Bryce Canyon National Park, Utah

CKD IN THE GENERAL POPULATION

In this chapter we assess the burden of CKD by using data from the National Health and Nutrition Examination Survey (NHANES), a valuable source of information for assessing disease prevalence and high-risk subsets among representative U.S. adults. The biochemical data collected by NHANES is an especially important resource for looking at CKD, which is defined in large part by the estimation of glomerular filtration rate (eGFR) and by evidence of albumin in the urine. As is done with other disease burdens assessed in the national survey, we define CKD at a single point prevalent point in time. Some estimates of CKD incorporate additional estimates of persistent albumin in the urine over weeks or months. But because such data was assessed only in the 1988–1994 NHANES sample, we have chosen to report the single measure to broadly define CKD on a population level. The clinical definition for a single patient may require greater precision and repeated measurements to be certain of actual disease and prognosis.

Recent publications by the CKD Consortium (Lancet, 2010) examine the risk of death, cardiovascular events, and ESRD based on eGFR and urine albumin levels. In past ADRs we have reported eGFR by two widely used methods, the MDRD approach and the newer CKD-EPI equation. As the latter has been shown to give more precise estimates with fewer false positives, this year we report eGFR using only the CKD-EPI equation.

We begin the chapter by showing the overall burden and interactions of diabetes, cardiovascular disease, and CKD — three interrelated diseases of clear public health relevance — and compare prevalence estimates based on an eGFR less than 60 ml/min/1.73 m^2 to those based on a urine albumin/creatinine ratio (ACR) of ≥30 mg/g. When defined by eGFR, the prevalence of CKD in 2005–2010 was 6.3 percent, compared to 9.3 and 8.5 percent for diabetes and cardiovascular disease, respectively. If kidney disease is defined, however, by ACR, the prevalence of CKD rises to 9.2 percent.

Exploring the implications of CKD, diabetes, and cardiovascular disease in the general population, this chapter sets the stage for Chapter Two, in which we discuss CKD as identified in datasets that are less well defined in terms of biochemical data, but that provide extensive information on morbidity, interventions, and costs.

Overall, the prevalence of CKD appears to have increased slightly from 1988–1994 to 2005–2010; the level of albuminuria, however, has not changed. Risk factors associated with CKD have declined slightly, but their overall pattern is similar. The main source of the increase in CKD appears to be defined by eGFRs

A conservationist is one who is humbly aware that with each stroke [of the axe] he is writing his signature on the face of the land.

ALDO LEOPOLD, *A Sand County Almanac*

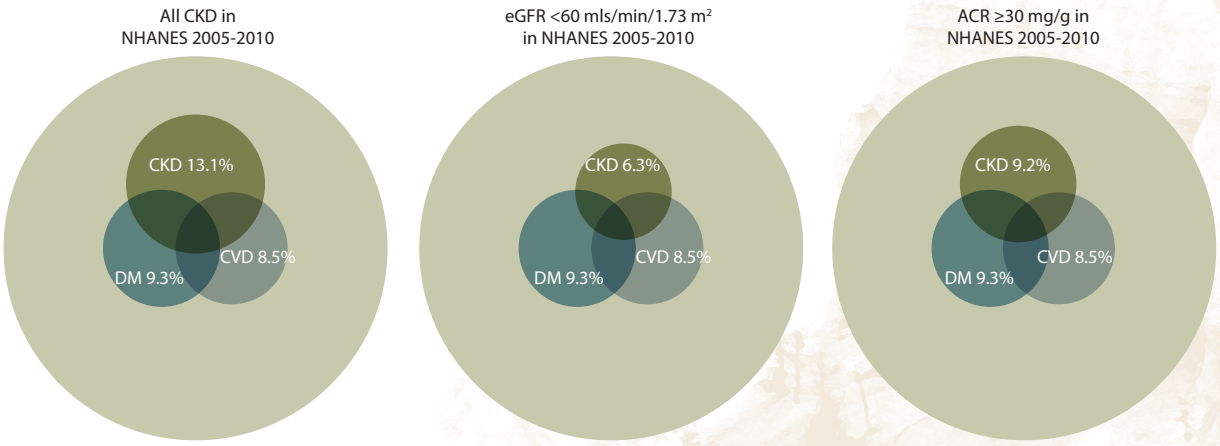
introduction

less than 60. Data on CKD within major risk populations with diabetes and cardiovascular disease show the common association of these three diseases, though findings are less prominent among those with a BMI of 30 kg/m² or above.

