



The Future Burden of CKD in the United States: A Simulation Model for the CDC CKD Initiative

Thomas J. Hoerger, PhD,¹ Sean A. Simpson, MA,¹ Benjamin O. Yarnoff, PhD,¹ Meda E. Pavkov, MD, PhD,² Nilka Ríos Burrows, MPH, MT,² Sharon H. Saydah, PhD,² Desmond E. Williams, MD, PhD,² and Xiaohui Zhuo, PhD²

Background: Awareness of chronic kidney disease (CKD), defined by kidney damage or reduced glomerular filtration rate, remains low in the United States, and few estimates of its future burden exist.

Study Design: We used the CKD Health Policy Model to simulate the residual lifetime incidence of CKD and project the prevalence of CKD in 2020 and 2030. The simulation sample was based on nationally representative data from the 1999 to 2010 National Health and Nutrition Examination Surveys.

Setting & Population: Current US population.

Model, Perspective, & Timeline: Simulation model following up individuals from current age through death or age 90 years.

Outcomes: Residual lifetime incidence represents the projected percentage of persons who will develop new CKD during their lifetimes. Future prevalence is projected for 2020 and 2030.

Measurements: Development and progression of CKD are based on annual decrements in estimated glomerular filtration rates that depend on age and risk factors.

Results: For US adults aged 30 to 49, 50 to 64, and 65 years or older with no CKD at baseline, the residual lifetime incidences of CKD are 54%, 52%, and 42%, respectively. The prevalence of CKD in adults 30 years or older is projected to increase from 13.2% currently to 14.4% in 2020 and 16.7% in 2030.

Limitations: Due to limited data, our simulation model estimates are based on assumptions about annual decrements in estimated glomerular filtration rates.

Conclusions: For an individual, lifetime risk of CKD is high, with more than half the US adults aged 30 to 64 years likely to develop CKD. Knowing the lifetime incidence of CKD may raise individuals' awareness and encourage them to take steps to prevent CKD. From a national burden perspective, we estimate that the population prevalence of CKD will increase in coming decades, suggesting that development of interventions to slow CKD onset and progression should be considered.

Am J Kidney Dis. 65(3):403-411. © 2015 by the National Kidney Foundation, Inc. Published by Elsevier Inc. All rights reserved.

INDEX WORDS: Chronic kidney disease (CKD); disease burden; simulation model; lifetime incidence; prevalence; disease trajectory; United States; CKD Health Policy Model; Centers for Disease Control and Prevention CKD Initiative; public health.

Chronic kidney disease (CKD) is a major cause of morbidity, mortality, and high medical costs in the United States, particularly among older adults.¹ Nearly 1 in 7 adults has CKD,² and recent data suggest that the number of deaths from CKD has doubled in the past 2 decades.³ In addition to its burden on health, CKD requires substantial US health care resources. End-stage renal disease (ESRD), the most severe stage of CKD, cost Medicare \$32.9 billion in 2010,¹ and earlier stages of CKD cost Medicare an estimated \$48 billion in 2010.⁴

Despite the increasing prevalence and high cost associated with CKD, awareness of the disease remains low in the United States.⁵ Many Americans do not know that they are at risk for CKD, and few estimates of the future burden of the disease exist for either individuals or the nation. In this study, we provide 2 measures of the future burden of CKD that represent individual and national perspectives on the future burden of the disease. First, we estimate the residual lifetime

incidence of CKD (ie, the probability that someone will develop CKD during his or her remaining lifetime) among current adult cohorts aged 30 to 49, 50 to 64, and 65 years or older. These estimates provide individuals with information on the risk of incurring CKD in their lifetime. Second, we estimate the prevalence of CKD among US adults 30 years or older and 65 years or older in 2020 and 2030, which provides a national perspective on the future burden at a population level.

From ¹RTI International, Research Triangle Park, NC; and ²Centers for Disease Control and Prevention, Atlanta, GA.

Received March 13, 2014. Accepted in revised form September 8, 2014. Originally published online November 25, 2014.

Address correspondence to Thomas J. Hoerger, PhD, RTI International, 3040 E Cornwallis Rd, PO Box 12194, Research Triangle Park, NC 27709. E-mail: tjh@rti.org

© 2015 by the National Kidney Foundation, Inc. Published by Elsevier Inc. All rights reserved.

0272-6386

<http://dx.doi.org/10.1053/j.ajkd.2014.09.023>

METHODS

Model Overview

We used the CKD Health Policy Model, a microsimulation model of CKD progression that has been described in detail elsewhere.⁶⁻⁸ Briefly, the model simulates the natural history of CKD for persons from age 30 years through death or the age of 90 years. The model includes 7 states: no CKD, CKD stages 1 through 5, and death. The CKD stages are defined by estimated glomerular filtration rates (eGFRs) and the presence of elevated albuminuria, following NKF-KDOQI (National Kidney

Foundation–Kidney Disease Outcomes Quality Initiative) guidelines.⁹ Figures S1 and S2 (provided as online supplementary material) outline the model structure. Model parameters were derived from the epidemiologic literature, clinical trials, and a previous cost-effectiveness study by Boulware et al.¹⁰ Key disease progression parameters are shown in Tables 1 and 2.

