent of the KEEP participants had a normal blood pressure, while almost 30 percent had Stage 1 hypertension.

Figure 4.3 • The proportion of KEEP participants with hypertension increased with increasing age, and was similar in both males and females.

Figure 4.5 • In males, blacks over 30 years of age tended to have the highest rates of hypertension, while the same held true for females regardless of age. Non-Hispanics younger than 60 years old tended to have higher rates of hypertension than Hispanics, regardless of gender.

Figure 4.6 • Up until age 75, the likelihood of diabetes increased with increasing age; males tended to have slightly higher rates of diabetes than females.

Figure 4.8 • With the exception of participants age 18–30, the proportion of individuals with diabetes was higher in Hispanics than in non-Hispanics.

Figure 4.9 • Of the Hispanic participants, the greatest proportion of diabetes occurred in male and female Puerto Ricans.

Figure 4.12 • Blacks had higher rates of obesity than whites.

Figure 4.14 • Patterns of obesity were remarkably similar in KEEP participants with hypertension or diabetes.

Figure 4.15 • The majority of KEEP participants had never smoked, and more females had never smoked compared to males.

Figure 4.16 • Compared to whites, a greater proportion of younger black participants had never smoked.

Figure 4.17 • Non-Hispanics age 60 or younger were more likely to have never smoked than Hispanics.

Figure 4.18 • The proportion of KEEP participants with anemia was highest for females, and increased with increasing age.

Figure 4.19 • Rates of anemia were higher in blacks than in whites, and in non-Hispanics compared to Hispanics.

Figure 4.20 • Compared to non-diabetics, anemia was more prominent in diabetics regardless of CKD status. This difference was most remarkable (39.3 vs. 18.4 percent) for participants with a CKD status of Stage 3–5.

Figure 4.22 • Rates of hypertension increased with increasing BMI in both diabetics and non-diabetics.

Figure 4.23 • When comparing participants by smoking status, hypertension rates were comparable across all BMI categories.

Figure 4.24 • Compared to non-anemic participants, rates of hypertension were higher in anemic participants who were either overweight, obese, or extremely obese.

Figure 4.25 • In both the KEEP and NHANES III populations, as the severity of CKD increased so did the proportion of patients with multiple risk factors.

Introduction

In the KEEP program, CKD was identified through microalbuminuria or an eGFR of <60 ml/min/1.73 m². Established risk factors for CKD include blood pressure, diabetes, cigarette smoking, obesity, and anemia.

CKD is typically suspected on the basis of elevated serum creatinine (>1.5 mg/dl in men and >1.3 in women), depressed eGFR (determined by the MDRD estimating equation or the Cockcroft-Gault creatinine clearance, which adjusts for body surface area (BSA-CG)), and/or

twice as many men with CKD as did the BSA-CG clearance. Both estimating equations showed incrementally higher estimates of depressed kidney function as age increases.

By race, both estimating equations showed higher rates of depressed kidney function in whites than in blacks. Calculations using the MDRD formula showed CKD to be most prevalent in whites and Native Americans, while those using the BSA-CG creatinine clearance showed the most CKD among Asians and whites. By ethnicity, prevalence estimates were generally similar for Hispanic and non-Hispanic participants. The number of Cuban participants

Chronic Kidney Disease

was relatively small, making their prevalence estimates highly unstable. And by region, both estimating equations showed the greatest prevalence of depressed kidney function occurring in the west, and the lowest in the Midwest (Figures 5.4–6).

The overall prevalence of CKD in the KEEP cohort was just under 50 percent. Interestingly, the majority of participants with evidence of CKD were identified not on the basis of a depressed eGFR, but rather on the presence of microalbuminuria with an MDRD eGFR of >60 ml/min/1.73 m² (Figure 5.7).

By age, estimates of the prevalence of CKD ranged from 40–66 percent for participants age 18–75+, and rates were similar in men and women. White participants had a lower prevalence of CKD than blacks and those of other races, while non-Hispanics had slightly higher rates than Hispanics (Figures 5.8–9).

CHAPTER FIVE

proteinuria or albuminuria (identified by dipstick or quantitative methods on spot urine samples).

Approximately one in twenty KEEP participants had elevated serum creatinine levels. Compared to those younger than 60, however, nearly four times as many participants age 60 and older had elevated levels, and there was a fifteen-fold difference in the prevalence of these levels between the youngest and oldest age groups. By race, the prevalence of elevated serum creatinine ranged from 2.3 percent in Pacific Islanders to 6.7 percent in Native Americans, and was 6.0 percent in blacks (Figures 5.1–2).

Prevalence of CKD

Figure 5.3 shows the prevalence of eGFR (calculated with the MDRD method) and creatinine clearance (BSA-CG method). In both methods, CKD was identified through a result of <60 ml/min/1.73 m². For women these two formulas provided nearly identical estimates of the CKD population, while the MDRD eGFR formula identified almost

Since I attended your program I learned to eat healthier & take care of my health more seriously.

I encourage you to continue the great job you are doing on behalf of the people that do not have health insurance. I am very grateful with all of you. God bless you!

Francisco Granados,
Arizona; May 2002

In Figure 5.10 we examine the association of CKD with BMI. Extremely obese persons had the highest prevalence of CKD, at 53.8 percent. Rates were much lower in persons of normal body weight (39.7 percent), and increased incrementally at higher BMIs.

Family history of CKD

Almost one in four KEEP participants reported a family history of kidney disease: 26.7 percent of women, and 20.5 percent of men. By race, Asians were least likely to report a family history of the disease, and Pacific Islanders the most likely (17.1 and 27.8 percent, respectively); one-quarter of black participants reported this family history. By ethnicity, one-quarter of non-Hispanics reported a family history of CKD, while in Hispanics the number ranged from 16.7 percent in people of Cuban ancestry to 35.2 percent in Mexican-Americans. Given the small number of Cuban participants, the prevalence estimates for this group were relatively unstable (Figures 5.11–13).

Concordance of MDRD eGFR and BSA-CG creatinine clearance with serum creatinine cut-points

Table 5.1 shows the agreement between serum creatinine and cut-points for identifying depressed kidney function, using both the MDRD formula and the BSA-CG creatinine clearance. Serum creatinine levels of >1.5 for men and >1.3 for women are considered elevated, and an eGFR or BSA-CG creatinine clearance of <60 ml/min/1.73 m² is considered depressed kidney function.

Gender-specific creatinine elevations were relatively insensitive in picking up depressed kidney function as determined by the MDRD eGFR (524/1,601 = 32.7 percent). The specificity of a normal serum creatinine, however, was quite high (9,111/9,124 = 99.9 percent). Ten percent of participants were discordantly classified using these two metrics. Virtually all were misclassified by serum creatinine as having non-depressed kidney function when, in fact, the MDRD eGFR was <60 ml/min/1.73 m².

Using the BSA-CG creatinine clearance, the sensitivity of serum creatinine levels for detecting depressed kidney function was 23.6 percent (317/1,342), and the specificity of a normal serum creatinine was 97.7 percent (9,061/9,272). Nearly 12 percent of participants had discordant serum creatinine and BSA-CG creatinine clearance levels (1,236/10,614). Again, the overwhelming majority of misclassification occurred with a normal serum creatinine level and a

depressed BSA-CG creatinine clearance. The BSA-CG creatinine clearance, however, appeared to agree less with gender-specific serum creatinine cut-points, as discordant classification, sensitivity, and specificity were all lower than in the comparison of serum creatinine to MDRD eGFR.

Interrelation of CKD risk factors with MDRD eGFR

Table 5.2 displays mean and median systolic and diastolic blood pressure levels and interquartile ranges, using the definitions set by K/DOQI. Using the MDRD calculation, median systolic levels were 18 mmHg greater in the lowest MDRD eGFR category compared to the highest (148 vs 130 mmHg). Diastolic blood pressure levels were only slightly lower at lower eGFRs, with a median in persons with eGFR >90 of 80 mmHg versus 78 mmHg in the lowest eGFR category. Pulse pressure (SBP – DBP), a known correlate of cardiovascular-renal injury, increased considerably at lower MDRD eGFR levels, primarily because of disproportionate higher systolic blood pressure levels and, to a lesser degree, because of the slightly lower diastolic pressures. Since medication status of the KEEP participants was not ascertained, the influence of antihypertensive medication on these associations is unknown.

A similar, though less pronounced, inverse relationship was seen in the relation of systolic blood pressure to BSA-CG creatinine clearance. The trend of slightly lower diastolic blood pressure at lower creatinine clearances was also reconfirmed.

Figure 5.14 displays the percent of KEEP participants with blood pressure levels at or above two cut-points (140/90 and 130/85 mmHg). As MDRD eGFR levels decreased, the prevalence of readings at or above these cut-points increased. In general, within an MDRD eGFR category, the prevalence of elevated blood pressure, particularly at or above the 130/85 mm Hg cut-point, was higher in KEEP participants with anemia than in those without (Figure 5.15).

Figure 5.16 displays the interaction of smoking and MDRD eGFR with the prevalence of elevated blood pressure ($>140/90$ mmHg). With the exception of the lowest eGFR category, current smokers had a lower prevalence of elevated blood pressure than either previous smokers or those who have never smoked. Similar trends were observed when the BP threshold was lowered to $>130/85$ mmHg.

