Nicolaes de Bry, 1601

1 Chronic kidney disease in the general population

In this chapter we assess single-sample, cross-sectional estimates of kidney function with 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 examining kidney function, usually by estimating glomerular filtration rates and rates of urinary albumin excretion. As with other disease burdens assessed in the national survey, we estimate kidney function at a single point in time. In clinical practice, defining CKD cases would typically require multiple estimates of kidney function over weeks or months. But because repeated measures of kidney function were only available in a voluntary subset of the 1988–1994 NHANES sample, we are forced to rely on single measurements to define current kidney function estimates in the U.S., as well as trends over time.

We begin the chapter by showing the overall burden and interactions of diabetes, cardiovascular disease, and single-sample ("spot") prevalence estimates of an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 m^2 or a urine albumin/creatinine ratio (ACR) of 30 mg/g or higher — three interrelated conditions of public health relevance — and compare prevalence estimates based on eGFR to those based on ACR. When defined by eGFR <60, the prevalence estimate in 2005–2010 was 6.3 percent, compared to 9.3 and 8.5 percent for diabetes and cardiovascular disease, respectively. Defined, however, by ACR ≥ 30, the prevalence estimate rises to 9.2 percent.

Diabetes, cardiovascular disease, and either a spot eGFR <60 or a spot ACR ≥ 30 were present in 9.3, 8.5, and 13.1 percent of NHANES participants in 2005–2010; 6.3 percent had an eGFR < 60, while 9.2 percent had an ACR ≥ 30.

Exploring the implications of kidney function, 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

CKD IN THE GENERAL POPULATION
introduction

In wisdom gathered over time I have found that every experience is a form of exploration.

Ansel Adams
A Manifesto for Living

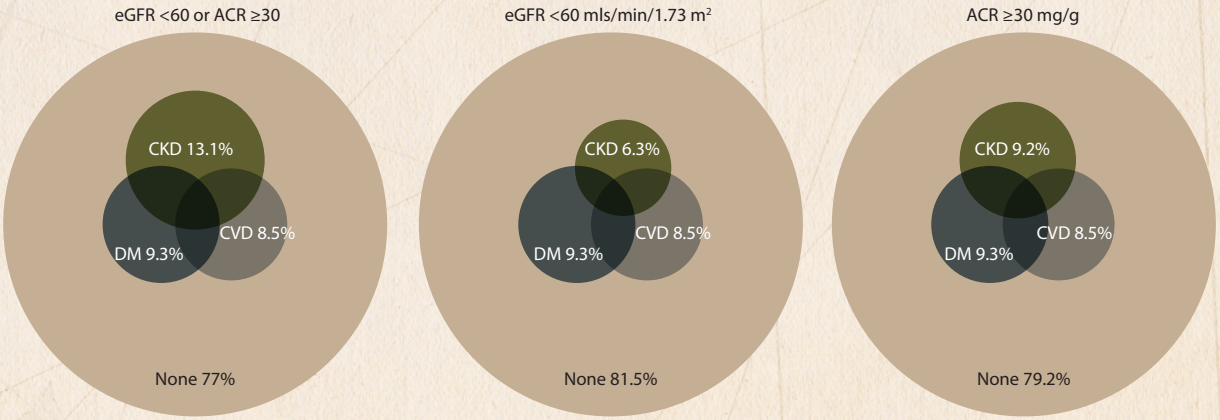
terms of biochemical data, but that provide extensive information on morbidity, interventions, and costs.

Overall, the prevalence of either eGFR < 60 or ACR ≥ 30 appears to have increased between 1988–1994 and 2005–2010; the prevalence of ACR ≥ 30 alone, however, has not changed, suggesting that a rise in non-proteinuric eGFR < 60 has occurred in the U.S. general population. Findings for eGFR < 60 or ACR ≥ 30 within populations at risk for CKD show similar patterns, though findings are less prominent among those with a BMI ≥ 30 kg/m².