For this analysis, we based the cohort to be simulated in the model on a nationally representative sample of adults 30 years or older. The data were drawn from persons who participated in NHANES (National Health and Nutrition Examination Survey) from 1999 through 2010. For the persons drawn, we simulated

Table 1. Model Variables

Variable	Value	Source
Population		
Age when disease progression begins	30 y	Assumption
Distribution by age, sex, race/ethnicity	NHANES observations	NHANES 1999-2010
Natural history		
Initial eGFR	NHANES observations	NHANES 1999-2010
Moderately increased albuminuria incidence	Estimated from NHANES; varies by age, sex, DM, HTN	NHANES data
Severely increased albuminuria transitions	Estimated from NHANES; varies by age, sex, DM, HTN	NHANES data; Adler et al ¹¹
Risk factors and complications		
Total cholesterol, HDL cholesterol, SBP, smoking	NHANES observations	NHANES 1999-2000
DM incidence	0.28%-1.61%; varies by age, sex, race/ethnicity	Cowie et al, ¹² Geiss et al ¹³
LVH, prevalence and incidence with CKD	Prevalence, 16%-33%; incidence, 51%-61%; varies by sex, race/ethnicity	Family Blood Pressure Program; Paoletti et al, ¹⁴ Cottone et al ¹⁵
Framingham CHD probability	Function of age, sex, SBP, cigarette use, total cholesterol, HDL cholesterol, DM, LVH	Anderson et al ¹⁶
Framingham MI probability	Function of age, sex, SBP, cigarette use, total cholesterol, HDL cholesterol, DM, LVH, prior CVD	Anderson et al ¹⁶
Framingham stroke probability	Function of age, sex, SBP, cigarette use, total cholesterol, HDL cholesterol, DM, LVH, prior CVD	Anderson et al ¹⁶
HR for cardiac events for existing CVD patients	2.19	Weiner et al ¹⁷
HR for stroke for existing CVD patients	1.86	Weiner et al ¹⁷
CKD multiplier for CVD risk	Ranges from 1 for eGFR \geq 60 to 4.8 at eGFR = 15	Go et al ¹⁸
Mortality		
Annual background mortality	Total–CVD mortality; varies by age, sex, race/ethnicity	2003 Census Life Tables (Arias ¹⁹); NCHS ²⁰
ESRD mortality	Varies by age, sex, race/ethnicity, DM, HTN	2010 USRDS data
CKD multiplier for background mortality	Ranges from 1 at eGFR \geq 60 to 4.8 at eGFR = 15	Go et al, ¹⁸ assumption
Excess mortality due to stroke, by age		
<65 y	0.14	Sacco et al ²¹
\geq 65 y	0.32	
Excess mortality due to MI, by age		
30-44 y	0.015 for first MI, 0.087 for other MI	Hunink et al ²² ;
45-54 y	0.034 for first MI, 0.112 for other MI	Weinstein et al ²³
55-64 y	0.073 for first MI, 0.145 for other MI	
65-74 y	0.159 for first MI, 0.187 for other MI	
\geq 75 y	0.295 for first MI, 0.295 for other MI	

Note: eGFR is expressed as mL/min/1.73 m².

Abbreviations: CHD, coronary heart disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HDL, high-density lipoprotein; HR, hazard ratio; HTN, hypertension; LVH, left ventricular hypertrophy; MI, myocardial infarction; NCHS, National Center for Health Statistics; NHANES, National Health and Nutrition Examination Survey; SBP, systolic blood pressure; USRDS, US Renal Data System.

Table 2. Annual eGFR Decrements by Age

Diabetes/Hypertension Status	eGFR	Age 30-49 y	Age \geq 50 y
Neither	No proteinuria	\geq 60	0.85
		<60	0.85
	Proteinuria	\geq 60	0.935
		<60	4.2
Hypertension	No proteinuria	\geq 60	0.935
		<60	1.4
	Proteinuria	\geq 60	1.02
		<60	3.9
Diabetes	No proteinuria	\geq 60	0.935
		<60	2.8
	Proteinuria	\geq 60	4.1
		<60	5.2

Abbreviation and definition: eGFR, estimated glomerular filtration rate expressed as mL/min/1.73 m². Rates for African Americans are multiplied by 1.25 and 1.5 for eGFRs of 30 to 59 and 15 to 29 mL/min/1.73 m², respectively; corresponding rates for non-African Americans are multiplied by 0.875 and 0.8 (Hoerger et al⁸).

Source: Boulware et al¹⁰ and authors' analysis of 1999 to 2010 National Health and Nutrition Examination Survey data.

future albuminuria and eGFR trajectories to estimate CKD stages 1 through 5. We focused on CKD prevalence among adults 30 years or older because eGFR typically begins declining after age 20 to 30 years.^{9,24} Measures of the prevalence of albuminuria, the other component in defining CKD, vary widely between childhood and early adulthood.⁹ Therefore, the model is designed to simulate disease progression beginning at age 30 years (the relatively few prevalent cases of CKD at age 30 are incorporated in the simulation starting values) and follows up persons as their eGFRs decline and/or they develop persistent albuminuria.