Figure 5.1 · percent distribution of KEEP participants with elevated serum creatinine levels, overall & by age

KEEP: n=10,725; excludes participants with missing serum creatinine values; elevated levels: >1.5 mg/dl in men, >1.3 mg/dl in women

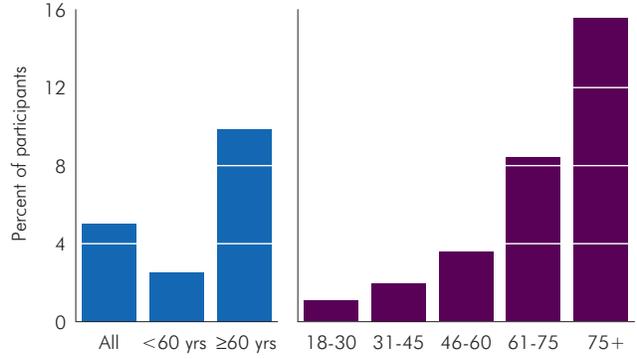


Figure 5.2 · percent distribution of KEEP participants with elevated serum creatinine levels, by race

KEEP: n=10,413; excludes participants with missing serum creatinine values or unknown or missing race; elevated levels: >1.5 mg/dl in men, >1.3 mg/dl in women

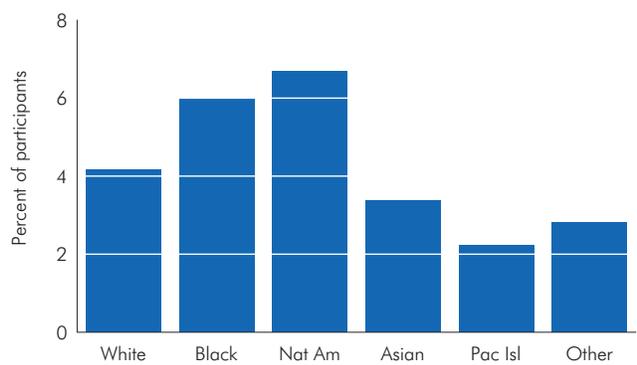


Figure 5.3 · percent distribution of KEEP participants with eGFR using MDRD and Cockcroft-Gault methods, overall & by age & gender

KEEP: MDRD eGFR, n=10,725; CG, n=10,614; excludes participants with missing values

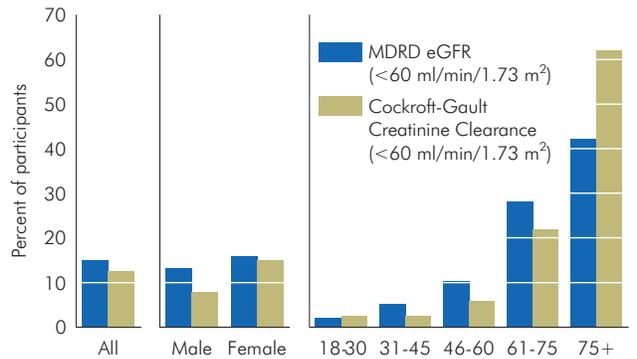


Figure 5.4 · percent distribution of KEEP participants with eGFR using MDRD and Cockcroft-Gault methods, by race

KEEP: MDRD eGFR, n=10,413; CG, n=10,308; excludes participants with missing values

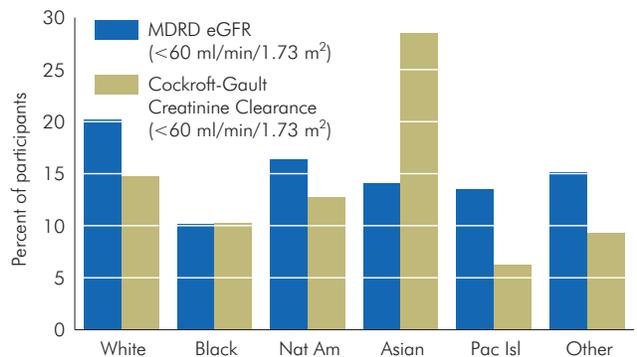


Figure 5.5 · percent distribution of KEEP participants with eGFR using MDRD and Cockcroft-Gault methods, by Hispanic ethnicity

KEEP: MDRD eGFR, n=7,195; CG, n=7,142; excludes participants with missing ethnicity

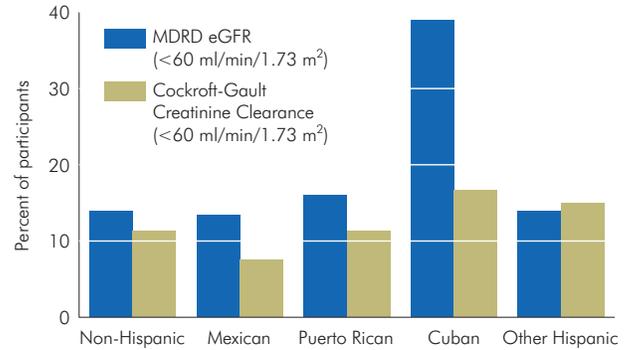


Figure 5.6 · percent distribution of KEEP participants with eGFR using MDRD and Cockcroft-Gault methods, by U.S. region

KEEP: MDRD eGFR, n=10,725; CG, n=10,614; excludes participants with missing values

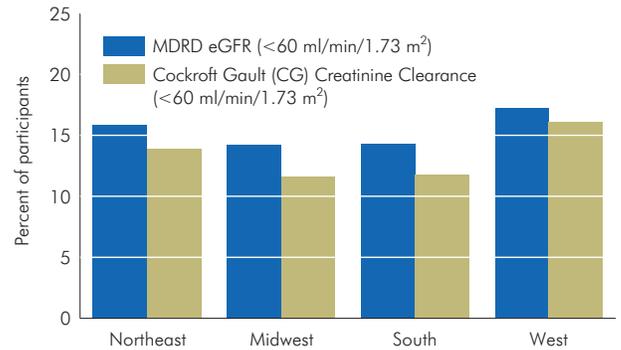


Figure 5.7 · percent distribution of KEEP participants with CKD, by CKD status

KEEP: n=10,651; excludes participants with missing eGFR; CKD defined by eGFR <60 ml/min/1.73 m² (MDRD formula) or presence of microalbuminuria if eGFR ≥60 ml/min/1.73 m²

CKD stages	
Stage 1:	CCR ≥ 90, microalbuminuria = +
Stage 2:	CCR 60–89, microalbuminuria = +
Stage 3:	CCR 30–59
Stage 4:	CCR 15–29
Stage 5:	CCR < 15 or patient on dialysis

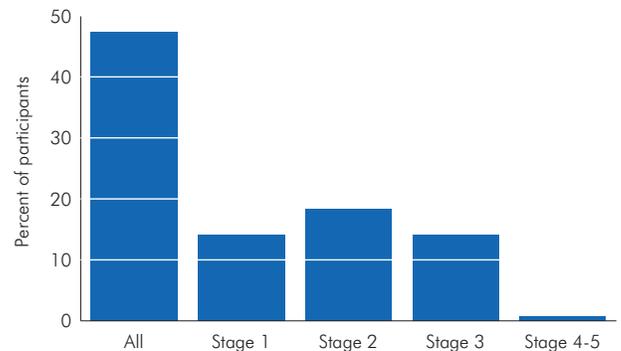


Figure 5.8 · percent distribution of KEEP participants with CKD, by age & gender

KEEP: n=10,651; excludes participants with missing eGFR; CKD defined by eGFR <60 ml/min/1.73 m² (MDRD formula) or presence of microalbuminuria if eGFR ≥60 ml/min/1.73 m²

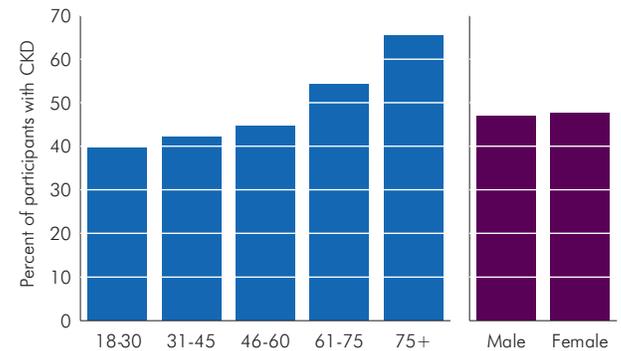


Figure 5.9 · percent distribution of KEEP participants with CKD, by race & Hispanic ethnicity

KEEP: n=10,343; excludes participants with missing eGFR or race; CKD defined by eGFR <60 ml/min/1.73 m² (MDRD formula) or presence of microalbuminuria if eGFR ≥60 ml/min/1.73 m². Race & Hispanic ethnicity are not mutually exclusive.

