Chronic kidney disease (CKD) in Wisconsin: Time to address this public health problem

A. Vishnu Moorthy, MD; Mark V. Wegner, MD, MPH

Over the past 30 years, the number of individuals with chronic kidney disease (CKD) has been growing silently to epidemic proportions, both in the United States and worldwide.[1-2] This increasing burden of CKD, both on patients and the health care system, is readily apparent when examining the significant increase in the number of patients with kidney failure who have required dialysis or kidney transplantation during the past 3 decades. The number of patients developing kidney failure annually in the United States has increased more than 7-fold, from 14,500 cases in 1978 to over 106,912 in 2005, (34.7/100,000 population).[3]

According to the US Renal Data System,[3] there were over 485,000 people living with kidney failure in the United States on December 31, 2005, and Medicare costs for the kidney disease program totaled $21.4 billion. The number of patients requiring dialysis or kidney transplantation in the United States is expected to be more than 661,000 by the year 2010 at a projected annual cost exceeding $28 billion dollars.[3]

In Wisconsin, the number of patients with kidney failure has increased 3-fold, from 8.6 per 100,000 population in 1982 to 27.9 per 100,000 population in 2003 (Figure 1).[4] This is well beyond the *Healthy People 2010* target of 21.7 cases per 100,000. Four new dialysis centers opened in Wisconsin in 2006, and in 2007, nearly 5000 patients received dialysis treatments in 113 Wisconsin dialysis centers. Despite improvement in the quality of dialysis therapy in recent years, patients on dialysis continue to experience significant morbidity, require extended hospitalization, and have a 2-year survival rate of 67% and a 5-year survival rate of 40%.[3]

March 13, 2008, is World Kidney Day.

Although the numbers for individuals with kidney failure are staggering on their own, they represent only a subset of the population with CKD. The number of patients with CKD in the United States has been estimated to be over 19 million.[5] In the United States, approximately 1 in 6 adults (16.8%) over the age of 20 years has CKD, according to the 1999-2004 National Health and Nutrition Examination Survey (NHANES) data. This is an alarming increase from the 1988-1994 NHANES data that indicated a prevalence of 14.5% in US adults.[6] CKD is a bigger problem in older adults. Prevalence of CKD was greatest at 39.4% in adults 60 years and older. It is also estimated that another 20 million Americans are at increased risk for developing CKD.[5]

The effects of CKD are far reaching, and recent data from several large, diverse population studies have shown that patients with CKD are up to 100 times more likely to die from cardiovascular disease than to ever require dialysis or kidney transplantation.[7-8] Despite this large burden, and the fact that the complications of CKD are easier to prevent than to treat, CKD has not been historically recognized as a serious public health problem and patients with CKD are rarely diagnosed until late in their disease. One reason for this is that CKD does not have symptoms in its early stages and can only be diagnosed by laboratory tests.

In recent years, diagnosis of CKD has been defined by the National Kidney Foundation—Kidney Disease Outcomes Quality Initiative.[9] Serum creatinine alone is

Author Affiliation: Nephrology Section, Department of Medicine, University of Wisconisin School of Medicine and Public Health, Madison, Wis (Moorthy); Wisconsin Division of Public Health, Madison, Wis (Wegner).

Corresponding Author: A. Vishnu Moorthy, MD, UW Nephrology, 3034 Fish Hatchery Rd, Fitchburg WI 53713; phone 608.270.5689; e-mail avm@medicine.wisc.edu.

considered inadequate to assess the kidney function. Timed urine collections to measure the creatinine clearance over a 24-hour period have been generally abandoned since they are time consuming, inconvenient, and are an inaccurate measure of the kidney function. The National Kidney Disease Education Program (NKDEP) recommends that equations be used to translate serum creatinine into an estimate of the glomerular filtration rate (GFR).[10] However, formulae to assess kidney function such as the Cockcroft-Gault equation have been found to be less than adequate in the patient with CKD.[11]