Lifetime Incidence of CKD

For the lifetime incidence estimates for the age groups 30 to 49, 50 to 64, and 65 years or older, we created cohorts of persons drawn from NHANES 1999 to 2010 data. For each person, we drew an actual observation from the cohort age group from NHANES, keeping a person's starting age, sex, race/ethnicity, eGFR, albuminuria status (normal, moderately increased albuminuria, or severely increased albuminuria), diabetes status, hypertension status, and cardiovascular disease status. We estimated eGFR using the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation.²⁵ Because CKD staging is based on persistent albuminuria and NHANES includes only one observation, we adjusted observed moderately increased albuminuria using an algorithm proposed by Coresh et al.²

Using these starting values for each person in the cohort, we simulated the person's progression through the model until the person dies or reaches the age of 90 years. The starting year for the simulation is 2010. During each year, a person can develop diabetes, hypertension, or albuminuria. The person's eGFR declines annually, with decrements higher for persons who have diabetes, hypertension, severely increased albuminuria, or eGFR < 60 mL/min/1.73 m² or who are 50 years or older (see Table 2).¹⁰ eGFR progression rates also are faster for African Americans with eGFRs < 60 mL/min/1.73 m².⁸ Persons with

diabetes or hypertension are more likely to develop moderately increased albuminuria, and persons with moderately increased albuminuria are more likely to develop severely increased albuminuria. A stochastic multiplicative variable allows eGFR progression to vary between persons with the same risk factors. Further details on progression are available elsewhere.⁶⁻⁸

We calculated residual lifetime risk of CKD as the probability of reaching any stage of CKD (stages 1-5) in persons who do not have CKD at the start of the simulation. We also estimated residual lifetime incidence of CKD stage 3a+ (eGFR < 60 mL/min/1.73 m²), stage 3b+ (eGFR < 45 mL/min/1.73 m²), stage 4+ (eGFR < 30 mL/min/1.73 m²), and stage 5 (eGFR < 15 mL/min/1.73 m²) for persons who are not in these stages at the start of the simulation. In the simulation, persons who reach stage 3b must first go through stage 3a; similarly, those who reach stage 4 must go through stages 3a and 3b, and those who reach stage 5 must go through stages 3a, 3b, and 4. However, it is possible to reach stage 3a or higher without going through stages 1 and 2 if a person never has elevated albuminuria.

In addition, we calculated the unconditional lifetime incidence of CKD as the probability of starting with or progressing to any stage of CKD; this calculation accounts for persons who have CKD at the start of the simulation, as well as the residual lifetime incidence for persons who do not have CKD at the start. We calculated unconditional lifetime incidence for CKD stages 3a+, 3b+, 4+, and 5 in an analogous fashion.

Projecting Prevalence in 2020 and 2030

To project the prevalence of CKD among adults 30 years or older in 2020 and 2030, we followed a similar simulation process for cohorts that currently are 30 years or older. We applied a slightly different process for cohorts that currently are younger than age 30 but will be 30 years or older in 2020 or 2030. We used NHANES to calculate the size and age, sex, and race/ethnicity proportions of the current 10- to 19- and 20- to 29-year-old cohorts, but we endowed them with eGFR, diabetes, hypertension, and albuminuria characteristics drawn from the current 18- to 29-year-old population. The cohorts then were progressed through the model beginning from the year they turned 30 years old; based on this approach, a few persons start with prevalent CKD at age 30 years. Prevalences of CKD in 2020 and 2030 were estimated as the proportion of persons with CKD among those who are 30 years or older and alive. The future prevalence among adults 65 years or older was estimated similarly. We used bootstrapping to estimate 95% confidence intervals for the 2020 and 2030 prevalence rates. For each year, we simulated the prevalence 100 times. From this sample, we used the 2.5th and 97.5th percentile results to calculate confidence intervals. For comparison purposes, we estimated current prevalence using all observations from the 1999 to 2010 NHANES. We used all observations from 1999 to 2010 to increase sample size.

Sensitivity Analyses

We conducted a number of one-way sensitivity analyses by varying key model parameters. We varied the eGFR decrements associated with diabetes, hypertension, and proteinuria by \pm 50%, following Boulware et al.¹⁰ These decrements affect the eGFR trajectory, which in turn affects the incidence of CKD. We varied mortality rates for stages 3 and 4 by \pm 10%, matching the confidence intervals for mortality effects in the Go et al¹⁸ study of CKD mortality. We also varied the mortality rates for ESRD by \pm 25%, the approximate improvement in ESRD mortality rates between 2000 and 2010.¹ In another analysis, we applied age-specific relative risks for CKD mortality for persons with eGFRs < 60 mL/min/1.73 m².²⁶ We applied higher relative risks for individuals at younger ages, holding eGFR constant. In separate analyses, we varied

Table 3. Residual Lifetime Incidence, Current Prevalence, and Unconditional Lifetime Incidence in Adults 30 Years or Older

Stage	Current Age 30-49 y			Current Age 50-64 y			Current Age \geq 65 y		
	Residual Lifetime Incidence	Current Prevalence	Unconditional Lifetime Incidence	Residual Lifetime Incidence	Current Prevalence	Unconditional Lifetime Incidence	Residual Lifetime Incidence	Current Prevalence	Unconditional Lifetime Incidence
CKD	54.13 (53.40-54.93)	4.02 (3.61-4.42)	55.98 (55.47-56.56)	52.01 (50.79-53.24)	9.86 (8.98-10.73)	56.74 (56.08-57.44)	41.80 (39.78-43.85)	39.65 (38.43-40.87)	64.88 (64.39-65.43)
CKD stage 3a+	47.06 (46.54-47.68)	0.71 (0.52-0.90)	47.44 (47.01-47.95)	44.70 (43.65-45.74)	4.83 (4.16-5.50)	47.37 (46.75-48.00)	37.37 (35.64-39.09)	30.06 (28.83-31.28)	56.20 (55.77-56.66)
CKD stage 3b+	24.19 (23.68-24.66)	0.19 (0.10-0.28)	24.33 (23.90-24.73)	23.74 (23.11-24.48)	0.95 (0.73-1.18)	24.47 (24.02-25.03)	19.67 (18.56-20.70)	10.61 (9.81-11.42)	28.19 (27.86-28.48)
CKD stage 4+	9.42 (9.02-9.80)	0.12 (0.06-0.17)	9.52 (9.18-9.85)	9.10 (8.63-9.61)	0.33 (0.21-0.45)	9.40 (9.04-9.79)	8.07 (7.38-8.71)	2.59 (2.17-3.01)	10.45 (10.16-10.69)
CKD stage 5	3.17 (2.95-3.37)	—	3.17 (2.95-3.37)	3.31 (3.00-3.53)	—	3.31 (3.00-3.53)	2.63 (2.45-2.79)	—	2.63 (2.45-2.79)