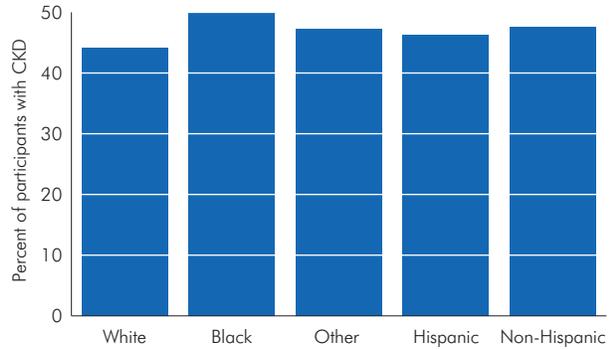
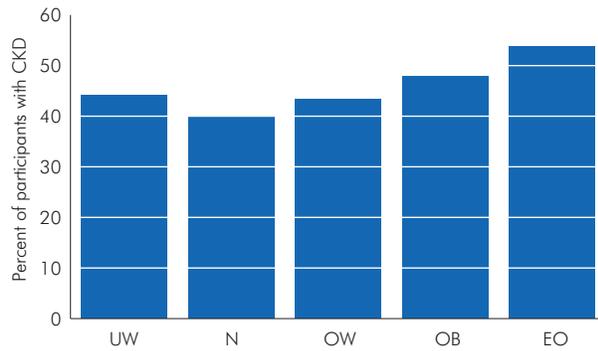


Figure 5.10 · percent distribution of KEEP participants with CKD, by BMI

KEEP: n=11,122; excludes participants with missing eGFR or BMI values; CKD defined by eGFR <60 ml/min/1.73 m² (MDRD formula) or presence of microalbuminuria if eGFR ≥60 ml/min/1.73 m²

BMI index
 BMI <18.5: UW: Underweight
 BMI 18.5–24.9: N: Normal
 BMI 25–29.9: OW: Overweight
 BMI 30–39.9: OB: Obese
 BMI ≥40: EO: Extremely Obese



FAMILY HISTORY OF KIDNEY DISEASE

Figure 5.11 · percent distribution of KEEP participants with a family history of kidney disease, overall & by gender

KEEP: n=10,960 total, 2,707 with a reported family history of kidney disease; excludes participants with missing family history

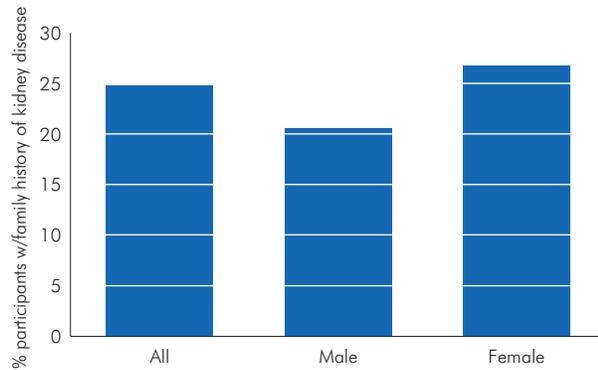


Figure 5.12 · percent distribution of KEEP participants with a family history of kidney disease, by race

KEEP: n=10,637, 2,608 with a reported family history of kidney disease; excludes participants with missing family history or race

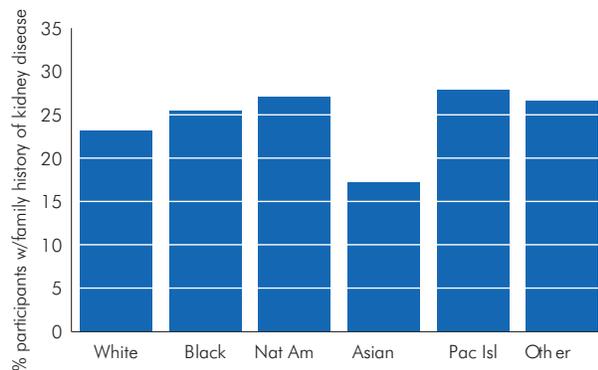
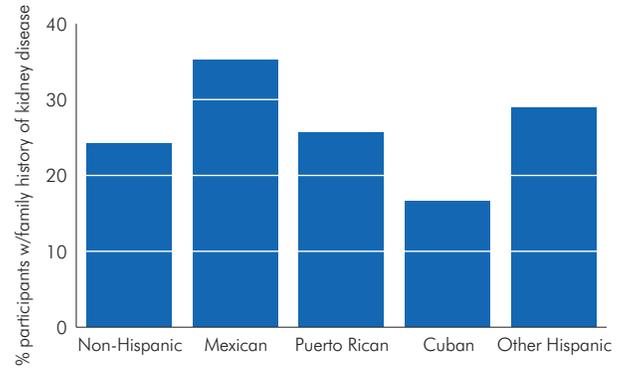


Figure 5.13 · percent distribution of KEEP participants with a family history of kidney disease, by Hispanic ethnicity

KEEP: n=7,356, 1,845 with a reported family history of kidney disease; excludes participants with missing family history or ethnicity



CATEGORIZING CKD

Table 5.1 · concordance of eGFR, BSA-CG creatinine clearance, & gender-specific cut-points for categorizing abnormal kidney function in KEEP participants

Serum creatinine	MDRD eGFR			BSA-CG creatinine clearance		
	<60	≥60	All	<60	≥60	All
Elevated	524	13	537	317	211	528
Not elevated	1,077	9,111	10,188	1,025	9,061	10,086
All	1,601	9,124	10,725	1,342	9,272	10,614

Elevated: men >1.5, women >1.3 mg/dl
 Not elevated: men ≤1.5, women ≤1.3 mg/dl
 eGFR <60 ml/min/1.73 m² = moderate reduction in kidney function

RISK FACTORS & eGFR

Table 5.2 · blood pressure levels, by stage of CKD, MDRD eGFR, & BSA-CG creatinine clearance in KEEP participants

CKD stages
 Stage 1: CCR ≥ 90, microalbuminuria = +
 Stage 2: CCR 60–89, microalbuminuria = +
 Stage 3: CCR 30–59
 Stage 4: CCR 15–29
 Stage 5: CCR <15 or patient on dialysis

	Systolic (mmHg)				Diastolic (mmHg)			
	Mean	Median	SD	Interquar. range	Mean	Median	SD	Interquar. range
MDRD								
Stage I	132.6	130.0	20.2	24.0	80.0	80.0	12.0	16.0
Stage II	135.7	133.0	20.8	28.0	80.5	80.0	11.8	16.0
Stage III	142.1	140.0	22.4	28.0	79.3	80.0	12.4	18.0
Stages IV–V	148.1	148.0	26.6	29.0	77.9	78.0	13.8	18.0
Missing	133.9	131.5	21.0	27.0	81.2	80.0	12.9	17.0
Cockcroft-Gault								
Stage I	134.8	132.0	20.2	26.0	81.4	80.0	11.9	17.0
Stage II	134.8	132.0	21.7	28.0	78.4	79.0	11.5	16.0
Stage III	140.7	140.0	23.1	30.0	77.5	78.0	12.2	15.0
Stages IV–V	144.3	142.0	24.9	30.0	75.4	77.0	11.9	14.0
Missing	134.5	132.0	21.4	28.0	80.7	80.0	12.9	18.5

Figure 5.14 · percent distribution of KEEP participants with elevated blood pressure, by CKD stage

KEEP: n=10,584; excludes participants with missing CKD stage or blood pressure value

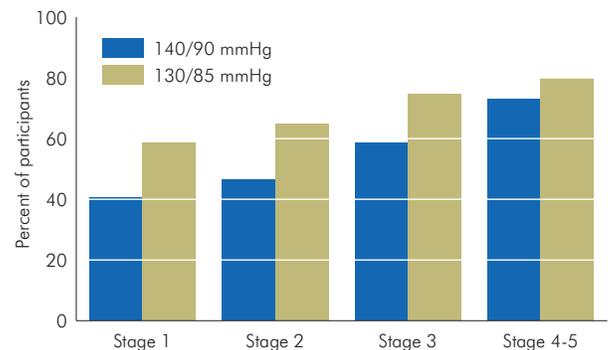


Figure 5.15 • percent distribution of KEEP participants with elevated blood pressure, by CKD stage, anemia, & eGFR

KEEP: n=10,319; excludes participants with missing CKD stage, anemia status, or blood pressure value; anemia defined by NKF-K/DOQI: males: Hgb <12 g/dl; females age >50: Hgb <12 g/dl; females age ≤50: Hgb <11 A= anemia, NA= no anemia

CKD stages

Stage 1: CCR ≥ 90, microalbuminuria = +
 Stage 2: CCR 60–89, microalbuminuria = +
 Stage 3: CCR 30–59
 Stage 4: CCR 15–29
 Stage 5: CCR <15 or patient on dialysis

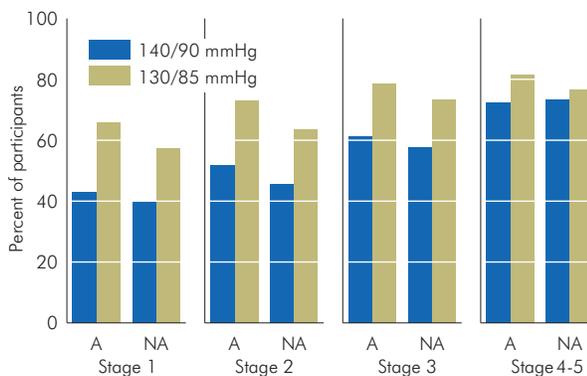
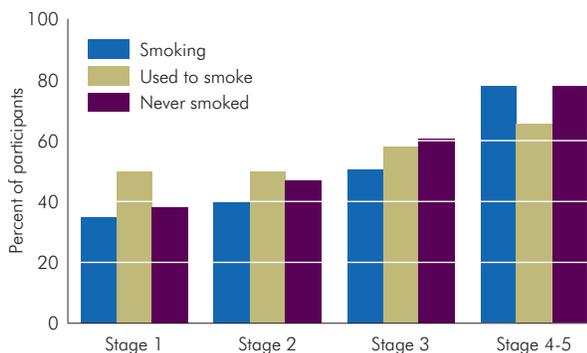


Figure 5.16 • percent distribution of KEEP participants with elevated blood pressure, by CKD & smoking status

KEEP: n=9,940; excludes participants with missing CKD status, blood pressure status, or smoking status. Hypertension based on JNC definition.