Currently the MDRD (Modification of Diet in Renal Disease) formula is the recommended method to estimate kidney function.[10] This formula produces an estimated GFR (eGFR) from the patient's age, gender, ethnicity, and measured serum creatinine level. A diagnosis of CKD is made when a patient has an eGFR of ≤60 ml/min for more than 3 months. Alternatively, a diagnosis of CKD may be made in a patient with any level of eGFR who has structural (ie, polycystic kidney disease) or functional (ie, proteinuria) kidney abnormalities that persist for more than 3 months. Although the MDRD formula is the current best method for early diagnosis of CKD, it is important to note its limitations. The formula is less accurate for estimating the GFR in subjects at higher level of kidney function (ie, GFR>60 ml/min).[12] Also, the formula is designed for use in patients with stable kidney function and thus is not useful in the hospitalized patient whose serum creatinine level can vary for a variety of reasons (due to both renal and extra renal disease). Finally, the need for the laboratory to calibrate the serum creatinine measurement to accepted standards is crucial in estimating the GFR (Table 1).[13]

Another early diagnostic test for the presence of kidney disease, particularly in a patient with diabetes mellitus, is testing for proteinuria. However, the traditional dipstick test for the presence of protein in the urine is insensitive. A protein/creatinine ratio can be useful as a surrogate for 24-hour collection of urine.[14] In the patient with diabetes mellitus, a more sensitive test for kidney damage is the detection of microalbuminuria. This can be detected in a random sample of urine (early morning sample is preferred) and expressed as mg of albumin per gram of creatinine. The urine albumin excretion in healthy individuals generally does not exceed 30 mg of albumin per gram of urinary creatinine. Microalbuminuria is present when urine albumin/creatinine ratio is between 30 to 300 mg of albumin per gram of creatinine. Persistent microalbuminuria is an early marker of kidney damage in the patient with diabetes mellitus and is also a predictor of cardiovascular disease.

An increasing number of laboratories are standardizing the reporting of blood and urine tests to diagnose CKD. Several report the eGFR automatically when a serum creatinine test is ordered. As the ethnicity of the patient is generally unknown to the laboratory, 2 values for the eGFR should be reported, one for African Americans and the second for all other races. Alternately, the physician could multiply the eGFR reported by the laboratory by 1.121 if the patient is of African American ethnicity. African Americans generally have a greater muscle mass and have slightly higher serum creatinine levels at all ages.

Because of low prevalence of CKD in the general population, it is recommended that screening programs for CKD be directed to patients at increased risk for this condition. Diabetes, hypertension, cardiovascular diseases, and a family history of CKD are the most common risk factors for CKD. In the United States, CKD is more prevalent in patients with diabetes (40.2%) than those without diabetes (15.4%), and in those with hypertension (24.6%) than those without (2.5%).[5] CKD is also more frequent in patients with cardiovascular disease (28.2%) than those without (15.4%).[5] The burden of CKD is greater among minority populations, particularly non-Hispanic blacks (19.9%) and Mexican Americans (18.7%).[5] Prevalence among non-Hispanic whites is 16.1%.[5]

Although the risk factors for CKD are well known (Table 2), the diagnosis is infrequently made even in patients at high risk for CKD. Although the risk for development of kidney failure is higher in African Americans, over 43% of African Americans with kidney failure were not aware of kidney disease until 1 week before their kidneys fail entirely.[16] Under-diagnosis was more common in non-Hispanic blacks, men, and those with hypertension. In a recent survey of more than 400 physicians, diabetes and hypertension were widely recognized as CKD risk factors. However, in a survey of 465 primary care physicians in 4 communities, family history of CKD was only identified as a risk factor by 66% of physicians and African American race was only identified by 78%.[17]

Despite the challenges of early diagnosis, it is the key to the management of the patient with CKD. Several large clinical trials have shown that adequate control of blood sugar levels in a patient with diabetes, maintaining blood

