

Diabetic Kidney Disease: A Report From an ADA Consensus Conference

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The incidence and prevalence of diabetes mellitus have grown significantly throughout the world, due primarily to the increase in type 2 diabetes. This overall increase in the number of people with diabetes has had a major impact on development of diabetic kidney disease (DKD), one of the most frequent complications of both types of diabetes. DKD is the leading cause of end-stage renal disease (ESRD), accounting for approximately 50% of cases in the developed world. Although incidence rates for ESRD attributable to DKD have recently stabilized, these rates continue to rise in high-risk groups such as middle-aged African Americans, Native Americans, and Hispanics. The costs of care for people with DKD are extraordinarily high. In the Medicare population alone, DKD-related expenditures among this mostly older group were nearly \$25 billion in 2011. Due to the high human and societal costs, the Consensus Conference on Chronic Kidney Disease and Diabetes was convened by the American Diabetes Association in collaboration with the American Society of Nephrology and the National Kidney Foundation to appraise issues regarding patient management, highlighting current practices and new directions. Major topic areas in DKD included (1) identification and monitoring, (2) cardiovascular disease and management of dyslipidemia, (3) hypertension and use of renin-angiotensin-aldosterone system blockade and mineralocorticoid receptor blockade, (4) glycemia measurement, hypoglycemia, and drug therapies, (5) nutrition and general care in advanced-stage chronic kidney disease, (6) children and adolescents, and (7) multidisciplinary approaches and medical home models for health care delivery. This current state summary and research recommendations are designed to guide advances in care and the generation of new knowledge that will meaningfully improve life for people with DKD. *Am J Kidney Dis.* 64(4):510-533. © 2014 by the American Diabetes Association and the National Kidney Foundation. Published by Elsevier Inc. All rights reserved.

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The incidence and prevalence of diabetes mellitus have grown significantly throughout the world, due primarily to the increase in type 2 diabetes. This increase in the number of people developing diabetes has had a major impact on the development of diabetic kidney disease (DKD).¹ Although kidney

disease attributable to diabetes is referred to as DKD, diabetes and various kidney diseases are common chronic conditions. Thus, people with diabetes may have other etiologies of chronic kidney disease (CKD) in addition to diabetes. Notably, DKD remains one of the most frequent complications of both types

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of diabetes, and diabetes is the leading cause of end-stage renal disease (ESRD), accounting for approximately 50% of cases in the developed world. Although incidence rates for ESRD attributable to DKD have stabilized over the past few years,² differences remain among high-risk subgroups. Middle-aged African Americans, Native Americans, and Hispanics continue to have higher rates of ESRD. These disparities in health care may be linked, in part, to the increasing rates of obesity and type 2 diabetes in youth, which disproportionately occur in these populations and allow for the development of diabetes complications earlier in life.

The overall costs of care for people with DKD are extraordinarily high, due in large part to the strong relationship of DKD with cardiovascular disease (CVD) and development of ESRD.³ For example, overall Medicare expenditures for diabetes and CKD in the mostly older (≥ 65 years of age) Medicare population were approximately \$25 billion in 2011. At the transition to ESRD, the per person per year costs were \$20,000 for those covered by Medicare and \$40,000 in the younger (< 65 years of age) group. Increased albuminuria and decreased glomerular filtration rate (GFR) are each independently and additively associated with an increase in all-cause and CVD mortality, and, in fact, most of the excess CVD of diabetes is accounted for by the population with DKD.

Due to very high human and societal costs, the Consensus Conference on Chronic Kidney Disease and Diabetes was convened by the American Diabetes Association (ADA) in collaboration with the American Society of Nephrology (ASN) and the National Kidney Foundation (NKF). The objectives of convening the conference and publishing this consensus report were to address vital issues regarding patient care, highlighting current practices, gaps in knowledge, and new directions for improving outcomes in this high-risk population.

The major sponsoring organization (ADA) and conference leadership (K.R.T. and M.E.M.) chose major topic areas meeting these objectives based on recent publications, public health trends, and input from stakeholders representing professional, academic, clinical, industry, and patient groups. This report contains summaries of the topic areas based on the conference proceedings and feedback from participants. Major topic areas in DKD included (1) identification and monitoring, (2) CVD and management of dyslipidemia, (3) hypertension and use of renin-angiotensin-aldosterone system (RAAS) blockade and mineralocorticoid receptor blockade, (4) glycemia measurement, hypoglycemia, and drug therapies, (5) nutrition and general care in advanced-stage CKD, (6) children and adolescents, and (7)

multidisciplinary approaches and medical home models for health care delivery.

This current state summary with research recommendations is designed to guide advances in patient care and the generation of new knowledge that will meaningfully improve life for people with DKD. This consensus conference and corresponding report are not all-inclusive of important considerations. For example, the topics of geriatrics, pregnancy, and kidney disease progression in DKD were not specifically addressed. However, these topics were comprehensively covered in the NKF-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines for diabetes and CKD and the evidence reviews and recommendations made therein remain germane.⁴

IDENTIFICATION AND MONITORING OF DKD

Laboratory Assessment of DKD

Identifying and monitoring DKD relies upon assessments of kidney function, usually with an estimated GFR (eGFR) < 60 mL/min/1.73 m², and kidney damage, usually by estimation of albuminuria > 30 mg/g creatinine. Widespread utilization of these simple laboratory measures has facilitated earlier recognition of DKD and has formed the basis for clinical staging. However, understanding the imprecision associated with these tests is critical to their appropriate utilization in clinical care.

Limitations of eGFR

Routine reporting of eGFR with serum creatinine concentration has been widely implemented. However, many clinicians and patients remain unaware of the uncertainty associated with GFR estimating equations. P_{30} , the performance measure for estimating equations, is the likelihood that the eGFR is within 30% of the measured GFR. The P_{30} for the most commonly used estimating equations is generally between 80% and 90%. Thus, the eGFR has, at best, a 90% chance of being within 30% of the measured GFR. In addition, the characteristics of the existing estimating equations make them significantly less precise at higher GFRs. This is of particular concern early in the course of DKD, which may be associated with an elevated GFR (also called hyperfiltration).⁵

Hyperfiltration is thought to be a manifestation of increased intraglomerular capillary pressure and has been implicated in the development and progression of experimental nephropathy in diabetic rodents. Reduction in intraglomerular capillary pressure and single nephron GFR by RAAS blockade in these animal models formed the basis for subsequent clinical trials.⁶ However, the link between glomerular hyperfiltration and subsequent albuminuria or eGFR

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