JNC VI hypertension

Stage I: systolic 140–159 or diastolic 90–99
 Stage II: systolic 160–179 or diastolic 100–109
 Stage III: systolic ≥180 or diastolic ≥110



CHAPTER SUMMARY

Figure 5.1 • Approximately five percent of KEEP participants had elevated serum creatinine levels.

Figure 5.2 • By race, the prevalence of elevated serum creatinine was highest in Native Americans and lowest in Pacific Islanders.

Figure 5.4 • Calculations using the MDRD formula show CKD to be most prevalent in whites and Native Americans, while the BSA-CG creatinine clearance shows CKD to be most prevalent in Asians and whites.

Figures 5.8 • By age, the prevalence of CKD ranged from 39.7–65.5 percent in KEEP participants.

Figure 5.10 • Extremely obese participants had the highest prevalence of CKD, while rates were much lower in individuals of normal body weight.

Figure 5.12 • By race, Asians were the least likely to report a family history of kidney disease.

Figure 5.13 • By ethnicity, one-quarter of non-Hispanics reported a family history of CKD, while in Hispanics rates ranged from 16.7 percent in individuals of Cuban ancestry to 35.2 percent in Mexican-Americans.

Figure 5.15 • Within an MDRD eGFR category, the prevalence of elevated blood pressure, particularly at or above 130/85 mmHg, was highest in KEEP participants with anemia.

Figure 5.16 • With the exception of the lowest eGFR category (Stages 4–5), current smokers had a lower prevalence of elevated blood pressure than participants who used to smoke or those who had never smoked.

Though anemia may be the result of different pathologic processes, in CKD patients its primary cause is an erythropoietin deficiency coupled with a resistance to erythropoietin. A number of investigators have shown the relationship between kidney destruction and the loss of erythropoietin production required for bone marrow cell maturation. Anemia here may also be related to increased inflammatory cytokines, which have recently been associated with CKD, and it appears as well to be a secondary complication in chronic inflammatory conditions, apparently due to the

The prevalence of anemia increased with age in both KEEP and NHANES III participants, as it does in the general U.S. population. As expected, because of the study's unique patient screening and its higher prevalence of CKD, almost twice as many KEEP participants were anemic. Nearly 20 percent of blacks in both KEEP and NHANES III had anemia, while in other racial and ethnic groups anemia was more common in KEEP participants, consistent with their higher degree of CKD (Figures 6.2–3).

CHAPTER SIX

inflammatory blockade of iron use from the reticuloendothelial system.

While anemia is a common complication of end-stage renal disease—more than half of all patients have hemoglobins less than 10 g/dl at the start of dialysis, and 75 percent have levels less than 11 g/dl (the lower end of the K/DOQI guidelines for treatment of anemia in ESRD)—the prevalence of anemia in different stages of CKD has only recently received attention. We explore here the associations between anemia and the characteristics of people with CKD. To define anemia, we use criteria set by WHO: in males: a hemoglobin <13 g/dl in men, and <12 g/dl in women.

Anemia

Using definitions of CKD proposed by the NKF, Figure 6.1 shows that Stage 2 CKD was the most common stage found in KEEP participants (38.9 percent), and Stage 3 was most common in NHANES III participants (38.0 percent).

Anemia & Chronic Kidney Disease

Anemia in CKD and non-CKD participants

Our next set of figures illustrates the prevalence of anemia in CKD and non-CKD populations. Anemia was most com-

mon in KEEP participants with CKD, and 1.3 times more likely in these participants than in their NHANES counterparts with CKD. Even in the population with normal renal function and no evidence of microalbuminuria, however, KEEP patients were 1.6 times more likely than NHANES participants to be anemic. Some of these differences may relate to variations in age, gender, and race between the KEEP participants and the general Medicare population (Figure 6.4).

Racial differences by the presence of CKD were also strong. In both KEEP and NHANES III participants, and regardless of CKD status, black participants were more likely than whites to be anemic. And as expected, women had a far greater degree of anemia than men, particularly among participants without CKD (Figures 6.5–6).

I learned something I didn't know was wrong with me. I am very glad I went & found out some things that I can get work on to help me stay healthy. Thanks.

Callie Rogers, Indiana;
February 2002

Anemia and stages of CKD

KEEP data by stages of CKD show that advancing levels of the disease were associated with a higher likelihood of anemia, and that, in participants with Stage 3 CKD and higher, diabetics had consistently higher degrees of anemia than those without diabetes. In Stage 3 CKD participants, for example, anemia occurred in more than four times as many diabetics as non-diabetics, and was 29 percent more likely in diabetics with CKD of Stage 4 or 5. In patients with CKD of these highest two stages, gender differences were also especially pronounced. The percentage of women with hemoglobin levels less than 11 g/dl was more than four times that of men. And by race, blacks and other minorities with CKD of Stage 4 or 5 were more than twice as likely as their white counterparts to be anemic (Figures 6.7–9).

Odds of anemia

Using a multivariate logistic regression model we investigated the odds of anemia. In both the KEEP and NHANES III populations, the odds ratios for anemia were 1.7 and 2.7 times higher in patients with an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 m² than in those with eGFRs \geq 90 ml/min/1.73 m². Anemia was more likely in older patients, particularly those age 75 and above, and in the KEEP population the likelihood of anemia in black diabetics was more than four times that in whites without diabetes (Figures 6.10–12).

Based on these findings, the KEEP participants show an expected pattern of consistency of anemia at more advanced stages of chronic kidney disease when compared to the general population. Diabetics appear to be more vulnerable to this anemia, particularly at Stage 3 and higher for more ad-

vanced chronic kidney disease. People of older age, females, and particularly the black population consistently had high odds ratios for anemia, at up to four times greater than that of the white population.

These findings show a strong relationship between anemia and the most advanced stages of CKD. They also, however, illustrate the degree of anemia in patients with Stage 3 CKD, indicated by an eGFR of 30–60 ml/min/1.73 m², and the increased occurrence of anemia in blacks. Given recent concerns that anemia may contribute to both congestive heart failure, a common complication of advancing CKD, as well as progressive loss of kidney function, clinical assessment of anemia and its correctable factors should be undertaken in these populations.

It is not clear whether the correction of anemia to levels greater than 13 g/dl in men and 12 g/dl in women would improve outcomes. Further interventional trials and additional epidemiologic studies are required to assess the long-term effects of mild to moderate anemia in CKD patients.

Mean C-reactive protein and anemia

In this chapter's final set of figures we investigate mean C-reactive protein levels (CRP) in NHANES III participants and their association with anemia. Data show that, with few exceptions, there is a cross-sectional relationship between stages of CKD and rising CRP levels. This study confirms these findings in a general population study. It is conceivable that inflammation could cause decreased GFR levels. It is also possible, however, that decreased GFR could cause an increase in CRP levels, and further studies are needed to determine the direction of the effect (Figures 6.13–15).

Figure 6.1 • percent distribution of KEEP & NHANES III participants with chronic kidney disease

KEEP: n=5,051, NHANES III: n=2,252; CKD status defined by calculated creatinine clearance using the MDRD formula. Stage 5 in NHANES III data does not include patients on dialysis

CKD stages

- Stage 1: CCR ≥ 90, microalbuminuria = +
- Stage 2: CCR 60–89, microalbuminuria = +
- Stage 3: CCR 30–59
- Stage 4: CCR 15–29
- Stage 5: CCR <15 or patient on dialysis

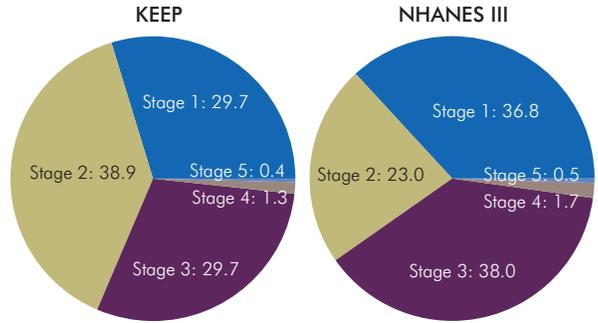


Figure 6.2 • percent distribution of KEEP & NHANES III participants with anemia (WHO definition), by age

KEEP: n= 10, 448, NHANES III: n=16,795; excludes participants with missing hemoglobin values

WHO anemia definition

- Male: Hemoglobin <13 g/dl
- Female: Hemoglobin <12 g/dl

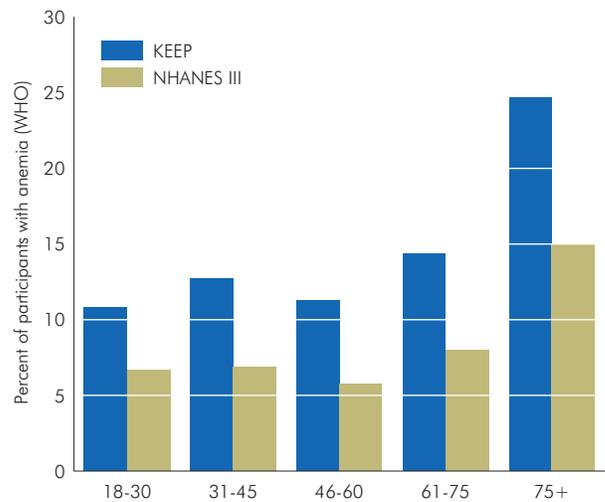


Figure 6.3 • percent distribution of KEEP & NHANES III participants with anemia (WHO definition), by race/ethnicity

KEEP: race, n=10,136, Hispanic ethnicity, n=10,448, NHANES III: n=16,795; excludes participants with missing race, ethnicity, or hemoglobin values. Race & Hispanic ethnicity are not mutually exclusive.