We conclude the chapter by examining awareness, treatment, and control of major risk factors for cardiovascular disease, looking at hypertension, lipid disorders, and glycemic control within populations eGFR < 60 or ACR ≥ 30. 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. Awareness of high LDL-cholesterol levels has doubled, and control has increased 15-fold. Finally, glycemic control among diabetic patients with eGFR < 60 or ACR ≥ 30 has also improved.

It will be important to determine whether 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; single-sample estimates of eGFR & ACR. eGFR calculated using the CKD-EPI equation.*

vol 1
1.1 **Distribution of NHANES 2005–2010 participants with diabetes, cardiovascular disease, & single-sample markers of CKD**



Spot estimates of GFR less than 60 ml/min/1.73 m² and ACR ≥30 mg/g for adult NHANES 1988–1994 and 2005–2010 participants are shown in Table 1.a. For the presence of either spot eGFR <60 or spot ACR ≥30, prevalence estimates rose from 12.3 to 14.0 percent.

The largest relative increase (1.6-fold) was seen in those with cardiovascular disease, for whom estimates rose from 25.4 percent to 40.8 percent.

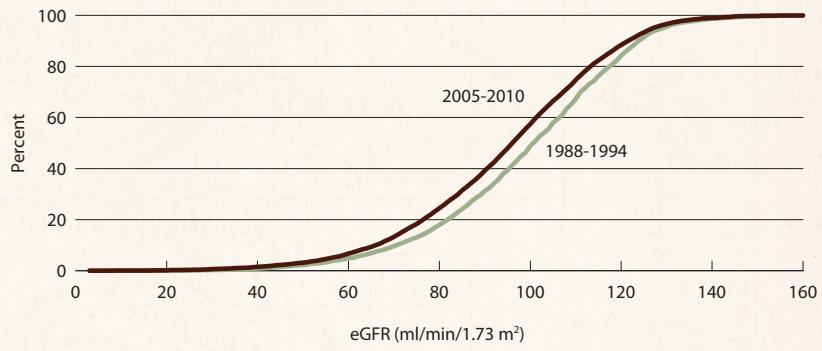
For spot eGFR <60, prevalence rose from 4.9 to 6.7 percent overall, with the largest relative increase (1.7-fold) in those age 40–59; prevalence for spot ACR ≥30 rose from 8.8 to 9.4 percent overall, and from 16.6 to 24.3 percent for those with cardiovascular disease.

Figure 1.2 shows cumulative distributions of spot eGFR in 1988–1994 and 2005–2010. Overall, a population shift towards lower spot eGFR levels was observed over time, with most of the leftward shift confined to spot eGFR levels between 50 and 125 ml/min/1.73 m². Figure 1.3, with corresponding findings for spot ACR, shows similar distribution patterns in both eras. • **Table 1.a & Figures 1.2–3;** see page 140 for analytical methods. *NHANES 1988–1994 & 2005–2010 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation.*

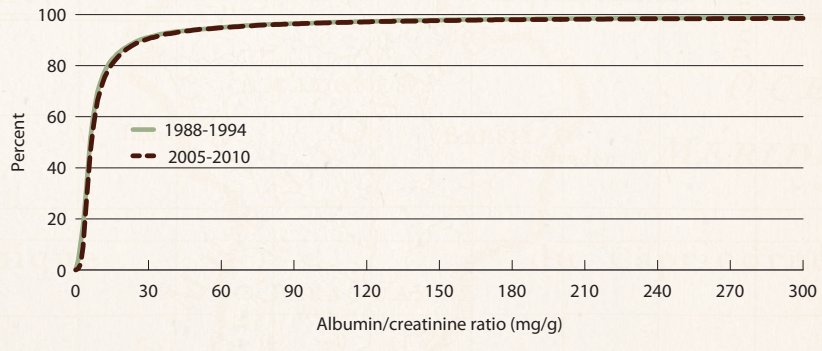
vol 1 **1.a** **Prevalence (%) of CKD in the NHANES population within age, gender, race/ethnicity, & risk factor categories**