We conclude the chapter by examining awareness, treatment, and control of major risk factors, looking at hypertension, lipid disorders, and glycemic control within CKD populations to see if any progress has been made. Hypertension was as common in 2005–2010 as it was in 1988–1994, though awareness of the condition has improved, and control of blood pressure to target levels has increased three-fold, a positive sign that patients and providers are addressing major risk factor for adverse events. Awareness of LDL cholesterol levels has doubled, and control has increased 15-fold, an important finding. And glycemic control among diabetic patients with CKD has improved as well, again demonstrating the marked improvement in care.

It will be important to determine if these changes in the awareness, treatment, and control of major risk factors translates into reduced rates of cardiovascular events, death, and progression of CKD to ESRD. » **Figure 1.1;** see page 140 for analytical methods. *NHANES participants 2005–2010, age 20 & older; eGFR calculated using CKD-EPI equation; urine albumin creatinine ratio (ACR).*

vol 1
1.1 **Distribution of NHANES participants with diabetes, congestive heart failure, & markers of CKD, 2005–2010**



Between 1988–1994 and 2005–2010, the overall prevalence estimate for CKD — defined by an eGFR <60 ml/min/1.73 m² or an ACR ≥30 mg/g — rose from 12.3 to 14.0 percent. The largest relative increase, from 25.4 to 40.8 percent, was seen in those with cardiovascular disease. For eGFR <60, prevalence rose from 4.9 to 6.7 percent, with the largest increase in those age 40–59; for ACR ≥30 mg/g, the estimate rose from 8.8 to 9.4. » **Table 1.a;** see page 140 for analytical methods. *NHANES III (1988–1994) & 2005–2010 participants age 20 & older; eGFR calculated using CKD-EPI equation; urine albumin creatinine ratio (ACR).*

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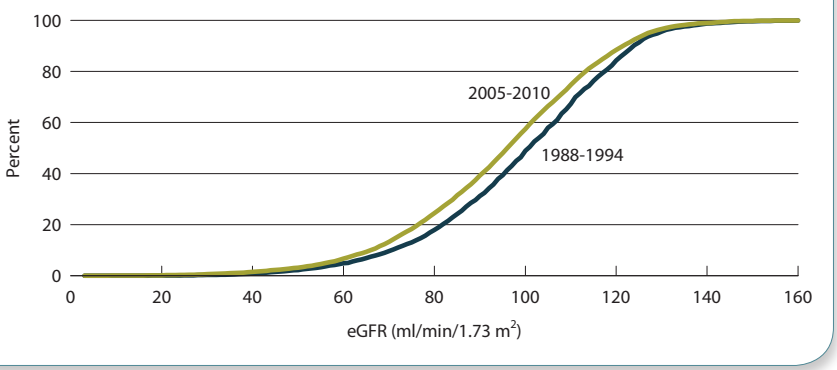
1.a **Prevalence (%) of CKD in the NHANES population within age, gender, race/ethnicity, & risk-factor categories**

	All CKD		eGFR <60 ml/min/1.73m²		ACR ≥30 mg/g	
	1988–1994	2005–2010	1988–1994	2005–2010	1988–1994	2005–2010
20-39	5.1	5.7	0.1	0.2	5.0	5.7
40-59	8.4	9.1	1.3	2.2	7.7	7.6
60+	32.2	35.0	19.5	24.1	18.3	18.4
Male	10.2	12.1	4.1	5.6	7.4	8.6
Female	14.2	15.8	5.6	7.7	10.2	10.2
Non-Hispanic white	12.3	14.3	5.5	7.9	8.2	8.6
Non-Hispanic Blk/Af Am	14.5	16.0	4.1	6.2	12.7	12.6
Other	10.5	11.9	2.2	2.6	9.2	10.6
Diabetes	43.1	40.1	15.6	19.3	36.3	29.9
Self-reported diabetes	42.7	41.6	16.4	20.4	35.9	30.8
Hypertension	22.2	23.2	10.4	12.9	15.4	14.8
Self-reported hypertension	25.3	26.8	12.9	15.6	17.1	16.7
CVD	25.4	40.8	14.5	27.9	16.6	24.3
BMI ≥30	16.6	16.8	6.2	7.4	12.3	11.7
All	12.3	14.0	4.9	6.7	8.8	9.4