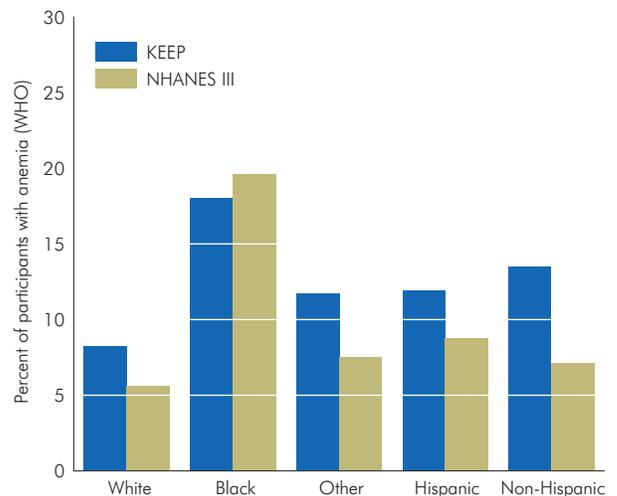


Figure 6.4 · percent distribution of KEEP & NHANES III participants with anemia (WHO definition), by CKD status

KEEP: total, n=10,332, anemia, n=1,376,
NHANES III: n=15,670

Definition of CKD

If calculated creatinine clearance by K/DOQI
MDRD < 60 ml/min/1.73 m² or;
If calculated creatinine clearance by K/DOQI
MDRD ≥ 60 ml/min/1.73 m² and
microalbuminuria +

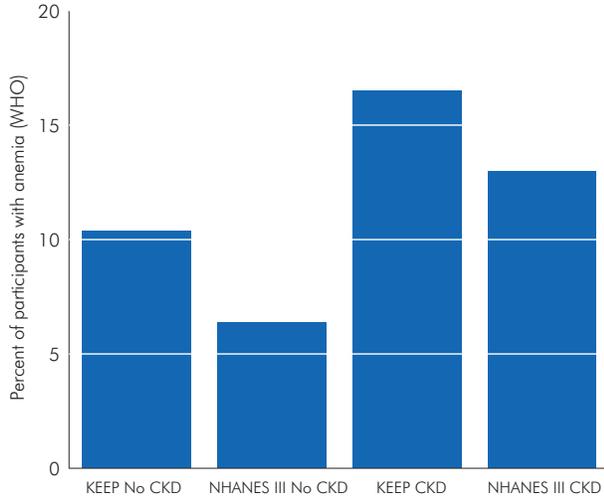


Figure 6.5 · percent distribution of KEEP & NHANES III participants with anemia (WHO definition), by race & CKD status

KEEP: non-CKD, n=5,248 CKD, n=4,779;
NHANES III: n=15,670; excludes participants with
missing race or hemoglobin values

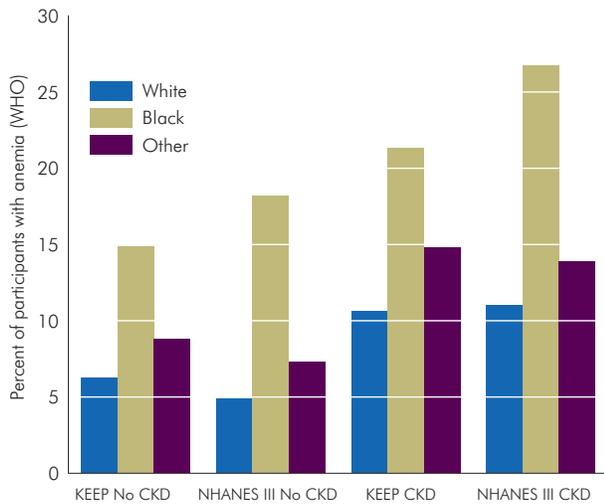


Figure 6.6 · percent distribution of KEEP & NHANES III participants with anemia (WHO definition), by gender & CKD status

KEEP: non-CKD, n=5,400, CKD, 4,932;
NHANES III: n=15,670; excludes participants with
missing hemoglobin values

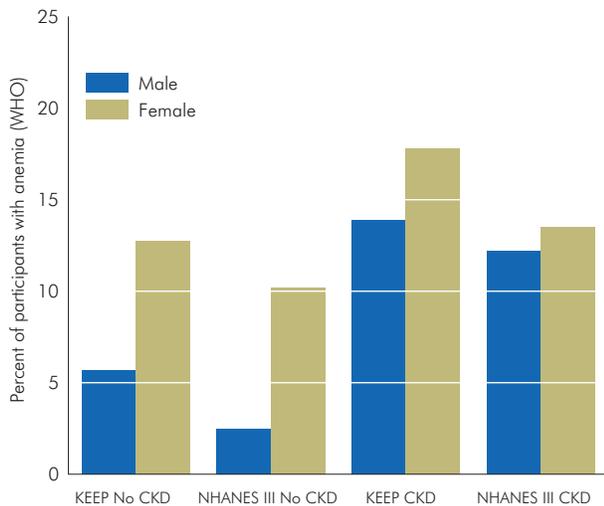


Figure 6.7 · distribution of KEEP participants with a hemoglobin less than 11 g/dl, by stage of CKD & self-reported diabetic status

KEEP: diabetics, n=2,481, non-diabetics, n=7,684; excludes participants with missing hemoglobin values or CKD stage

CKD stages
 Stage 1: CCR ≥ 90, microalbuminuria = +
 Stage 2: CCR 60–89, microalbuminuria = +
 Stage 3: CCR 30–59
 Stage 4: CCR 15–29
 Stage 5: CCR < 15 or patient on dialysis

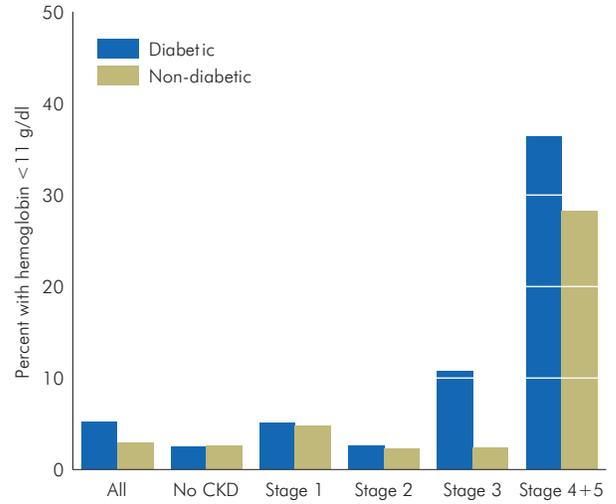


Figure 6.8 · distribution of KEEP participants with a hemoglobin less than 11 g/dl, by stage of CKD & gender

KEEP: males, n=3,424, females, n=6,908; excludes participants with missing hemoglobin values or CKD status

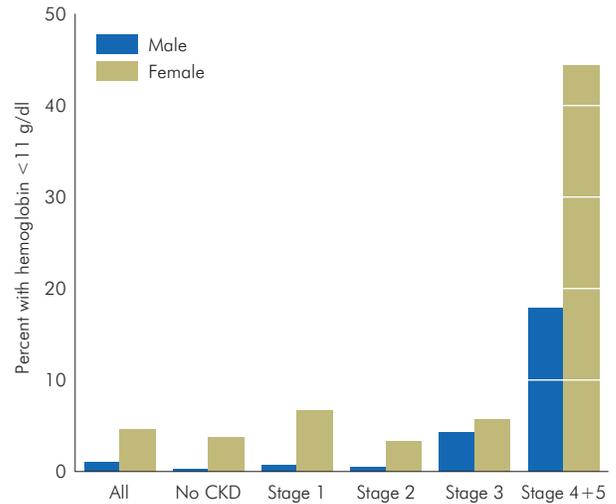
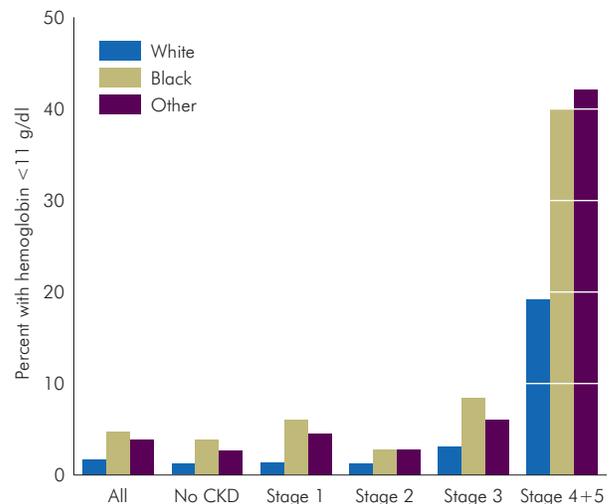