	All CKD		eGFR <60 ml/min/1.73 m²		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 black/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

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



vol 1 **1.3** **Cumulative urine albumin/creatinine ratio (ACR) distribution curves of NHANES participants**



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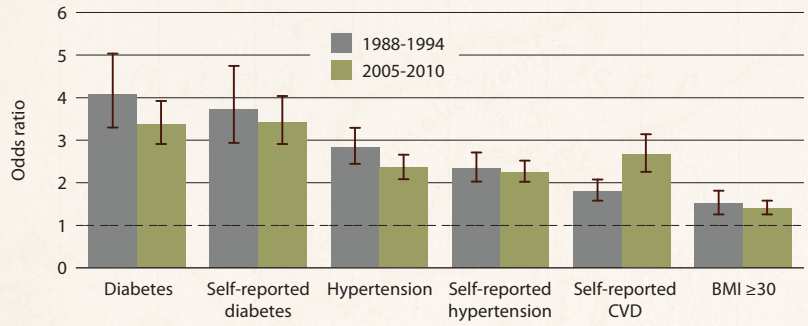
Adjusted odds ratios of CKD in NHANES participants, by risk factor



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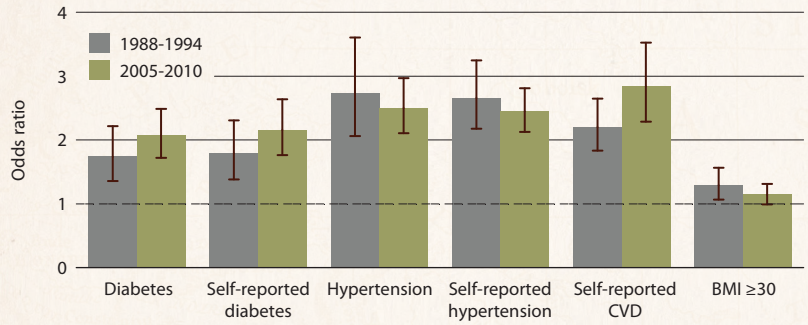
Adjusted odds ratios of spot eGFR <60 ml/min/1.73 m² in NHANES participants, by risk factor



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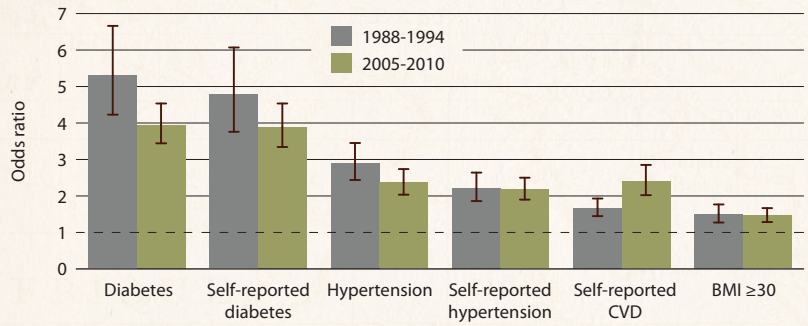
Adjusted odds ratios of spot urine albumin/creatinine ratio (ACR) ≥30 mg/g in NHANES participants, by risk factor



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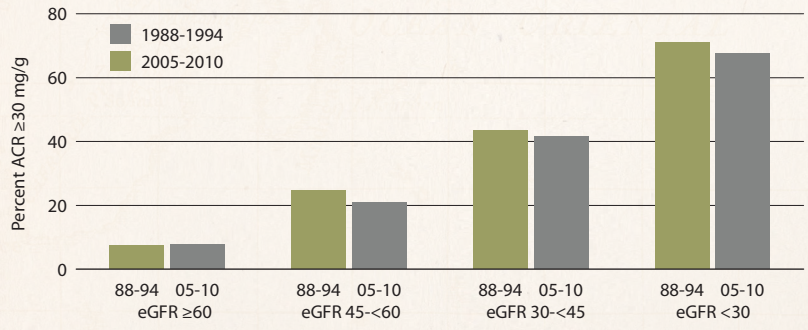
NHANES participants with spot urine albumin / creatinine ratio (ACR) ≥ 30 mg/g, by spot eGFR range



Adjusted odds ratios for spot eGFR <60 ml/min/1.73 m² or spot ACR ≥30 mg/g were lower in NHANES 2005–2010 participants than in 1988–1994 participants for all associations except self-reported cardiovascular disease, where adjusted odds ratios rose from 1.81 to 2.66.