Note: Values are given as percentage (95% confidence interval). Residual lifetime incidence for CKD shows the projected percentage of persons who do not currently have CKD and who will develop CKD in their lifetime. Residual lifetime incidence for CKD stage 3a+ shows the projected percentage of persons with current eGFR \geq 60 mL/min/1.73 m² who will develop eGFR < 60 mL/min/1.73 m² in their lifetime. Residual lifetime incidence for CKD stages 3b+, 4+, and 5 are defined in a similar manner, with eGFR cutoff points of 45, 30, and 15 mL/min/1.73 m², respectively. Current prevalence estimates come from NHANES data from 1999 to 2010; NHANES does not have enough observations to support separate estimates for stage 5. Unconditional lifetime incidence of CKD accounts for persons who currently have CKD (based on NHANES) and persons currently alive who will develop CKD in their lifetime (as projected by the model).

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NHANES, National Health and Nutrition Examination Survey.

incidence rates for 3 risk factors that affect CKD stage: diabetes, albuminuria, and hypertension. We varied diabetes, albuminuria, and hypertension incidence rates by $\pm 33\%$ (the approximate increase in age-adjusted diabetes incidence between 2000 and 2010; Centers for Disease Control and Prevention [CDC]; 2013),²⁷ $\pm 15\%$ (the increase in albuminuria prevalence between NHANES III [1988-1994] and NHANES 1999-2004; Coresh et al,² 2007), and $\pm 10\%$ (by assumption; little evidence is available on US hypertension incidence trends; prevalence is expected to increase by 7.2% between 2013 and 2030),²⁸ respectively.

RESULTS

Lifetime Incidence of CKD

Table 3 presents the estimated residual lifetime incidence, current prevalence, and unconditional lifetime incidence of CKD in current US adults 30 years or older. The residual lifetime incidence of CKD is 54.1% for ages 30 to 49, 52.0% for ages 50 to 64, and 41.8% for ages 65 years or older. The residual lifetime incidence of CKD stage 3a+ is nearly as high as the residual lifetime incidence of any CKD for all 3 age groups, ranging from 37.4% to 47.1%, but the residual lifetime incidences for CKD stages 3b+ (ranging from 19.7%-24.2%), 4+ (ranging from 8.1%-9.4%), and CKD stage 5 (ranging from 2.6%-3.2%) are much lower. Because the current prevalence of CKD is very low and moderately low for persons aged 30 to 49 and 50 to 64 years, respectively, unconditional lifetime incidences of CKD are

very similar to residual lifetime incidences for these ages. For persons older than 65 years, current prevalence is relatively high, and unconditional lifetime incidence therefore is substantially higher than residual lifetime incidence. Separate results by race are presented in Table S1.

Future Prevalence of CKD

Table 4 shows the projected future prevalence of CKD in adults 30 years or older and adults 65 years or older in 2020 and 2030, as well as the current prevalence estimated from NHANES data. For all adults 30 years or older, the prevalence of CKD is projected to increase from 13.2% currently to 14.4% in 2020 and 16.7% in 2030. Among persons with CKD, stage 3a will be the most common stage at all points in time (5.5%, 5.9%, and 8.1%, respectively) and account for the largest absolute increase in prevalence between current levels and 2030. Stages 2, 1, and 3b are the next most common. Estimates for stages 4 and 5 show relatively small changes over time. For adults 65 years or older, the prevalence of CKD is projected to decrease from 39.6% currently to 36.4% in 2020 before increasing to 37.8% in 2030. Among persons with CKD, stage 3a will remain the most common stage at all times (19.4%, 18.1%, and 20.7%, respectively). Separate results by race are shown in Table S2.

Table 4. Projected Prevalence of CKD in 2020 and 2030

Stage	Current Prevalence ^a	2020	2030
Age \geq 30 y			
No CKD	86.79 (86.20-87.39)	85.64 (85.47-85.80)	83.30 (83.09-83.51)
CKD	13.21 (12.61-13.80)	14.35 (14.20-14.53)	16.70 (16.49-16.91)
Stage 1	2.10 (1.88-2.32)	2.32 (2.26-2.39)	1.81 (1.74-1.88)
Stage 2	3.03 (2.78-3.28)	3.49 (3.40-3.60)	4.10 (3.94-4.23)
Stage 3a	5.47 (5.06-5.88)	5.92 (5.85-6.00)	8.08 (7.97-8.20)
Stage 3b	1.91 (1.72-2.10)	1.90 (1.85-1.97)	1.98 (1.89-2.08)
Stage 4	0.70 (0.60-0.80)	0.51 (0.48-0.54)	0.51 (0.46-0.56)
Stage 5	—	0.20 (0.18-0.22)	0.21 (0.19-0.24)
Age \geq 65 y			
No CKD	60.35 (59.13-61.57)	63.36 (62.86-63.82)	62.16 (61.66-62.70)
CKD	39.65 (38.43-40.87)	36.64 (36.18-37.14)	37.84 (37.30-38.34)
Stage 1	1.16 (0.86-1.45)	0.97 (0.88-1.09)	0.76 (0.67-0.84)
Stage 2	8.43 (7.65-9.22)	8.26 (7.92-8.58)	8.59 (8.26-8.96)
Stage 3a	19.44 (18.34-20.55)	18.09 (17.80-18.44)	20.70 (20.33-21.15)
Stage 3b	8.03 (7.34-8.71)	6.90 (6.63-7.14)	5.77 (5.50-6.05)
Stage 4	2.59 (2.17-3.01)	1.90 (1.76-2.03)	1.49 (1.31-1.67)
Stage 5	—	0.51 (0.42-0.60)	0.53 (0.44-0.65)

Note: Values are given as percentage (95% confidence interval).