Figure 6.9 · percent of KEEP participants with a hemoglobin less than 11 g/dl, by stage of CKD & race

KEEP: white, n=3,730; black, n=4,577; other, n=1,720; excludes participants with missing hemoglobin values or CKD status



ODDS OF ANEMIA

Figure 6.10 · influence of eGFR on anemia (WHO definition)

KEEP: n=8,686, NHANES III: n=16,011; method: logistic regression, adjusted for age, gender, race, family history, & smoking status; reference is eGFR ≥ 90 ml/min/1.73 m²

WHO anemia definition

Male: Hemoglobin < 13 g/dl
Female: Hemoglobin < 12 g/dl

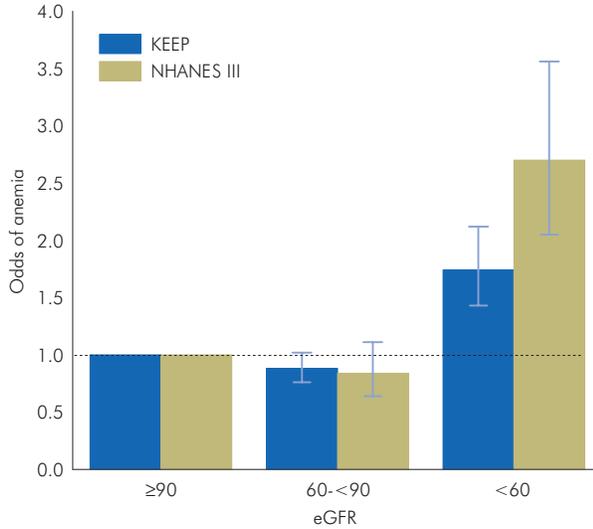


Figure 6.11 · odds of anemia (WHO definition), by age & self-reported diabetic status

KEEP: n=8,686, NHANES III: n=16,011; method: logistic regression, adjusted for gender, race, family history, & smoking status; reference is age 46-60

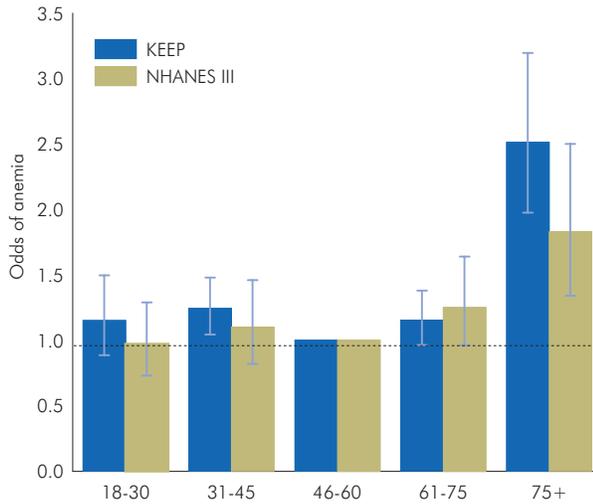
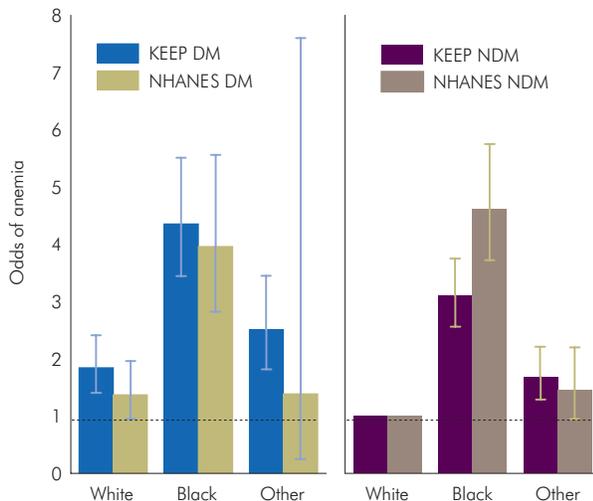


Figure 6.12 · odds of anemia (WHO definition), by race & study population

KEEP: n=8,686, NHANES III: n=16,011; method: logistic regression, adjusted for age, gender, family history, & smoking status; reference is white non-diabetics



**MEAN C-REACTIVE
PROTEIN & ANEMIA**

Figure 6.13 · mean C-reactive protein in all NHANES III patients, by CKD stage & anemia status (WHO definition)

NHANES III: *n*=16,293

CKD stages
 Stage 1: CCR ≥ 90
 Stage 2: CCR 60–89
 Stage 3: CCR 30–59
 Stage 4: CCR 15–29
 Stage 5: CCR < 15

WHO anemia definition
 Male: Hemoglobin < 13 g/dl
 Female: Hemoglobin < 12 g/dl

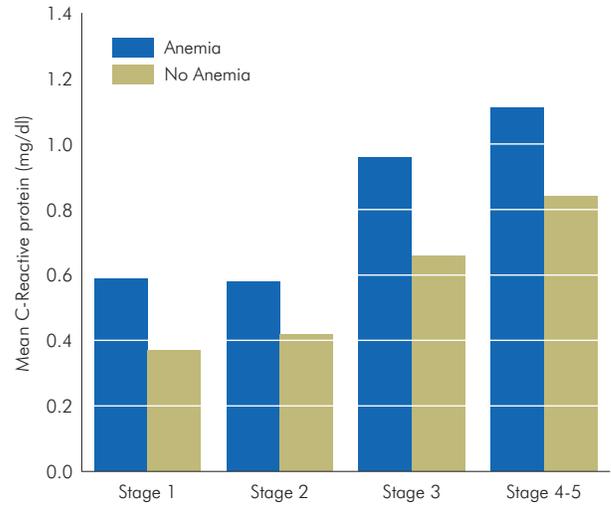


Figure 6.14 · mean C-reactive protein in NHANES III males, by CKD stage & anemia status (WHO definition)

NHANES III: *males*, *n*=7,617

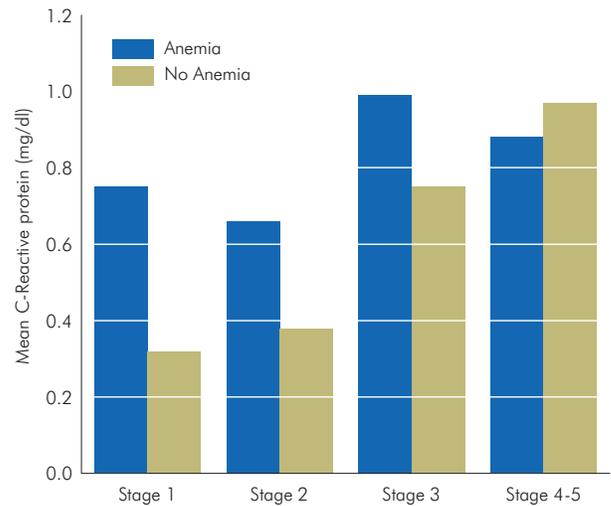
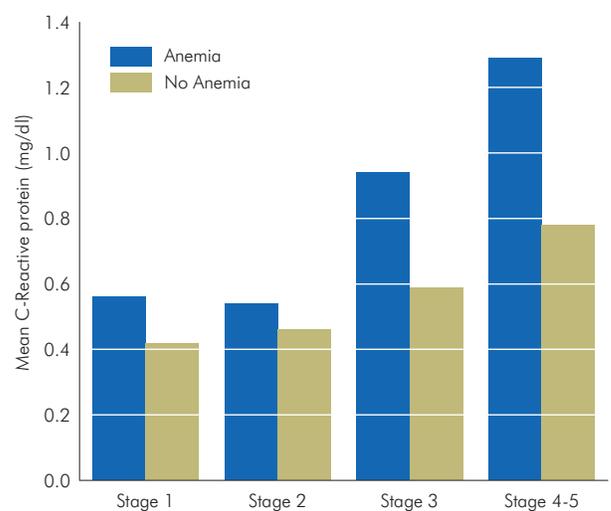


Figure 6.15 · mean C-reactive protein in NHANES III females, by CKD stage & anemia status (WHO definition)

NHANES III: *females*, *n*=8,676



CHAPTER SUMMARY

Figure 6.1 • Stage 2 CKD was the most prominent (38.9 percent) level of CKD in the KEEP participants, and Stage 3 was most common in the NHANES III population.

Figure 6.2 • The proportions of participants with anemia (WHO definition) were higher in the KEEP population compared to the NHANES III population, regardless of age.

Figure 6.3 • Black participants had the highest rates of anemia in both the KEEP and NHANES III study populations.

Figure 6.4 • Compared to non-CKD patients, rates of anemia were more pronounced in those with CKD in both the KEEP and NHANES III study populations.