Figure 1.5 shows a similar analysis for spot eGFR <60; adjusted odds ratios rose for both diabetes categories and for self-reported cardiovascular disease, and fell for both measured and self-reported hypertension and for obesity.

For spot ACR ≥30, adjusted odds ratios fell for all characteristics except self-reported cardiovascular disease. ✦ **Figures 1.4–6;** see page 140 for analytical methods. *NHANES 1988–1994 & 2005–2010 participants age 20 & older; single-sample estimates of eGFR & ACR. Adj: age, gender, & race; eGFR calculated using the CKD-EPI equation.*

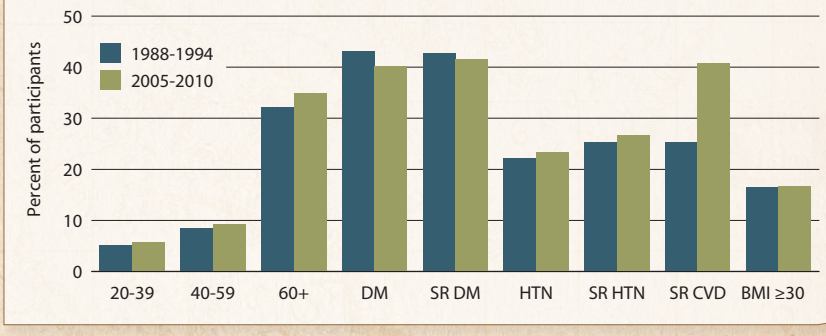
In NHANES participants from both 1988–1994 and 2005–2010, the likelihood of spot ACR ≥30 increased as spot eGFR fell, with 68 percent of 2005–2010 participants having a spot ACR ≥30 when spot eGFR was <30, compared to 7.8 percent when spot eGFR was above 60. ✦ **Figure 1.7;** see page 140 for analytical methods. *NHANES 1988–1994 & 2005–2010 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation.*

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

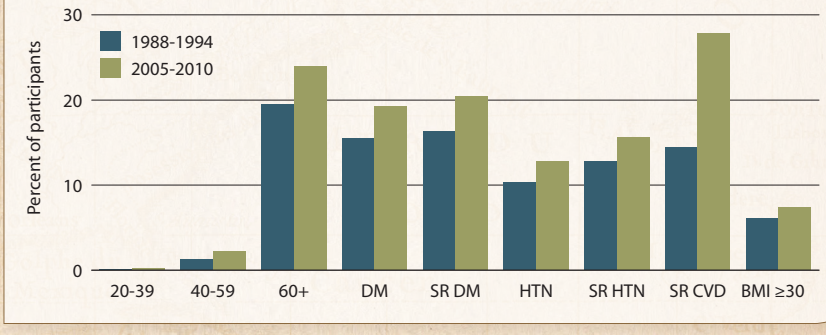
For spot eGFR <60 alone, prevalence estimates are higher in later years in all subgroups studied. For spot ACR ≥30 alone, a substantial decline is seen among those in each diabetes category (from 36 to 30 percent), while a substantial increase is seen in those with self-reported cardiovascular disease (from 16.6 to 24 percent).