Figure 1.2 shows cumulative distributions of eGFR in 1988–1994 and 2005–2010. Overall, a population shift towards lower eGFR levels was observed over time, with most of the leftward shift confined to levels between 50 and 125 ml/min/1.73 m². Corresponding findings for albumin/creatinine ratio (ACR) in Figure 1.3 show that a slight leftward shift occurred for ACR values less than 20 mg/g. » **Figures 1.2–3;** see page 140 for analytical methods. *NHANES III (1988–1994) & 2005–2010 participants age 20 & older; eGFR calculated using CKD-EPI equation.*

vol 1
1.2 **Cumulative eGFR distribution curves of NHANES participants**



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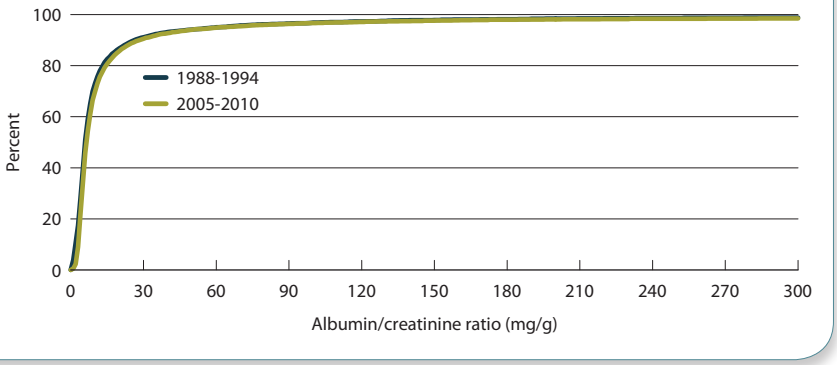
1.3 **Cumulative urine albumin/creatinine ratio (ACR) distribution curves of NHANES participants**



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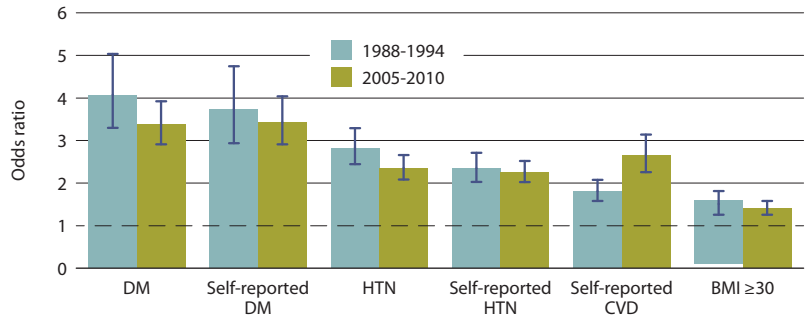
Adjusted odds ratios of CKD in NHANES participants, by risk factor



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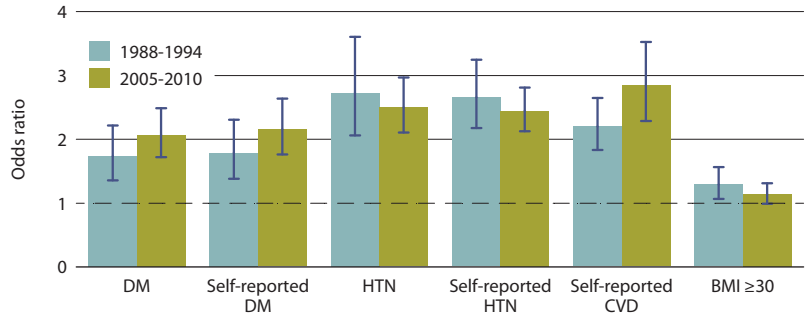
Adjusted odds ratios of eGFR <60 in NHANES participants, by risk factor



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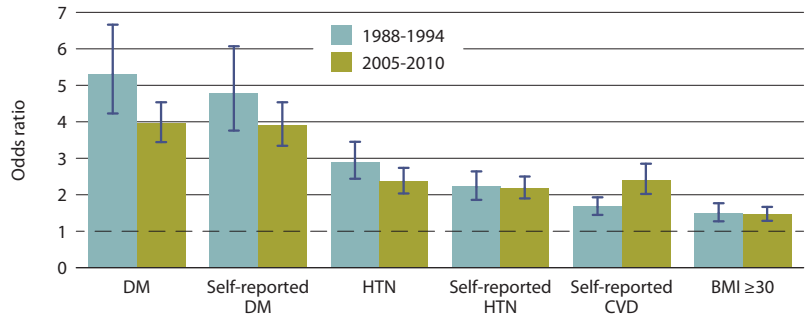
Adjusted odds ratios of urine albumin/creatinine ratio (ACR) ≥30 mg/g in NHANES participants, by risk factor