Abbreviations: CKD, chronic kidney disease; NHANES, National Health and Nutrition Examination Survey.

^aStage 1 through stage 4 rows for current prevalence are estimated from NHANES data. NHANES contains insufficient data to estimate stage 5 prevalence. CKD stages are defined according to NKF-KDOQI (National Kidney Foundation–Kidney Disease Outcomes Quality Initiative) guideline.⁹

Table 5. Sensitivity Analyses of Residual Lifetime Incidence of CKD in Adults Aged 30 to 49 Years

Analysis	CKD	Stage 3a+	Stage 3b+	Stage 4+	Stage 5
Baseline	54.61	47.30	24.26	9.24	3.14
eGFR slope +50%	80.90	79.39	61.32	34.92	13.34
eGFR slope -50%	27.11	11.48	2.98	0.98	0.38
Stages 3 and 4 mortality +10%	54.61	47.33	23.40	8.71	2.85
Stages 3 and 4 mortality -10%	54.59	47.28	24.99	9.88	3.46
Stage 5 mortality +25%	54.62	47.30	24.26	9.25	3.14
Stage 5 mortality -25%	54.61	47.31	24.26	9.25	3.14
Age-specific CKD mortality rates	54.61	47.29	23.91	9.00	3.25
Diabetes incidence +33%	55.20	47.65	25.42	10.50	3.66
Diabetes incidence -33%	53.99	46.95	22.89	7.99	2.58
Proteinuria incidence +15%	55.53	47.50	24.35	9.39	3.19
Proteinuria incidence -15%	53.59	47.19	24.04	9.08	3.04
Hypertension incidence +10%	54.65	47.31	24.23	9.23	3.09
Hypertension incidence -10%	54.62	47.38	24.10	9.34	3.19

Note: Values are given as percentage. Residual lifetime incidence for CKD shows the projected percentage of persons who do not currently have CKD who will develop CKD in their lifetime. Residual lifetime incidence for CKD stage 3a+ shows the projected percentage of persons with current eGFR ≥ 60 mL/min/1.73 m² who will develop eGFR < 60 mL/min/1.73 m² in their lifetime. Residual lifetime incidence for CKD stages 3b+, 4+, and 5 are defined in a similar manner, with eGFR cutoff points of 45, 30, and 15 mL/min/1.73 m², respectively.

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

Sensitivity Analyses

One-way sensitivity analyses for residual lifetime incidence of CKD for the cohort currently aged 30 to 49 years are shown in [Table 5](#). Increasing or decreasing eGFR decrements has a large effect on the residual lifetime incidence of CKD. Increasing the decrements leads to more persons reaching CKD stages 3a+, 3b+, 4+, and 5 and fewer persons ending progression in stages 1 and 2. With smaller decrements, the proportion of persons reaching CKD stages 3a+, 3b+, 4+, and 5 decreases, and the proportion ending in CKD stages 1 or 2 increases. Varying mortality rates for stages 3a, 3b, 4, and 5 has little impact on residual incidence of CKD because these variables affect persons who have already experienced CKD; however, mortality rates for stages

3a, 3b, and 4 have a moderate effect on the residual lifetime incidence of CKD stages 4+ and 5. Age-specific relative risks for CKD mortality also have relatively small effects on the cumulative incidence of CKD and CKD stages 3a+, 3b+, 4+, and 5. Although increasing or decreasing diabetes incidence has relatively small effects on cumulative CKD incidence, it has a somewhat larger impact on the proportion of patients ending in CKD stages 4+ and 5. Varying the incidence rates for albuminuria and hypertension has relatively little impact on the residual incidence of CKD or the proportion of patients ending in any CKD stage.

One-way sensitivity analyses for 2030 prevalence are shown in [Table 6](#). Varying assumptions about eGFR decrements by $\pm 50\%$ has the largest effect on CKD prevalence relative to our baseline estimates. Increasing the decrements by 50% moves an additional 7.7% of the population to CKD, with the proportion of persons in CKD stages 3a, 3b, 4, and 5 increasing and the proportions in stages 1 and 2 decreasing (because persons with albuminuria now will be more likely to progress to eGFRs < 60 mL/min/1.73 m²). There are corresponding reductions when eGFR decrements are decreased by 50%. In our baseline analyses, persons in CKD stages 3a, 3b, 4, and 5 have higher mortality rates than persons without CKD. Increasing or decreasing the stage 3a, 3b, and 4 mortality rates by 10% or the stage 5 mortality rate by 25% has relatively little impact on CKD prevalence. Age-specific relative risks for CKD mortality also have relatively little effect on CKD prevalence. Varying incidence rates for diabetes, albuminuria, and hypertension all have relatively small effects on the 2030 prevalence of CKD and individual CKD stages.