While differences in categorization for cardiovascular disease may explain some of the disparities in prevalence estimates for markers of CKD, these substantial differences have yet to be adequately explained. ◆ **Figures 1.8–10;** see page 140 for analytical methods. *NHANES 1988–1994 & 2005–2010 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation. Diabetes defined as A1c <7 percent, self-reported (SR), or currently taking glucose-lowering medications. Hypertension defined as BP ≥130/≥80 for those with diabetes or CKD, otherwise BP ≥140/≥90, or taking medication for hypertension.*

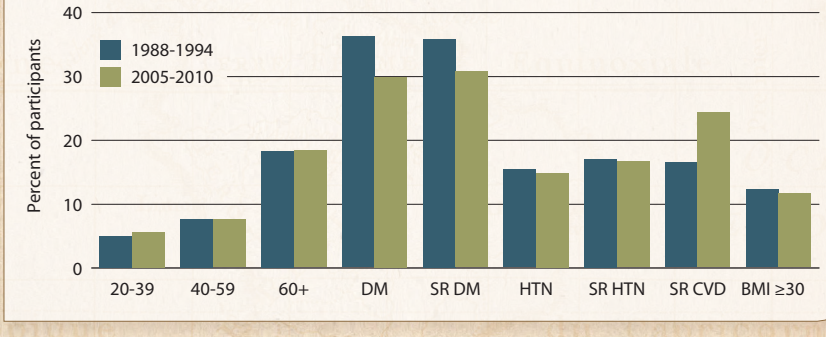
vol 1 **1.8** **NHANES participants with CKD, by age & risk factor**



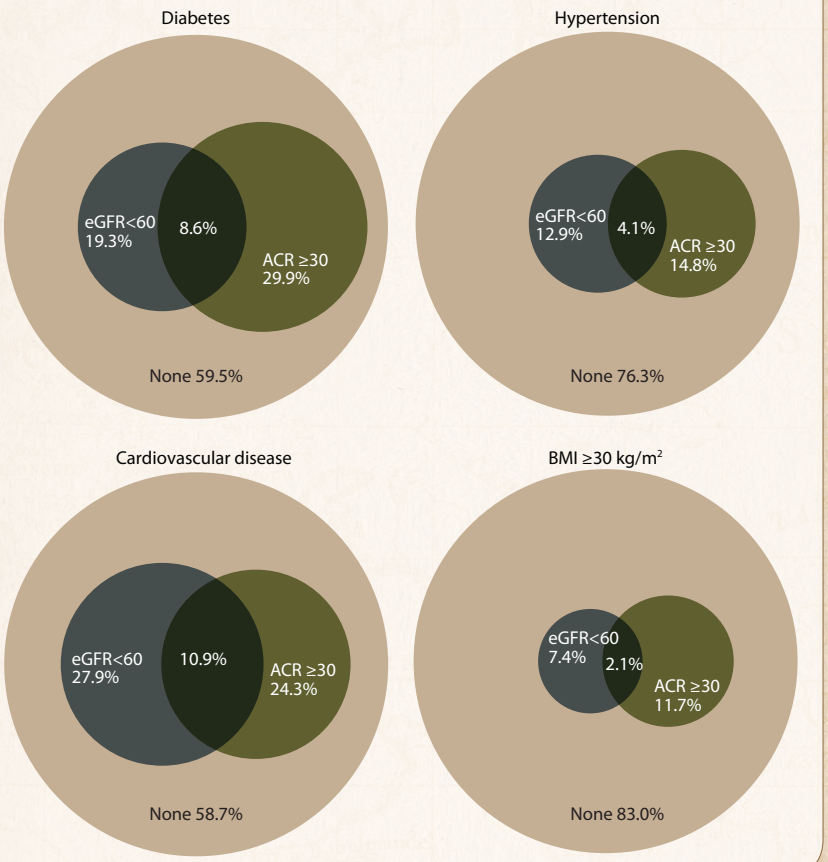
vol 1 **1.9** **NHANES participants with spot eGFR <60 ml/min/1.73 m², by age & risk factor**



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



vol 1
I.11 **Distribution of markers of CKD in NHANES participants with diabetes, hypertension, cardiovascular disease, & obesity, 2005–2010**