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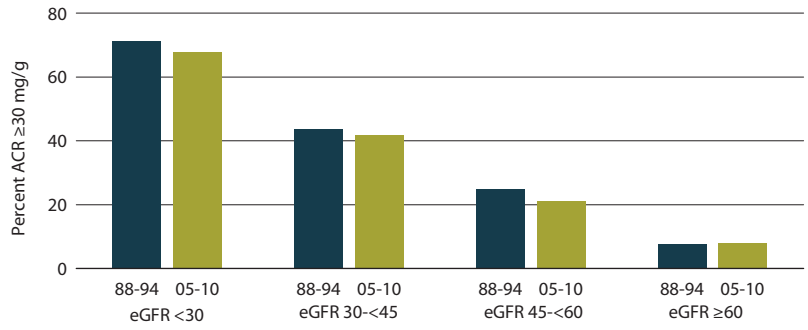
NHANES participants with urine albumin /creatinine ratio (ACR) ≥ 30 mg/g, by eGFR range



Figures 1.4–6 show comorbidity associations of CKD in two time frames, presented as odds ratios that are adjusted for age, gender, race, and ethnicity.

While diabetes, hypertension, cardiovascular disease and body mass index ≥30 kg/m² are all associated with CKD, the highest odds ratios occur in participants with diabetes, at 4.08 in 1988–1994 and 3.38 in 2005–2010.

In participants with eGFR <60, hypertension showed the highest odds ratio (2.73) in 1988–1994, and cardiovascular disease the highest odds ratio (2.84) in 2005–2010. For ACR ≥30, diabetes showed the highest odds ratios (5.31 and 3.95) in both periods. » **Figures 1.4–6;** see page 140 for analytical methods. *NHANES III (1988–1994) & 2005–2010 participants age 20 & older. Adj: age/gender/race; for Figure 1.5, eGFR calculated using CKD-EPI equation.*

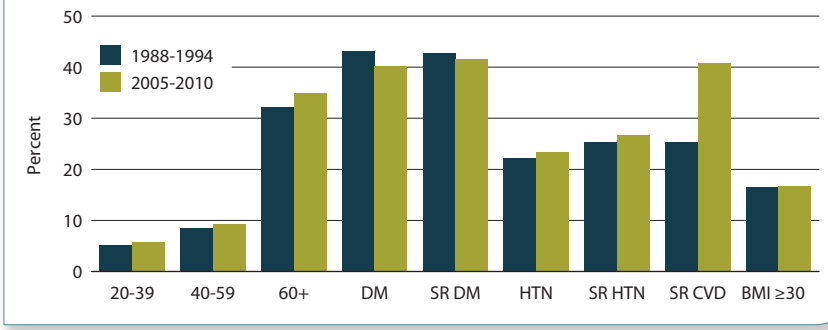
The percentage of NHANES participants with an ACR ≥30 mg/g increases with the severity of kidney disease. Among 2005–2010 NHANES participants with eGFRS <30 ml/min/1.73 m², for example, 68 percent had an elevated ACR. In those with eGFRS of 30–<45, 45–<60, or ≥60, 42, 21, and 8 percent, respectively, had elevated ACRS. » **Figure 1.7;** see page 140 for analytical methods. *NHANES III (1988–1994) & 2005–2010 participants age 20 & older; eGFR calculated using CKD-EPI equation.*

Many studies have shown that diabetes, hypertension, cardiovascular disease, higher body mass index, and advancing age are associated with the presence of CKD. Figure 1.8, showing the percentage of NHANES participants with either eGFR <60 ml/min/1.73 m² or ACR ≥30 mg/g, confirms a higher prevalence of CKD when each of these risk factors is present. While prevalence estimates are generally similar between time periods, the proportion with CKD among subjects with self-reported cardiovascular disease increased substantially, from 25.4 percent to 40.8 percent.

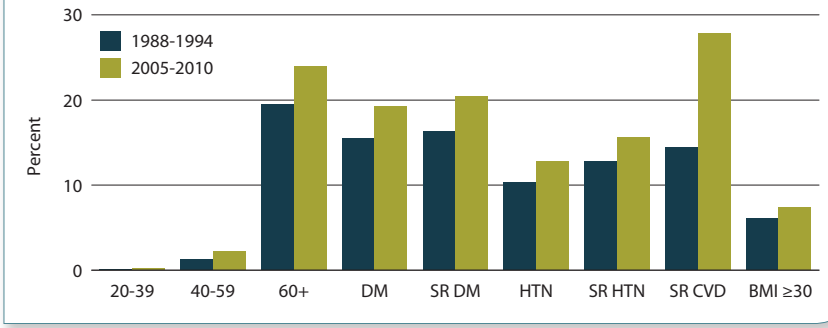
Figures 1.9–10 show similar analyses for eGFR <60 ml/min/1.73 m² and ACR ≥30 mg/g. For eGFR, prevalence estimates are higher in later years in all subgroups studied, especially age 60 and older (24.1 versus 19.5 percent), diabetes (19.3 versus 15.6 percent), and self-reported cardiovascular disease (14.5 versus 27.9 percent). For ACR ≥30 mg/g, a meaningful decline is seen in participants with diabetes (36.3 versus 29.9 percent), while a large increase is seen in those with self-reported cardiovascular disease (16.6 versus 24.3 percent).