DISCUSSION

We provide 2 perspectives on the future burden of CKD. From the individual perspective, we estimate the probability that a person will experience CKD during his or her lifetime, given the person's current age. This analysis shows that a person's residual lifetime probability of developing CKD is relatively high. For example, the residual lifetime incidence of CKD is 54% for someone who currently is aged 30 to 49 years. This compares to lifetime incidences of 12.5% for breast cancer in women,²⁹ 33% to 38% for diabetes,³⁰ and 90% for hypertension in middle-aged men and women.³¹ Information on a person's lifetime incidence of CKD may help raise individuals' awareness of the disease and encourage them to take steps to prevent or delay CKD onset.

Our projections for residual lifetime incidence for persons aged 30 to 49 years are higher than the value (47.1% for a 30-year-old person) we generated using

Table 6. Sensitivity Analyses of 2030 Prevalence for Adults 30 Years or Older

Analysis	CKD	Stage 3a+	Stage 3b+	Stage 4+	Stage 5
Baseline	16.52	10.72	2.74	0.73	0.22
eGFR slope +50%	24.26	19.64	6.52	1.76	0.51
eGFR slope -50%	11.32	4.42	1.03	0.23	0.06
Stages 3 and 4 mortality +10%	16.31	2.61	0.69	0.69	0.20
Stages 3 and 4 mortality -10%	16.75	10.96	2.89	0.78	0.23
Stage 5 mortality +25%	16.49	10.68	2.70	0.69	0.18
Stage 5 mortality -25%	16.58	10.78	2.80	0.79	0.28
Age-specific CKD mortality rates	16.39	10.58	2.65	0.70	0.21
Diabetes incidence +33%	16.68	10.72	2.82	0.77	0.22
Diabetes incidence -33%	16.38	10.72	2.61	0.68	0.20
Proteinuria incidence +15%	17.00	10.72	2.74	0.73	0.22
Proteinuria incidence -15%	16.01	10.70	2.72	0.72	0.22
Hypertension incidence +10%	16.57	10.71	2.75	0.73	0.22
Hypertension incidence -10%	16.49	10.74	2.75	0.73	0.22

Note: Values are given as percentage. CKD stage 3a+ shows the projected percentage of persons with eGFR < 60 mL/min/1.73 m² in 2030. CKD stages 3b+, 4+, and 5 are defined in a similar manner, with eGFR cutoff points of 45, 30, and 15 mL/min/1.73 m², respectively.

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

an earlier version of the model.⁶ Two factors account for this difference. First, our present analysis assumes a faster average annual reduction in eGFR for persons with neither diabetes nor hypertension. The current decrements of -0.85 mL/min/1.73 m² before age 50 and -1.0 mL/min/1.73 m² for 50 years or older are based on an analysis of NHANES data in which eGFR was calculated using the CKD-EPI equation. Previously, we used the MDRD (Modification of Diet in Renal Disease) Study equation, which may be biased at high true GFR values. Second, starting eGFR values for the simulation now are drawn from individual respondents to NHANES.

Recently, Grams et al³² estimated the lifetime incidence of CKD stages 3 through 5. A number of methodological differences complicate comparisons between our results and those of Grams et al.³² We estimated overall CKD incidence (including stages 1 and 2), whereas Grams et al³² focused on stages 3 and

higher. We applied a microsimulation model of disease progression in persons that accounts for risk factors such as diabetes, hypertension, and albuminuria, whereas Grams et al³² applied a Markov model based on aggregate incidence and prevalence rates. Mortality in our model depends on relative risks for CKD that are independent of age or albuminuria; relative risks in Grams et al³² vary with age and albuminuria. We provide estimates for persons aged 30 to 49 years, whereas Grams et al³² provide aggregate US estimates from birth (they also report residual rates by sex and race for different ages, including age 30). Bearing these and other differences in mind, Grams et al³² estimated a residual lifetime risk of 59.1% for eGFR < 60 mL/min/1.73 m², 11.5% for eGFR < 30 mL/min/1.73 m², and 3.6% for ESRD. The most comparable numbers from our study come from the residual lifetime incidence estimates of CKD stage 3a+, 4+, and 5 for persons aged 30 to 49 years: 47.13%, 9.4%, and 3.2%. Although our estimates are somewhat lower than estimates of Grams et al,³² the estimates are reasonably close despite being derived from different models using different methods.

From a national perspective, we project the prevalence of CKD in the US population 30 years or older in 2020 and 2030. We show that population prevalence will increase in the coming decades. In addition to the increased proportion with CKD, the US population 30 years or older is projected to increase to 204 million in 2020 and nearly 225 million in 2030.³³ Combining our projections of CKD prevalence with the overall population projections, we project that the number of Americans 30 years or older with CKD will reach 28 million in 2020 and nearly 38 million in 2030. This increase suggests that CKD health care costs and quality-of-life losses will increase accordingly and further emphasizes the need to develop new interventions to slow the onset and progression of CKD.

For the population 65 years or older, our estimates show a dip in prevalence between now and 2020, but an increase in prevalence thereafter. The reduction between now and 2020 is surprising given that prevalence in the overall adult population is projected to increase. However, prevalence projections for 65 years or older are especially sensitive to variation in the age distribution of persons across ages 65 to 90 years because prevalence increases rapidly within this age group.

Prevalence depends on incidence, but also on mortality and the age distribution of the population at any point in time. In the model, most persons develop CKD at older ages, when death is an important competing risk versus further progression. As a result, relatively few persons with CKD progress to stages 4 and 5. For those who reach these stages, mortality is

high, both because the patients are older and have high mortality even in the absence of CKD and because mortality is elevated further in the stages. Because of these factors, relatively few person-years are spent in these stages, keeping their prevalence low. However, the US population is aging, and the larger share of the population in older age groups, in which CKD is more common, accounts for most of the increased prevalence in later decades.