Here we look at the occurrence of spot eGFR <60 ml/min/1.73 m² and spot ACR ≥30 mg/g among adult NHANES 2005–2010 participants with diabetes, hypertension, cardiovascular disease, and body mass index ≥30 kg/m². Spot eGFR <60 was most prevalent in those with cardiovascular disease, at 27.9 percent, followed by those with diabetes, hypertension, and high body mass index, at 19.3, 12.9 and 7.4 percent, respectively. Spot ACR ≥30 was most common in those with diabetes, at 29.9 percent, followed by those with cardiovascular disease, hypertension, and high body mass index, at 24.3, 14.8, and 11.7 percent.

The joint presence of spot eGFR <60 and spot ACR ≥30 was most common with cardiovascular disease, at 10.9 percent, followed by diabetes, hypertension, and high body mass index, at 8.6, 4.1, and 2.1 percent.✦ **Figure 1.11;** see page 140 for analytical methods. *NHANES 2005–2010 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation.*

vol 1
1.b **Awareness, treatment, & control of hypertension, hyperlipidemia, HDL, total cholesterol, & diabetes (% of NHANES participants)**

	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

Table 1.b shows awareness, treatment, and control of hypertension, hyperlipidemia, and diabetes in NHANES 1988–1994 and 2005–2010 adult participants with spot eGFR <60 ml/min/1.73 m² or spot ACR ≥30 mg/g.

While the prevalence of hypertension was similar in both time frames, at 73 versus 74 percent, the proportion of participants unaware of their hypertension declined from 36 percent to 24 percent, while the proportion that was aware, treated, and controlled rose from 7.9 to 26 percent.

For hyperlipidemia, overall prevalence declined from 75 to 67 percent, while lack of awareness fell from 62 to 34 percent, and the proportion categorized as aware, treated, and controlled increased almost 15-fold, from 2.1 to 31 percent.

In the subgroup with diabetes, glycemic control improved from 31 to 48 percent. ✦ **Table 1.b;** see page 140 for analytical methods. *NHANES 1988–1994 & 2005–2010 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation.*

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.

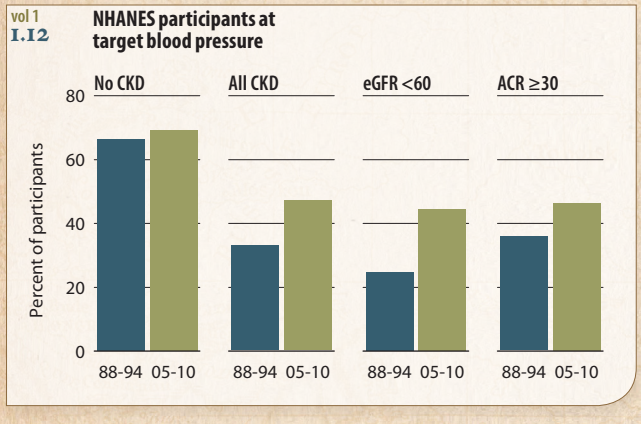
4 Awareness and treatment self-reported. Control defined as meeting the National Cholesterol Education Program (NCEP) ATP III LDL target: <100 mg/dl (high risk), <130 mg/dl (moderate risk), or <160 mg/dl (low risk).

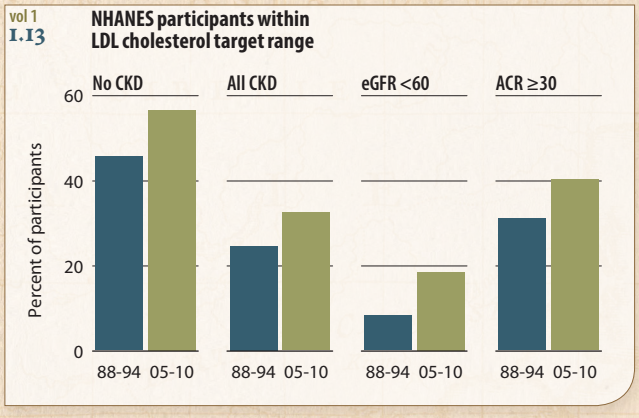
5 HDL cholesterol classified according to ATP III guidelines.