While differences in categorization for cardiovascular disease may explain some of the disparities in prevalence estimates for markers of CKD, the differences appear large from a numerical standpoint. » **Figures 1.8–10;** see page 140 for analytical methods. *NHANES III (1988–1994) & 2005–2010 participants age 20 & older; for Figure 1.9, eGFR calculated using CKD-EPI equation. SR: self-reported.*

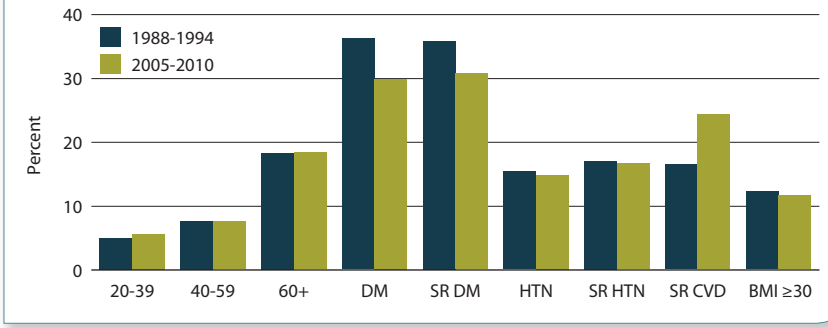
vol 1 **1.8** **NHANES participants with CKD, by age & risk factor**



vol 1 **1.9** **NHANES participants with eGFR <60 ml/min/1.73 m², by age & risk factor**



vol 1 **1.10** **NHANES participants with urine albumin/creatinine ratio (ACR) ≥30 mg/g, by age & risk factor**



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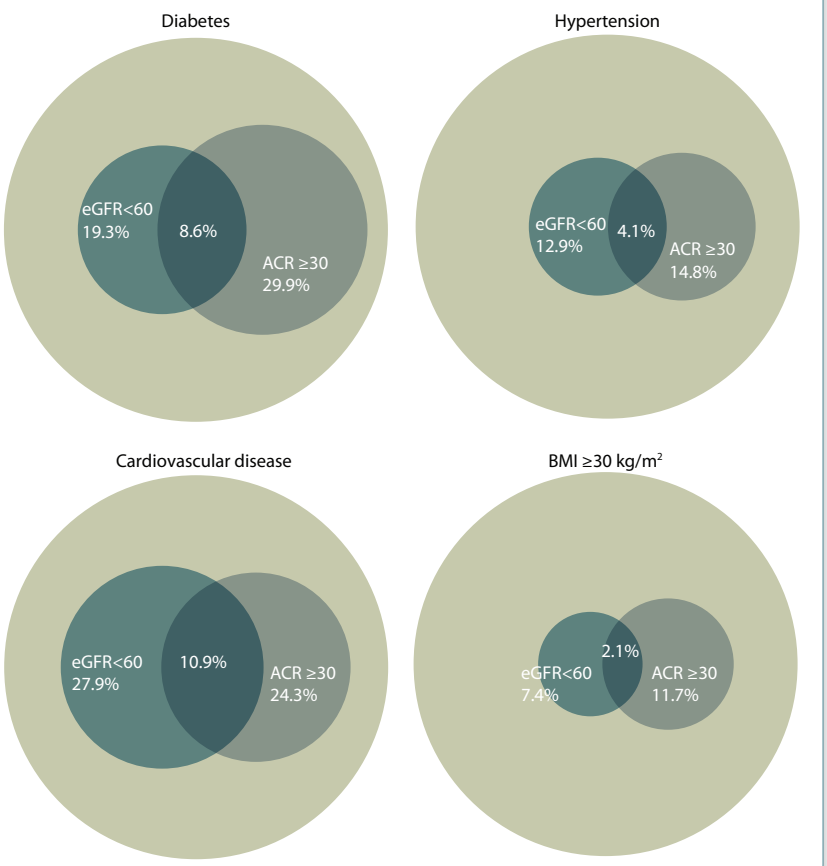
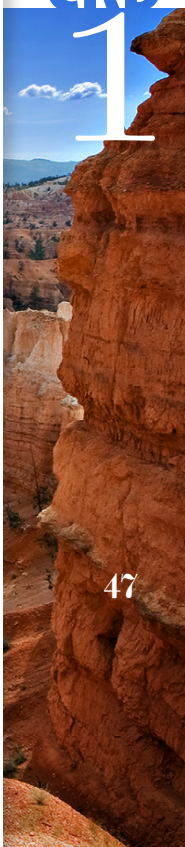
1.11