The clinical significance of CKD stage 3 has been questioned for elderly persons with eGFRs close to 60 mL/min/1.73 m², the upper cutoff for the stage.³⁴ We divided stage 3 into stages 3a and 3b. We find that the residual lifetime incidence of stage 3+ is approximately twice as high as that of stage 3b+, and at any point in time, stage 3a is the most common stage.

Our analysis is subject to several limitations. We focus on CKD in adults 30 years or older because eGFR is relatively constant before that age. Consequently, we do not provide estimates for CKD in younger adults. Data from NHANES indicate that CKD prevalence is ~2% in adults aged 18 to 29 years, with virtually all these individuals having albuminuria and eGFRs > 60 mL/min/1.73 m² (ie, stage 1 or 2).

Our analysis simulates CKD resulting from sustained disease progression over time. It does not account for acute kidney infections causing abrupt and sometimes permanent decreases in eGFR. To the extent that acute kidney infection is a major source of CKD, we may underestimate CKD incidence and prevalence.

Our estimates are based on assumptions about the effects of risk factors on annual eGFR decrements. Absent changes in risk factors, a person's eGFR is assumed to decline at a constant rate between the ages of 30 and 49 years, with a slightly faster decline beginning at age 50 years. The assumption of constant rates probably is an oversimplification. Better data for eGFR trajectories could lead to better model projections; moreover, adding more variation in the rates likely would lead to wider confidence intervals around our estimates. Unfortunately, longitudinal data sets that follow up persons' eGFRs over time are relatively rare and sometimes consist of selected patients (eg, endocrinology patients with known CKD) who may not represent the general population.

Finally, our estimates are based on current treatment patterns, risk factor prevalence, and mortality rates. If these factors change in the future, our estimates may over- or underpredict the cumulative lifetime incidence for individuals and the overall future prevalence of CKD. This limitation applies to almost all forecasts of future incidence

and prevalence, including estimates of life expectancy at birth.

In conclusion, better forecasts of the future burden of CKD can help planners prepare for future health care needs, raise individuals' awareness about the importance of keeping kidneys healthy, and stimulate research on interventions to slow the progression of CKD. Overall, our results show that adults 30 years or older who currently do not have CKD have a residual lifetime incidence of CKD ranging from 54.1% for age 30 to 49 years to 41.8% for age 65 years or older. By 2030, the prevalence of CKD among adults 30 years or older may reach 16.7%.

ACKNOWLEDGEMENTS

The authors thank Anne M. O'Hare, MD, of Veteran Affairs, Puget Sound Health Care, Seattle, for analytical support and thoughtful comments, and Lawrence Baker, PhD, of CDC, Division of Diabetes, for insightful comments on an early version of the manuscript. Susan Murchie from RTI International provided editorial support. Former RTI International employee John Wittenborn played a key role in the development of the CKD Health Policy Model.

Support: This research was supported by funding (contract 200-2008-27958) from the CDC. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

Financial Disclosure: The authors declare that they have no other relevant financial interests.

Contributions: Research idea and study design: TJH, DEW, XZ; data acquisition: TJH, SAS, BY, MEP, NRB, XZ; data analysis/interpretation: TJH, SAS, BY, MEP, NRB, SHS, XZ; statistical analysis: TJH, SAS, BY; supervision or mentorship: TJH, MEP, DEW, XZ. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. TJH takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

SUPPLEMENTARY MATERIAL

Table S1: Residual lifetime incidence, current prevalence, and unconditional lifetime incidence in adults ≥ 30 years, by race.

Table S2: Projected prevalence of CKD in 2020 and 2030 in adults ≥ 30 years, by race.

Figure S1: Broad overview of the CKD Health Policy Model.

Figure S2: Detailed view of the normal CKD stage subtree.

Note: The supplementary material accompanying this article (<http://dx.doi.org/10.1053/j.ajkd.2014.09.023>) is available at www.ajkd.org

REFERENCES

- Collins AJ, Foley RN, Herzog C, et al. US Renal Data System 2012 annual data report. *Am J Kidney Dis*. 2013;61(1)(suppl 1):e1-e480.
- Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA*. 2007;298(7):2038-2047.