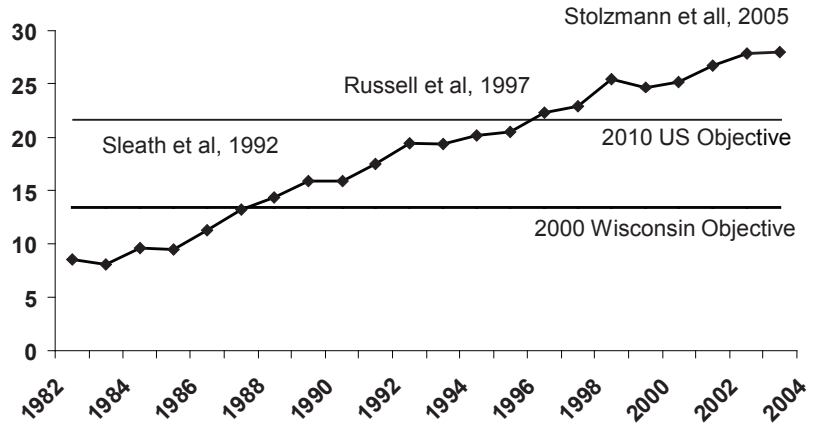

Figure 1. The trends in the age-adjusted end-stage renal disease incidence rate in Wisconsin, 1982-2003. (Courtesy of Patrick Remington, MD, MPH.)

Table 1. Criteria for the Definition of Chronic Kidney Disease

1. Estimated GFR of <60 ml/min/1.73 m^2
2. Abnormalities of the kidneys (with any eGFR) for at least 3 months that could be:
   a. Functional—as noted by urinary abnormalities such as proteinuria (or microalbuminuria in a patient with diabetes)
   b. Structural—such as polycystic kidney disease

National Kidney Foundation Kidney Disease Outcomes Quality Initiative 2005 (Adapted from reference 9).

Table 2. Prevalence of Risk Factors for Chronic Kidney Disease in United States

Risk Factor for CKD	Estimated Prevalence in United States (% of adults >20 years)
Diabetes Mellitus	7.8
Hypertension	24.0
Obesity	19.8
African American	12.3
Hispanic	12.5
Age >60 years	16.5

(Adapted from reference 15.)

pressure (BP) < 130/80 mm Hg in a patient with hypertension, use of medications to block the renin angiotensin system, lowering elevated lipid levels, and smoking cessation can slow the progression of kidney failure and also decrease cardiovascular morbidity and mortality.[18] However, these impressive results from clinical trials have not been generally translated into clinical practice.[19-20]

The enormous number of patients with CKD necessitates that the care of the patient in the early stages of CKD has to be provided by the primary care physician. Thus there is an increasing need for primary care providers to have a greater awareness of CKD risk factors and evidence-based treatment guidelines to care for patients with CKD. Patients with advanced CKD (ie, with GFR <30 ml/min) need to be referred to a nephrologist for management of the patient's medical problems as well as preparation for renal replacement therapy. In 1 recent study, only 17% of patients were seen by a nephrologist more than 3 months prior to starting dialysis.[21] This delay in referral of the patient has been shown to increase medical expense and shorten lifespan in the patient after initiation of dialysis. Kinchen et al studied 828 patients with new onset kidney failure starting dialysis in 81 dialysis facilities in the United States. Compared to patients who were referred to kidney specialists early (ie, >12 months before initiation of dialysis) the patients referred late (ie, <4 months) had a higher risk of early death. The 1-year mortality rate in the late referral group was 13.3% when compared to a rate of 4.3% in the early referral group.[22] Predialysis education of the patient with CKD has been shown to increase survival when dialysis is initiated. Devins et al noted in a 20-year follow up study that 172 patients randomly assigned to predialysis psychoeducational intervention survived significantly longer (mean of 9.36 years) than 163 patients receiving routine care (mean of 5.07 years).[23]

CKD is being recognized as a growing global public health problem. In 2006, the International Society of Nephrology and the International Federation of Kidney Foundations declared that the second Thursday in March every year is to be observed as the World Kidney Day. This is a recognition of the need for greater worldwide awareness of CKD.[24] Recent estimates suggest that the burden of CKD is also high in the developing countries including China and India.[1] CKD has been described as "common, harmful, and treatable."[1] Addressing the growing epidemic of CKD is essential and would be aligned with the government's public health goals in *Healthy People 2010*. ▼

Funding/Support: None declared.
Financial Disclosures: None declared.