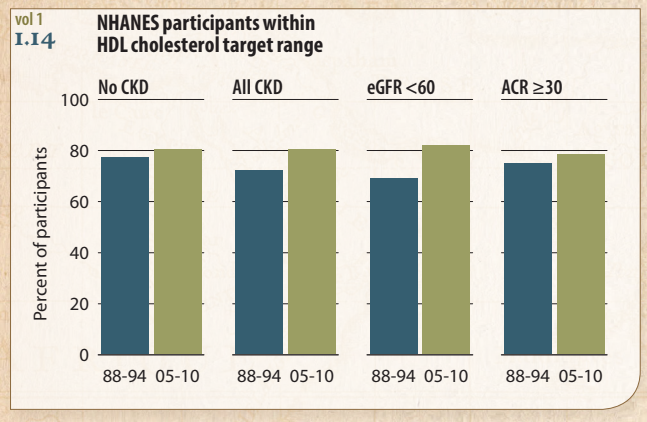
6 Total cholesterol classified according to ATP III guidelines.

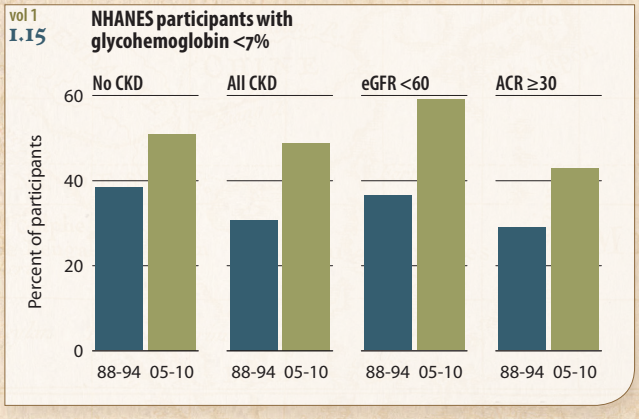
7 Glycohemoglobin classified according to American Diabetes Association guidelines.

Between 1988–1994 and 2005–2010, improvements in the management of hypertension, hyperlipidemia, hyperglycemia, and diabetes were present regardless whether spot eGFR or spot ACR was used for subgroup definition. In terms of absolute and relative changes over time, cardiovascular risk factor management improvements were greater in the population with CKD than in the population without. ✦ **Figures 1.12–1.15;** see page 140 for analytical methods. *NHANES 1988–1994 & 2005–2010 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation. Dialysis patients excluded from NHANES 2005–2010. Values in Figure 1.12 cannot be directly compared to those in Table 1.b. The table represents NHANES participants who are classified as hypertensive (measured/treated) but some of those are at target blood pressure. Figure 1.12 represents all hypertensives plus those hypertensives who are at target blood pressure, probably due to medication.*