Distribution of markers of CKD in NHANES participants with diabetes, hypertension, cardiovascular disease, & obesity, 2005–2010



Here we look at several subgroups of NHANES 2005–2010 participants, showing the percentage in each population with an eGFR <60 m/min/1.73 m² and an ACR ≥30 mg/g. Nearly 28 percent of participants with cardiovascular disease (CVD) had an eGFR less than 60, compared to 19.3, 12.9, and 7.4 percent of those with diabetes, hypertension, and a high body mass index, respectively. Participants with diabetes were the most likely to have an ACR ≥30 mg/g, at 29.9 percent, compared to 24.3, 14.8, and 11.7 percent among those with CVD, hypertension, and a high BMI.

Nearly 11 percent of participants with CVD had both an eGFR <60 and an ACR ≥30, compared to 8.6 percent of those with diabetes and 4.1 and 2.1 percent, respectively, of those with hypertension and a high BMI. » **Figure 1.11;** see page 140 for analytical methods. *NHANES III (1988–1994) & 2005–2010 participants age 20 & older; eGFR calculated using CKD-EPI equation; urine albumin/creatinine ratio (ACR).*



vol 1
1.b Awareness, treatment, & control of hypertension, hyperlipidemia, HDL, total cholesterol, & diabetes

	All CKD		eGFR <60 ml/min/1.73m²		ACR ≥30 mg/g	
	1988–1994	2005–2010	1988–1994	2005–2010	1988–1994	2005–2010
Hypertension, by current hypertensive status[1]						
Non- hypertensive status	27.3	26.2	16.1	15.5	31.2	30.4
Hypertensive (measured/treated)	72.7	73.8	83.9	84.5	68.8	69.6
Control of hypertension among hypertensive patients[2]						
Unaware	35.5	23.5	27.3	18.3	36.6	25.5
Aware, not treated	15.3	6.9	12.1	3.2	16.7	9.4
Aware, treated, uncontrolled	41.3	43.7	50.7	46.5	40.0	44.6
Aware, treated, controlled	7.9	25.9	9.9	32.0	6.7	20.5
Hyperlipidemia (LDL): LDL cholesterol[3]						
Within ATP-III target LDL range	24.8	32.6	8.3	18.6	31.2	40.3
Hyperlipidemia (measured or treated)	75.2	67.4	91.7	81.4	68.8	59.7
Control of hyperlipidemia (LDL) among participants with hyperlipidemia (LDL)[4]						
Unaware	62.1	33.8	61.2	35.6	64.4	31.7
Aware, not treated	24.3	10.8	27.4	12.2	20.7	8.1
Aware, treated, uncontrolled	11.5	24.2	11.2	25.0	11.8	24.4
Aware, treated & controlled	2.1	31.2	0.1	27.2	3.1	35.8
HDL cholesterol in ATP III target range[5]						
HDL <40 mg/dl (ATP III target)	27.8	19.6	30.8	18.0	25.2	21.6
HDL 40 mg/dl or higher (at/above ATP III target)	72.2	80.4	69.2	82.0	74.8	78.4
Total cholesterol[6]						
<200 (desirable)	35.0	57.6	27.6	62.1	36.5	56.4
200–239 (borderline high)	33.2	26.4	32.2	23.2	30.9	27.4
240+ (high)	31.7	16.1	40.1	14.7	32.6	16.2
Control of diabetes among patients with diabetes						
Glycohemoglobin <7% (controlled)	30.8	48.0	36.5	58.2	28.9	42.1
Glycohemoglobin 7% or higher (uncontrolled)	69.2	52.0	63.5	41.9	71.1	57.9

Here we examine awareness, treatment, and control of hypertension, hyperlipidemia, and diabetes in U.S. adults with CKD in 1988–1994 and 2005–2010. While the prevalence of hypertension was similar in both time frames, at 73 compared to 74 percent, the proportion unaware of their hypertension fell from 36 to 24 percent, while the proportion that was aware, treated, and controlled rose from 7.9 to 26 percent.