References

1. C Levey AS, Andreoli SP, DuBose T, Provenzano R, Collins AJ. Chronic kidney disease: common, harmful and treatable—World Kidney Day. *Clin J Am Soc Nephrol*. 2007;2:401-405.
2. Couser WJ. Chronic kidney disease—the promise and the perils. *J Am Soc Nephrol.* 2007;18:2803-2805.
3. USRDS data. Available at: www.usrds.org. Accessed January 16, 2008.
4. A Stolzmann KL, Camponeschi JL, Remington PL. The increasing incidence of end-stage renal disease in Wisconsin from 1982-2003: an analysis by age, race and primary diagnosis. *Wis Med J.* 2005;104:66-71.
5. Prevalence of Chronic Kidney Disease and Associated Risk Factors—United States, 1999-2004. *MMWR*. 2007;56:161-165.
6. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis.* 2003;41:1-12.
7. Keith D, Bicholls G, Guillion C, Brown JB, Smith DH. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. *Arch Intern Med.* 2004;164:659-663.
8. Collins AJ, Li S, Gilbertson DT, Liu J, Chen SC, Herzog CA. Chronic kidney disease and cardiovascular disease in the Medicare population. *Kidney Int Suppl.* 2003;S24-31.
9. National Kidney Foundation: K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis.* 2002;39:S1-S266.
10. Hostetter TH, Lising M. National kidney disease education program. *J Am Soc Nephrol.* 2003;14:S114-S116.
11. Shoker A, Hossain MA, Koru-Sengul T, Raju TL, Cockcroft D. Performance of creatinine clearance equations on the original Cockroft-Gault population. *Clin Nephrol.* 2006;66:89-97.
12. Rule AD, Larson TS, Bergstralh EJ, et al. Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and in chronic kidney disease. *Ann Intern Med.* 2004;41;12:929-937.
13. Levey AS, Coresh J, Greene T, et al. Chronic kidney disease epidemiology collaboration: using standardized serum creatinine values in the MDRD study equation for estimating glomerular filtration rate. *Ann Intern Med.* 2006;145:247-254.
14. Gaspari F, Perico N, Remuzzi G. Timed urine collections are not needed to measure urine protein excretion in clinical practice. *Am J Kidney Dis.* 2006;47:8-14.
15. Vassalotti JA, Stevens LA, Levey AS. Testing for chronic kidney disease: a position statement from the National Kidney Foundation. *Am J Kidney Dis.* 2007;50:169-180.
16. DuBose TD Jr. American Society of Nephrology Presidential Address 2006: chronic kidney disease as a public health threat—new strategy for a growing problem. *J Am Soc Nephrol.* 2007;18:1038-1045.
17. Lea JP, McClellan WM, Melcher C, Gladstone E, Hostetter T. CKD risk factors reported by primary care physicians: do guidelines make a difference? *Am J Kidney Dis.* 2006;47:72-77.
18. Ruggenenti P, Remuzzi G. Kidney failure stabilizes after a two-decade increase: Impact on global (renal and cardiovascular) health. *Clin J Am Soc Nephrol.* 2007;2:146-150.
19. Rosen AB, Karter AJ, Liu JY, Selby JV, Schneider EC. Use of angiotensin-converting enzyme inhibitor and angiotensin receptor blockers in high-risk clinical and ethnic groups with diabetes. ***J** Gen Intern Med.* 2004;19:669-675.
20. Bailie GR, Eisele G, Liu L, et al. Patterns of medication use in the RRI-CKD study: focus on medications with cardiovascular effects. *Nephrol Dial Transplant.* 2005;20:1110-1115.
21. Obialto CI, Ofili EO, Quarshie A, Martin PC. Ultra late referral and presentation for renal replacement therapy: socioeconomic implications. *Am J Kidney Dis.* 2005;46:881-886.
22. Kinchen KS, Sadler J, Fink N, et al. The timing of specialist evaluation in chronic kidney disease and mortality. *Ann Intern Med.* 2002;137:479-486.
23. Devins GM, Mendelssohn DC, Barre PE, Taub K, Binik YM. Predialysis psycho educational intervention extends survival in CKD: a 20-year follow up. *Am J Kidney Dis.* 2005;46:1088-1098.
24. World Kidney Day. Available at: www.worldkidneyday.org. Accessed January 17, 2008.

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 1098-1861) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

Visit www.wmjonline.org to learn more.