Figure 6.5 • When compared to rates in whites and those of “other” races, rates of anemia in CKD and non-CKD patients were highest for blacks in both the KEEP and NHANES III populations. Overall, rates of anemia were higher in CKD patients compared to non-CKD patients.

Figure 6.6 • Females in both the KEEP and NHANES III study populations had the highest rates of anemia, regardless of CKD status.

Figure 6.7 • The proportion of participants with a hemoglobin of less than 11 g/dl was highest in both

diabetics and non-diabetics with Stage 4 or 5 CKD.

Figure 6.8 • The proportion of males and females with a hemoglobin less than 11 g/dl was highest in participants with Stage 4 or 5 CKD.

Figure 6.9 • Blacks and participants of “other” races with Stage 4 or 5 CKD represent the greatest proportion of patients with hemoglobins less than 11 g/dl.

Figure 6.10 • When compared to participants with an eGFR of greater than or equal to 90 ml/min, the odds of anemia were significantly higher in those with an eGFR of less than 60 ml/min for both the KEEP and NHANES III populations.

Figure 6.11 • Participants age 75 or older in both the KEEP and NHANES III populations had the greatest odds of anemia.

Figure 6.12 • When compared to white non-diabetics, the odds of anemia were greatest for blacks in both the KEEP and NHANES III populations, regardless of diabetic status.

Figure 6.13 • Mean CRP levels generally increased as the severity of CKD increased in both anemic and non-anemic patients.

Figure 6.15 • Mean CRP levels increases linearly in females with CKD, and this effect is most pronounced in female participants with anemia.

Chapter 1: Program Introduction

Figures 1.1–7 present KEEP (and NHANES III) participant distribution by NKF affiliate, census region and division, state, age, gender, and race. Ages were grouped into 18–30, 31–45, 46–60, 61–75, and 75+, and races into white, black, and other (Native American, Asian, Pacific Islander, and other known race). We excluded those with unknown or missing race when calculating the percent of participants by race. Hispanics included Mexican, Puerto Rico, Cuban, and other known Hispanics; those with missing data on ethnicity were categorized as non-Hispanic. Race and Hispanic

ANALYTICAL METHODS

ethnicity were not mutually exclusive, and definitions by age and race were used throughout the chapter.

Figures 1.8–12 illustrate the distribution of participants by education level, grouped as grade school or less, some high school, high school graduate, some college, college graduate, and post-graduate or professional degree. Participants with missing data on educational status were excluded.

In Figures 1.13–20 we explore participant insurance coverage and insurance type. Insurance types were grouped into Medicare only, Medicare and Medicaid, Medicare with other insurance, Non-Medicare, and unknown or missing. When calculating the distribution of participants based on insurance coverage we excluded those with unknown coverage (Figures 1.13–15); in calculations by insurance type, however, all participants are included (Figures 1.16–20).

Figures 1.21–24 illustrate KEEP participant access to medical care. Physician specialties included family practice, inter-

nal medicine, endocrinology, obstetrics/gynecology, gerontology, nephrology, and other. We have excluded participants with missing or unknown answers to this question.

Chapter 2: Participant Characteristics

Figures 2.1–5 examine the history of diabetes in KEEP and NHANES III participants. The KEEP database contains a variable denoting self-reported diabetic status; participants not reporting their status were excluded in these figures, and in figures illustrating blood pressure values participants with missing values were excluded as well. The definitions of age and racial groups in this chapter are the same as those used in Chapter 1. Figures 2.3–5 show the interaction between self-reported diabetic status and measured blood pressure, defined using classifications of JNC VI: Stage 1 (systolic 140–159 or diastolic 90–99 mmHg), Stage 2 (systolic 160–179 or diastolic 100–109), Stage 3 (systolic \geq 180 or diastolic \geq 110), and normal (systolic less than 140 mmHg or diastolic less than 90 mmHg). Elevated blood pressures include those of Stages 1 to 3.

Figures 2.6–7 present the percent of participants with self-reported hypertension, while Figures 2.8–9 illustrate participant distribution by measured blood pressure, using the JNC VI categories. In Figures 2.10–11 we compare self-reported hypertension and measured hypertension.

Figures 2.12–17 present KEEP (and NHANES III) participant characteristics by obesity, defined by body mass indices (BMIs). Underweight, normal weight, overweight, obesity, and extreme obesity were defined by BMIs $<$ 18.5, 18.5–24.9, 25–29.9, 30–39.9, and \geq 40 kg/m², respectively. Participants with missing BMIs were excluded in the analyses. Figure 2.16 also excludes participants with missing information on self-reported diabetes or hypertension, and Figure 2.17 excludes those without a measured blood pressure.

Figures 2.18–22 present the distribution of KEEP participants by smoking status, and the interaction of smoking status with self-reported diabetes and hypertension and with measured chronic kidney disease (CKD). Smoking status was

categorized as smoking, used to smoke, and never smoked, and participants not describing their status were excluded. CKD was identified by a calculated creatinine clearance (K/DOQI MDRD formula) of < 60 ml/min/1.73 m², or by a clearance ≥ 60 accompanied by evidence of microalbuminuria. We excluded participants with unknown or missing disease status, and unless otherwise noted, the calculated creatinine clearance was computed with the MDRD formula.

Figures 2.23–27 show the distribution of KEEP participants by CKD status. CKD was defined as above, and grouped into stages by calculated creatinine clearance (using the K/DOQI MDRD formula): Stage 1, ≥ 90 ml/min/1.73 m² accompanied by evidence of microalbuminuria; Stage 2, 60–89 ml/min/1.73 m² accompanied by evidence of microalbuminuria; Stage 3, 30–59 ml/min/1.73 m²; Stage 4, 15–29 ml/min/1.73 m²; and Stage 5, < 15 ml/min/1.73 m². Participants with missing creatinine clearances were excluded. We calculated the distribution of people with CKD by dividing the number with CKD in each category (i.e. male and female) by the total number in KEEP with CKD. We calculated the prevalence of CKD by dividing the number with CKD in each category by the total number in the category. Participants with missing values in each category were excluded.

Figures 2.28–31 examine family history of comorbidities: diabetes, hypertension, and kidney disease. The association between a family history of these diseases and participants' disease status is presented by illustrating their interactions in Figures 2.29, 2.30, and 2.31, respectively. Participants with unknown or missing disease status were excluded.

Chapter 3: Obesity & BMI

Figures 3.1–3 look at body frame size and BMI. Body frame size was measured by having participants place their middle finger and thumb around their wrist, and defined as small if the two overlapped, medium if they just met, or large if they did not meet. BMI categories were defined as in Chapter 2. Participants with missing body frame size or missing BMI value were excluded, and definitions of age and racial groups identical to those used in Chapter 1.

Figures 3.4–6 present the distribution of KEEP participants by BMI and self-reported diabetic status, Figures 3.7–9 look at BMI and self-reported hypertension status, and Figures 3.10–12 illustrates the relation of BMI to self-reported kidney disease. All participants with missing values were excluded.

Chapter 4: Major Risk Factors for CKD

Figure 4.1 presents trends in the numbers of incident and prevalent ESRD patients and prevalent dialysis patients in the U.S., from 1978 to 2000.

Figures 4.2–5 look at the distribution of KEEP participants by measured blood pressure, self-reported hypertension status, and family history of hypertension. Age and race/ethnicity were defined as in Chapter 1, and measured blood pressure was defined as in Chapter 2.

Figures 4.6–7 illustrate the prevalence of self-reported diabetes in KEEP participants and family members. Figure 4.8 presents the percent of self-reported diabetes by two-way interactions of race with age and ethnicity with age. Figure 4.9 presents the distribution of Hispanic participants with diabetes, by gender, and Figure 4.10 illustrates the percent of self-reported diabetes by the two-way interaction of gender with BMI. In each figure, we have excluded participants with missing values in the corresponding variables.

Figures 4.11–14 present obesity status in KEEP participants. Obesity status was categorized as in Figures 3.1–3, and obesity defined as a BMI ≥ 25 kg/m². Figure 4.11 shows participant distribution by obesity status among age and gender groups, while Figure 4.12 shows distribution of obesity status by two-way interactions of age with race, and age with ethnicity. Figure 4.13 shows the distribution of Hispanics with obesity, by gender. Figure 4.14 shows the distribution of participant obesity status by the presence of self-reported diabetes and hypertension. In each figure, we have excluded participants with missing values in the associated variables.

Figures 4.15–17 present participant distribution by smoking status, defined as in Chapter 2. Age and race were defined as in Chapter 1. In each figure we have excluded participants with missing values in the corresponding variables.

Figures 4.18–19 show the distribution of KEEP participants by anemia status. Figure 4.20 illustrates the occurrence of anemia by each interaction group of self-reported diabetic status and measured CKD stage. Anemia was defined, using NKF K/DOQI guidelines, as a hemoglobin < 12 g/dl for males or < 12 g/dl for females age > 50 years old, or a hemoglobin < 11 g/dl for females age ≤ 50 years old. Definitions of CKD stages were the same as those in Chapter 2.