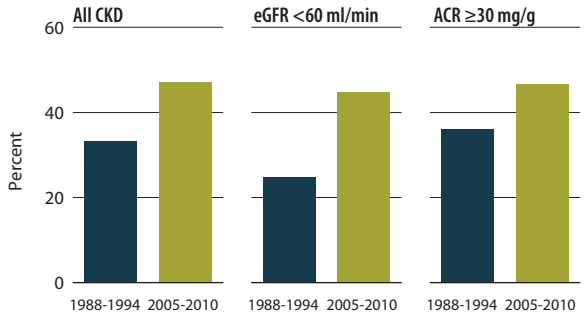
For hyperlipidemia, the overall prevalence declined from 75 to 67 percent, while the lack of awareness fell from 62 to 34 percent. The proportion categorized as aware, treated, and controlled increased almost 15-fold, from 2.1 to 31 percent. Among participants with diabetes, glycemic control improved from 31 to 48 percent. » **Table 1.b;** see page 140 for analytical methods. *NHANES III (1988–1994) & 2005–2010 participants age 20 & older; dialysis patients excluded from NHANES 2005–2010; eGFR calculated using CKD-EPI equation; urine albumin/creatinine ratio (ACR).*

Analysis definitions

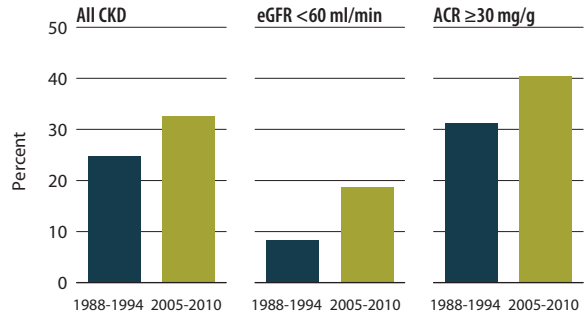
1. Hypertension defined as blood pressure ≥130/≥80 for those with CKD and diabetes; otherwise ≥140/≥90, or self-reported treatment for hypertension.
2. Awareness and treatment are self-reported. Control defined as <130/<80 for those with CKD and diabetes; otherwise <140/<90.
3. Hyperlipidemia based on elevated LDL following Adult Treatment Panel III (ATP III) guidelines, with CKD considered a risk equivalent for chronic heart disease, self-reported treatment, or self-reported dieting to lower cholesterol.
4. Awareness and treatment self-reported. Control defined as meeting the National Cholesterol Education Program (NCEP) ATP III LDL target: <100 mg/dl (high risk), <130 mg/dl (moderate risk), or <160 mg/dl (low risk).
5. HDL cholesterol classified according to ATP III guidelines.
6. Total cholesterol classified according to ATP III guidelines.
7. Glycohemoglobin classified according to American Diabetes Association guidelines.

Between 1988–1994 and 2005–2010, management of hypertension, hyperlipidemia, hyperglycemia, and diabetes in the NHANES cohorts improved, regardless of how CKD is defined — by eGFR or by ACR. » **Figures 1.12–15;** see page 140 for analytical methods. *NHANES III (1988–1994) & 2005–2010 participants age 20 & older; dialysis patients excluded from NHANES 2005–2010; eGFR calculated using CKD-EPI equation; urine albumin/creatinine ratio (ACR).*

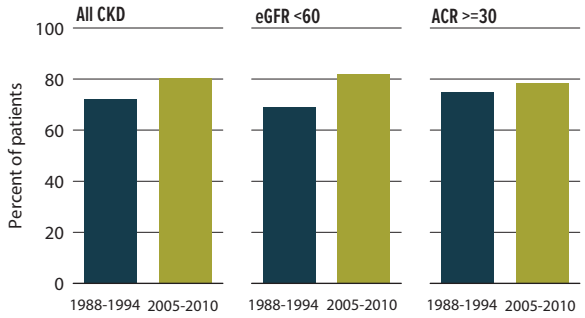
vol 1
1.12 NHANES participants at target blood pressure



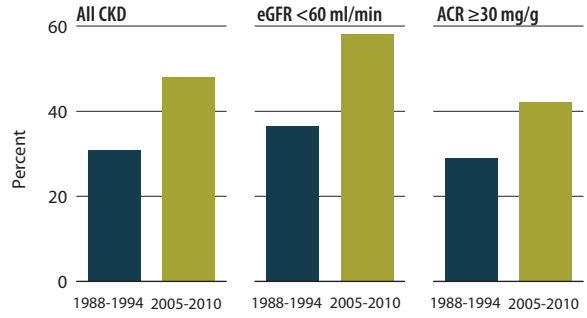
vol 1
1.13 NHANES participants within LDL cholesterol target range



vol 1
1.14 NHANES participants within HDL cholesterol target range



vol 1
1.15 NHANES participants with glycohemoglobin <7%



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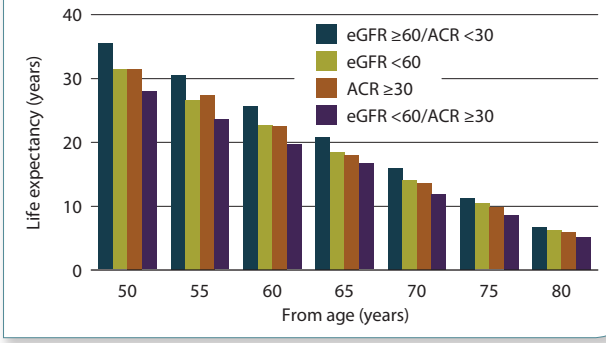
1.16 Life expectancy of NHANES participants with or without CKD, 1999–2004