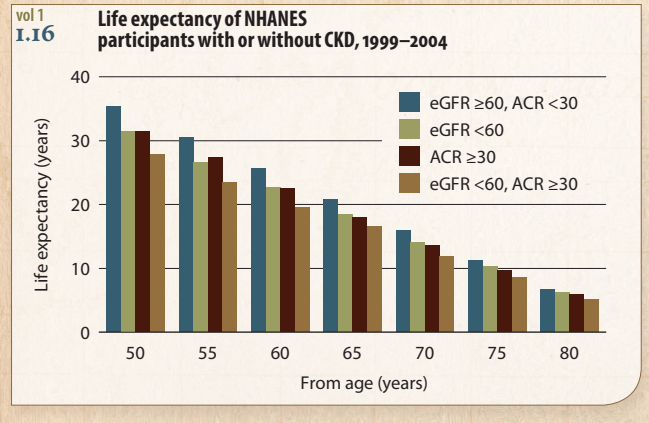


Figure 1.16 shows life expectancy estimates for adult NHANES 1999–2004 participants with single-sample estimates of GFR <60 ml/min/1.73 m² and ACR ≥30 mg/g. At age 50, estimated life expectancy for subjects with eGFR ≥ 60 and ACR <30 was 35.5 years; the reduction in life expectancy associated with eGFR <60, ACR ≥30 and both conditions were 4.1 years (11.4% of 35.5 years), 4.0 years (11.3%) and 7.5 years (21.2%), respectively. When life expectancy is calculated from successively older starting points, absolute reductions decline and percentage reductions remain similar. ✦ **Figure 1.16;** see page 140 for analytical methods. *NHANES 1999–2004 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation.*

prevalence of chronic kidney disease

ADJUSTED ODDS RATIOS OF CKD IN NHANES PARTICIPANTS, BY RISK FACTOR (FIGURE 1.4)

	DM	self-reported DM	HTN	self-reported HTN	self-reported CVD	BMI ≥30
NHANES 1988–1994	4.1	3.7	2.8	2.4	1.8	1.5
NHANES 2005–2010	3.4	3.4	2.4	2.3	2.7	1.4

ADJUSTED ODDS RATIOS OF SPOT eGFR <60 ML/MIN/1.73 M² IN NHANES PARTICIPANTS, BY RISK FACTOR (FIGURE 1.5)

	DM	self-reported DM	HTN	self-reported HTN	self-reported CVD	BMI ≥30
NHANES 1988–1994	1.7	1.8	2.7	2.7	2.2	1.3
NHANES 2005–2010	2.1	2.2	2.5	2.5	2.8	1.1

ADJUSTED ODDS RATIOS OF SPOT ACR ≥30 MG/G IN NHANES PARTICIPANTS, BY RISK FACTOR (FIGURE 1.6)

	DM	self-reported DM	HTN	self-reported HTN	self-reported CVD	BMI ≥30
NHANES 1988–1994	5.3	4.8	2.9	2.2	1.7	1.5
NHANES 2005–2010	3.9	3.9	2.4	2.2	2.4	1.5

comorbidity

DISTRIBUTION OF MARKERS OF CKD IN NHANES PARTICIPANTS WITH DIABETES, HTN, CVD, & OBESITY, 2005–2010 (FIGURE 1.11)

	diabetes	hypertension	CVD	BMI ≥30
spot eGFR <60	19.3%	12.9%	27.9%	7.4%
spot ACR ≥30	29.9%	14.8%	24.3%	11.7%
spot eGFR <60 & spot ACR ≥30	8.6%	4.1%	10.9%	2.1%

awareness, treatment, & control

NHANES PARTICIPANTS AT TARGET BLOOD PRESSURE (FIGURE 1.12)

	no CKD	CKD	spot eGFR <60	spot ACR ≥30
NHANES 1988–1994	67%	33%	25%	36%
NHANES 2005–2010	69%	47%	45%	47%

NHANES PARTICIPANTS WITHIN LDL CHOLESTEROL TARGET RANGE (FIGURE 1.13)

	no CKD	CKD	spot eGFR <60	spot ACR ≥30
NHANES 1988–1994	46%	25%	8.3%	31%
NHANES 2005–2010	57%	33%	19%	40%

NHANES PARTICIPANTS WITHIN HDL CHOLESTEROL TARGET RANGE (FIGURE 1.14)

	no CKD	CKD	spot eGFR <60	spot ACR ≥30
NHANES 1988–1994	77%	72%	69%	75%
NHANES 2005–2010	81%	80%	82%	78%

NHANES PARTICIPANTS WITH GLYCOHEMOGLOBIN <7 PERCENT (FIGURE 1.15)

	no CKD	CKD	spot eGFR <60	spot ACR ≥30
NHANES 1988–1994	38%	31%	37%	29%
NHANES 2005–2010	51%	49%	59%	43%