Figures 4.21–25 explore risk factors for CKD. Figure 4.21 shows the percent distribution of KEEP and NHANES III participants by the number of pre-existed risk factors: self-reported diabetes, elevated blood pressure, obesity, smoking history, and anemia. In Figure 4.24 anemia was defined as a hemoglobin < 11 g/dl, regardless of gender; in all other figures, it was defined by World Health Organization (WHO) criteria: a serum hemoglobin concentration < 13 g/dl in men and < 12 g/dl in women. The percent distribution of participants with elevated blood pressure by interactions of BMI with self-reported diabetes, smoking status, or anemia status are presented in Figures 4.22, 4.23, and 4.24, respectively. In each figure we have excluded participants with missing values in the corresponding variables.

Chapter 5: CKD

Figures 5.1–2 present the distribution of KEEP participants with elevated serum creatinine levels, by age and race. Elevated serum creatinine was defined as a value > 1.5 mg/dl in men and > 1.3 mg/dl in women. Participants with missing values for serum creatinine or race were excluded.

Figures 5.3–6 show the percent of KEEP participants with eGFRs < 60 ml/min/1.73 m², using both the MDRD and Cockcroft-Gault formulas. Figures 5.7–10 present the prevalence of CKD by age, gender, race, ethnicity, and BMI. In each figure, we have excluded participants with missing values in the corresponding variables.

Figures 5.11–13 illustrate the distribution of KEEP participants with a family history of kidney disease. Participants with an unknown or missing race, ethnicity, or family history of kidney disease were excluded.

Figures 5.14–15 show the prevalence of elevated blood pressure by CKD stage and anemia status. Elevated blood pressure was defined in two ways: $\geq 140/90$ mmHg, or $\geq 130/85$ mmHg. Figure 5.16 presents prevalence of elevated blood pressure (JNC VI definition) by CKD and smoking status. Participants with missing values of blood pressure, calculated creatinine clearance, hemoglobin, and or smoking status were excluded in the corresponding figures.

Table 5.1 shows the concordance of eGFR by MDRD and BSA-CG formulas using cut-points of calculated creatinine clearance (< 60 or ≥ 60 ml/min/1.73 m²). Table 5.2 presents means, medians, standard deviations, and interquartile ranges of blood pressures by CKD stage, calculated by both MDRD and Cockcroft-Gault formulas.

Chapter 6: Anemia & CKD

Figure 6.1 shows the percent distribution of KEEP participants by CKD stage, using the MDRD formula as described for Chapter 2. Figures 6.2–3 present the prevalence of anemia (using the WHO definition, as in Chapter 5) among KEEP and NHANES III participants by age, race, and ethnicity. Participants with missing values of hemoglobin and or race were excluded.

Figures 6.4–6 present the prevalence of anemia (WHO definition) among KEEP and NHANES III participants by CKD status, which was defined as in Chapter 2. Participants with missing values of hemoglobin, calculated creatinine clearance, or race were excluded.

Figures 6.7–9 illustrates the percent distribution of KEEP participants with a hemoglobin < 11 g/dl by CKD stage. Participants with missing values of hemoglobin, calculated creatinine clearance, diabetes status, or race were excluded.

Figures 6.10–12 present odds ratios of anemia (WHO definition) for KEEP and NHANES III participants by eGFR, age, and interaction of race with self-reported diabetes status. A logistic regression was used, with a total sample size of 8,686 after excluding all missing values. The explanatory variables were age; ethnicity; family history of diabetes, hypertension, and kidney disease; interaction of race and self-reported diabetic status; and eGFR. Age was grouped into 18–30, 31–45, 46–60 (reference), 61–75, and 75+. Ethnicity was grouped into Hispanic and non-Hispanic (reference), and races into white, black, and other. Family history of disease was defined

as “yes” or “no” (reference). White non-diabetics were chosen as the reference group for the interaction between race and self-reported diabetic status. Estimate GFR levels were grouped into < 60, 60–<90, and ≥ 90 (reference).

Figures 6.13–15 present mean C-reactive protein levels for NHANES III participants by CKD stage and gender.

NHANES III

DATABASE DESIGN, SETTING, & STUDY PARTICIPANTS

NHANES III, the Third National Health and Nutrition Examination Survey, was the seventh in a series of large health examination surveys conducted in the United States beginning in 1960. The survey was conducted in two phases from 1988 to 1994 by the National Center of Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC).

NHANES III used a stratified, multi-stage probability design, and included oversampling of Mexican Americans, non-Hispanic blacks, the elderly, and children to allow the calculation of more precise prevalence estimates of health indicators in these groups. During the six years, 39,695 persons were selected; of these, 33,994 were interviewed in their homes to obtain information about sociodemographic factors, medical history, nutrition history, and family history. All interviewed persons were invited to the mobile examination center (MEC) for a detailed medical examination. Seventy-eight percent of the selected persons were examined in the MEC, and an additional 493 persons were given a special, limited examination in their homes.

This cross-sectional survey provides national representative data on the health and nutritional status of the civilian, non-institutionalized population in the U.S. For comparison purposes, all samples analysed used data collected in both Phase I and Phase II (19,618 participants age 18 or older).

MEASUREMENTS

Age, gender, race, ethnicity, and census region

Age was defined as the participant’s age at the time of the household interview, and grouped into 18–30, 31–45, 46–60, 61–75, and 76+. Race was defined as white, black and other, and ethnicity as Hispanic (including Mexican-American and other Hispanic) and non-Hispanic. Census regions were identified as Northeast, Midwest, South, and West.

Education level

Education level was defined by the number of school years completed, including grade school or less (0–6 years), some high school (7–11 years), high school graduate (12 years), some college (13–15 years), college graduate (16 years), and post-graduate or professional degree (17+ years).

Insurance

Participants were considered insured if they answered yes to any of the following questions: “During the last month was covered by Medicare?” “During the last month was covered by Medicaid?” “During the last month was covered by

CHAMPUS, CHAMPVA, the VA or military healthcare?”
 “During the last month was covered by one or more health insurance plans obtained privately or through an employer or union?”

Diabetes

Self-reported diabetes was defined by an affirmative answer to the question: “Have you ever been told by a doctor that you had diabetes or sugar diabetes?”

Hypertension

Self-reported hypertension was identified by an affirmative answer to the question: “Have you ever been told by a doctor that you had hypertension, also called high blood pressure?” Diagnosed hypertension was defined as in Chapter 2.

Obesity

BMI (weight in kilograms / height in m²) was calculated from the recorded physical examination data. To examine the effects of body size, participants were grouped by BMI category, as defined for Chapter 2.

Smoker status

Smokers were identified by an affirmative answer to the question: “Have you smoked at least 100 cigarettes during your entire life?” This definition is used in Chapter 4 for risk factor analyses. Smokers were grouped further based on their answers to the question: “Do you smoke cigarettes now?” If the answer was “No,” the participant was classified as an “ex-smoker.” If the answer was “Yes,” the participant was defined as a “current smoker.” This definition is used in Chapter 6 for logistic model analyses.

Anemia

Using criteria from WHO, anemia was defined as a serum hemoglobin concentration below 13 g/dl in men and below 12 g/dl in women.

Microalbuminuria

Urine albumin concentration (mg/l) was measured by solid-phase fluorescent immunoassay. Urinary creatinine concentration in (mg/dl) was measured by the modified kinetic method of Jaffe using a Beckman Synchron AS/ASTRA analyzer (Beckman Instruments Inc, Brea, CA). Participants with valid ratios of urinary albumin to urinary creatinine (ACR) were classified as having microalbuminuria if this value was 30–300 mg/g.

CKD

Serum creatinine was measured by the modified kinetic Jaffe reaction using a Hitachi 737 analyzer (Boehringer Mannheim Corp, Indianapolis, IN) at White Sands Research Center (Almogordo, NM), and was recalibrated to the results at the Cleveland Clinic (Cleveland, OH). Glomerular filtration rate (ml/min/1.73 m²) was estimated by the MDRD method based on adjusted creatinine value:

$$\text{Estimated GFR} = 186.3 * (\text{serum creatinine})^{-1.154} * \text{age}^{-0.203} * (0.742 \text{ for women}) * (1.21 \text{ if African American})$$

CKD was defined as an eGFR less than 60 ml/min/1.73m², or an eGFR greater than or equal to 60 ml/min/1.73m² in the presence of microalbuminuria.

For Figures 6.13–15 in Chapter 6, participants were classified into four CKD groups, based on eGFR levels in ml/min/1.73 m²: Stage 1 (eGFR ≥ 90), Stage 2 (60 ≤ eGFR < 90), Stage 3 (30 ≤ eGFR < 60) and Stage 4–5 (eGFR < 30).

STATISTICAL ANALYSIS

To obtain national estimates of each statistic in these complex sample surveys, including prevalence and odds ratios, sampling weights, and survey design were implemented by SUDAAN (Research Triangle Institute, Research Triangle Park, NC). A weighted logistic regression model was used to examine the relationship between WHO anemia and eGFR. Estimated GFR was grouped as 0–59.9, 60–89.9 and 90+ ml/min/1.73 m². Estimated GFR was examined in the model, and adjusted for risk factors of age (grouped as before), ethnicity (Hispanic/Non-Hispanic), race (white/black/other), smoking status (non-smoker, ex-smoker, current smoker), relatives having diabetes (yes/no), and the interaction term between race and self-reported diabetes.

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