Many studies have shown that markers of CKD are associated with higher mortality rates, but few, if any, attempted to translate this mortality excess into easily understandable terms. Figure 1.16 shows life expectancy estimates for U.S. adults with CKD, using NHANES data from 1999–2004. At age 50, estimated life expectancy for subjects with eGFR ≥60 and ACR <30 is 35.5 years; the reductions in life expectancy associated with eGFR <60, ACR ≥30, and both conditions are 4.1 years (11.4 percent of 35.5 percent), 4.0 years (11.3 percent) and 7.5 years (21.2 percent), respectively. When life expectancy is calculated from successively older starting points, absolute reductions decline and percentage reductions remain broadly similar. » **Figure 1.16;** see page 140 for analytical methods. *NHANES participants, 1999–2004; eGFR calculated using CKD-EPI equation; urine albumin/creatinine ratio (ACR).*

PREVALENCE OF CKD

adjusted odds ratios of CKD in NHANES participants, by risk factor (Figure 1.4)

NHANES III	» diabetes · 4.1 » self-reported diabetes · 3.7 » hypertension · 2.8
	» self-reported hypertension · 2.4 » self-reported CVD · 1.8 » BMI ≥30 · 1.5
NHANES 2005–2010	» diabetes · 3.4 » self-reported diabetes · 3.4 » hypertension · 2.4
	» self-reported hypertension · 2.3 » self-reported CVD · 1.7 » BMI ≥30 · 1.4

adjusted odds ratios of eGFR <60 in NHANES participants, by risk factor (Figure 1.5)

NHANES III	» diabetes · 1.7 » self-reported diabetes · 1.8 » hypertension · 2.7
	» self-reported hypertension · 2.7 » self-reported CVD · 2.2 » BMI ≥30 · 1.3
NHANES 2005–2010	» diabetes · 2.1 » self-reported diabetes · 2.2 » hypertension · 2.5
	» self-reported hypertension · 2.5 » self-reported CVD · 2.8 » BMI ≥30 · 1.1

adjusted odds ratios of ACR ≥30 in NHANES participants, by risk factor (Figure 1.6)

NHANES III	» diabetes · 5.3 » self-reported diabetes · 4.8 » hypertension · 2.9
	» self-reported hypertension · 2.2 » self-reported CVD · 1.7 » BMI ≥30 · 1.5
NHANES 2005–2010	» diabetes · 4.0 » self-reported diabetes · 3.9 » hypertension · 2.4
	» self-reported hypertension · 2.2 » self-reported CVD · 2.4 » BMI ≥30 · 1.5

COMORBIDITY

distribution of markers of CKD in NHANES participants with diabetes, HTN, CVD, & obesity, 2005–2010 (percent; Figure 1.11)

eGFR <60	» diabetes · 19.3	» HTN · 12.9	» CVD · 27.9	» BMI ≥30 · 7.4
ACR ≥30	· 29.9	· 14.8	· 24.3	· 11.7
eGFR <60 & ACR ≥30	· 8.6	· 4.1	· 10.9	· 2.1

AWARENESS, TREATMENT, AND CONTROL

NHANES participants at target blood pressure (percent; Figure 1.12)

NHANES III	» all CKD · 33.1	» eGFR <60 · 24.7	» ACR ≥30 · 35.9
NHANES 2005–2010	· 47.2	· 44.6	· 46.5

NHANES participants within LDL cholesterol target range (percent; Figure 1.13)

NHANES III	» all CKD · 24.8	» eGFR <60 · 8.3	» ACR ≥30 · 31.2
NHANES 2005–2010	· 32.6	· 18.6	· 40.3

NHANES participants within HDL cholesterol target range (percent; Figure 1.14)

NHANES III	» all CKD · 27.8	» eGFR <60 · 30.8	» ACR ≥30 · 25.2
NHANES 2005–2010	· 19.6	· 18.0	· 21.6

NHANES participants with glycohemoglobin <7% (percent; Figure 1.15)

NHANES III	» all CKD · 30.8	» eGFR <60 · 36.5	» ACR ≥30 · 28.9
NHANES 2005–2010	· 48.0	· 58.2	· 42.1