3. U.S. Burden of Disease Collaborators. The state of US health, 1990–2010: burden of diseases, injuries, and risk factors. *JAMA*. 2013;310(6):591-608.
4. Honeycutt AA, Segel JE, Zhuo X, Hoerger TJ, Imai K, Williams D. Medical costs of CKD in the Medicare population. *J Am Soc Nephrol*. 2013;24(9):1478-1483.
5. Tuot DS, Plantinga LC, Hsu CY, et al; Centers for Disease Control Chronic Kidney Disease Surveillance Team. Chronic kidney disease awareness among individuals with clinical markers of kidney dysfunction. *Clin J Am Soc Nephrol*. 2011;6(8):1838-1844.
6. Hoerger TJ, Wittenborn JS, Segel JE, et al; Centers for Disease Control and Prevention CKD Initiative. A health policy model of CKD: 1. Model construction, assumptions, and validation of health consequences. *Am J Kidney Dis*. 2010;55(3):452-462.
7. Hoerger TJ, Wittenborn JS, Segel JE, et al; Centers for Disease Control and Prevention CKD Initiative. A health policy model of CKD: 2. The cost-effectiveness of microalbuminuria screening. *Am J Kidney Dis*. 2010;55(3):463-473.
8. Hoerger TJ, Wittenborn JS, Zhuo X, et al. Cost-effectiveness of screening for microalbuminuria among African Americans. *J Am Soc Nephrol*. 2012;23(12):2035-2041.
9. National Kidney Foundation. Kidney Disease Outcomes Quality Initiative: part 4. Definition and classification of stages of chronic kidney disease. *Am J Kidney Dis*. 2002;39(2)(suppl 1):S46-S75.
10. Boulware LE, Jaar BG, Tarver-Carr ME, Brancati FL, Powe NR. Screening for proteinuria in US adults: a cost-effectiveness analysis. *JAMA*. 2003;290(23):3101-3114.
11. Adler AI, Stevens RJ, Manley SE, et al. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). *Kidney Int*. 2003;63(1):225-232.
12. Cowie CC, Rust KF, Bryd-Hold DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. Population: National Health and Nutrition Examination Survey 1999–2002. *Diabetes Care*. 2006;29(6):1263-1268.
13. Geiss LS, Pan L, Cadwell B, Gregg EW, Benjamin SM, Engelgau MM. Changes in incidence of diabetes in US adults, 1997–2003. *Am J Prev Med*. 2006;30(5):371-377.
14. Paoletti E, Bellino D, Cassottana P, Rolla D, Cannella G. Left ventricular hypertrophy in nondiabetic predialysis CKD. *Am J Kidney Dis*. 2005;46(2):320-327.
15. Cottone S, Nardi E, Mule G, Vadala A. Association between biomarkers of inflammation and left ventricular hypertrophy in moderate chronic kidney disease. *Clin Nephrol*. 2007;67(4):209-216.
16. Anderson KM, Odell PM, Wilson PWF, Kannell WB. Cardiovascular disease risk profiles. *Am Heart J*. 1991;121(1, pt 2):293-298.
17. Weiner DE, Tabatabai S, Tighiouart H, et al. Cardiovascular outcomes and all-cause mortality: exploring the interaction between CKD and cardiovascular disease. *Am J Kidney Dis*. 2006;48(3):392-401.
18. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351(13):1296-1305.
19. Arias E. United States life tables, 2003. *Natl Vital Stat Rep*. 2006;54(14). http://www.cdc.gov/nchs/data/nvsr/nvsr54/nvsr54_14.pdf. Accessed July 30, 2007.
20. National Center for Health Statistics (NCHS). Worktable 210R: death rates for 113 selected causes, alcohol-induced causes, drug-induced causes, and injury by firearms by 5-year age groups, race, and sex: United States 2003. http://www.cdc.gov/nchs/data/statab/Mortfinal2003_worktable210r.pdf March 2006. Accessed July 30, 2007.
21. Sacco RL, Shi T, Zamanillo MC, Kargman DE. Predictors of mortality and recurrence after hospitalized cerebral infarction in an urban community: the Northern Manhattan Stroke Study. *Neurology*. 1994;44(4):626-634.
22. Hunink MG, Goldman L, Tosteson AN, et al. The recent decline in mortality from coronary heart disease, 1980–1990. *JAMA*. 1997;277(7):535-542.
23. Weinstein MC, O'Brien B, Hornberger J, et al. Principles of good practice for decision analytic modeling in health-care evaluation. Report of the ISPOR Task Force on Good Research Practices—Modeling Studies. *Value Health*. 2003;6(1):9-17.
24. Hoang K, Tan JC, Derby G, et al. Determinants of glomerular hypofiltration in aging humans. *Kidney Int*. 2003;64(4):1417-1424.
25. Levey AS, Stevens LA, Schmid CH, et al; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612.
26. Hallan SI, Matsushita K, Sang Y, et al; Chronic Kidney Disease Prognosis Consortium. Age and association of kidney measures with mortality and end-stage renal disease. *JAMA*. 2012;308(22):2349-2360.
27. Centers for Disease Control and Prevention. Crude and age-adjusted incidence of diagnosed diabetes per 1,000 population aged 18–79 years, United States, 1980–2011. 2012. <http://www.cdc.gov/diabetes/statistics/incidence/fig2.htm>. Accessed March 23, 2013.
28. American Heart Association. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation*. 2013;127:e6-e245.
29. Howlander N, Noone AM, Krapcho M, et al., eds. *SEER Cancer Statistics Review, 1975–2009 (Vintage 2009 Populations)*. Bethesda, MD: National Cancer Institute; 2012. http://seer.cancer.gov/archive/csr/1975_2009_pops09/. Accessed September 7, 2012.
30. Narayan KMV, Boyle JP, Thompson TJ, Sorensen SW, Williamson DF. Lifetime risk for diabetes mellitus in the United States. *JAMA*. 2003;290(14):1884-1890.
31. Vasan RS, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: the Framingham Heart Study. *JAMA*. 2002;287(8):1003-1010.
32. Grams ME, Chow EK, Segev DL, Coresh J. Lifetime incidence of CKD stages 3–5 in the United States. *Am J Kidney Dis*. 2013;62(2):245-252.
33. United States Census Bureau. 2012 national population projections: summary tables; Table 12, Projections of the Population by Age and Sex for the United States: 2015 to 2060; Middle Series. Updated May 2013. <http://www.census.gov/population/projections/data/national/2012/summarytables.html>. Accessed January 6, 2014.
34. Rutkowski M, Mann W, Derosé S, et al. Implementing KDOQI CKD definition and staging guidelines in Southern California Kaiser Permanente. *Am J Kidney Dis*. 2009;53(3 suppl 3):S86-S99.