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A Brief History of KDIGO: Now in Our Seventh Year of Independence

Since its founding in 2003, KDIGO has been inextricably linked with the development of global clinical practice guidelines in nephrology. Significant advances in guideline methodologic approaches and in our understanding of kidney disease pose new challenges on how best to synthesize and appraise the ever expanding data and distill expert guidance into guidelines that are most useful to clinicians. In the following series of articles, we present brief summaries of KDIGO's recent accomplishments and outline their vision plan for maintaining guidelines up-to-date and improving their knowledge translation.

By John Davis

KDIGO's history is a history of guidelines in nephrology. There were none in 1994 when a conference called Controversies in the Quality of Dialysis Care was held under the auspices of the National Kidney Foundation (NKF, United States). It was co-chaired by Dr. Gary Eknoyan. One recommendation from that event was the call for the development of nephrology guidelines. That thought resonated with various stakeholders, who provided funding and expertise to enable the NKF to develop evidence-based clinical practice guidelines. Four guidelines under the banner of the DOQI (Dialysis Outcomes Quality Initiative) were published in 1997.

Those guidelines made a major impression on American nephrologists and were used in everyday practice. The government data entity, the United States Renal Data System (USRDS), tracked areas covered by the guidelines and reported significant improvement in the uniformity of care. The NKF continued to develop guidelines, although Dr. Eknoyan amended the name to KDOQI (Kidney Disease Outcomes Quality Initiative) to better reflect on all aspects of chronic kidney disease (CKD) care rather than just dialysis care. Several more guidelines were produced between 1997 and 2002.

Publication of the Chronic Kidney Disease Guideline in 2002 strengthened the concept that guidelines should be developed globally, rather than country by country. Care was taken to vet this idea with non-American opinion leaders, and after 2 years of study, their opinions were enthusiastically positive. So, the concept for an international nephrology guideline body—KDIGO (Kidney Disease: Improving Global Outcomes)—was born. It was to be truly global, not just the expansion of an American effort. Thus, the organization was incorporated in Brussels and became a foundation in the public interest under Belgian law, with NKF continuing to provide management support.

KDIGO's first guideline on the management of hepatitis C in patients with CKD was published in 2008. It was followed by Mineral and Bone Disorders and Care of the Transplant Recipient in 2009. During these years KDIGO's other core program, Controversies Conferences, began to thrive. The format was established where 60 to 70 international experts were brought together to discuss and debate important issues that weren't totally resolved and these conferences were well known for not only providing clinical guidance in controversial areas but helped advance the fu-

Table 1.

KDIGO Guidelines published since independence	
Topic	**Year**
Evaluation and Management of Chronic Kidney Disease	2013
Lipid Management in Chronic Kidney Disease	2013
Evaluation and Care of Living Kidney Donors	2017
Diagnosis, Evaluation, Prevention and Treatment of CKD–MBD	2017
Prevention, Diagnosis, Evaluation, and Treatment of Hepatitis C in Chronic Kidney Disease	2018
Upcoming	
Evaluation and Management of Candidates for Kidney Transplantation	2020
Management of Diabetes and Chronic Kidney Disease	2020
Update: Management of Blood Pressure in Chronic Kidney Disease	2020
Update: Glomerulonephritis	2020
Update: Anemia	2021 (Initiating work)
Diagnosis, Evaluation, Management and Treatment of ADPKD	2021 (Initiating work)

KDIGO Controversies Conferences held since independence	
Topic	**Year**
Revisiting CKD–MBD	2013
Supportive Care in Chronic Kidney Disease	2013
ADPKD	2014
ADTKD (Consensus Conference)	2014
Cystinosis	2014
Iron Management in Chronic Kidney Disease	2014
Complement-Mediated Kidney Disease: C3G and aHUS	2015
Diabetes and Chronic Kidney Disease	2015
Fabry Nephropathy	2015
Understanding Kidney Care Needs and Implementation Strategies in Low- and Middle-Income Countries	2015
Challenges in Conducting Clinical Trials in Nephrology	2016
Chronic Kidney Disease and Arrhythmias	2016
Common Elements in Rare Kidney Diseases	2016
Gitelman and Tubulopathies	2016
Improving the Prognosis of Patients with Advanced Chronic Kidney Disease	2016
Blood Pressure in Chronic Kidney Disease	2017
Heart Failure in Chronic Kidney Disease	2017
Kidney Disease in the Setting of HIV infection	2017
Management and Treatment of Glomerular Diseases	2017
Coronary Artery & Valvular Disease and Chronic Kidney Disease	2018
Dialysis Initiation, Modality Choice, Access, and Prescription	2018
Onconephrology	2018
Potassium Homeostasis and Management of Dyskalemia	2018
Acute Kidney Injury	2019
Blood Pressure and Volume Management in Dialysis	2019
Early Identification and Intervention in Chronic Kidney Disease	2019
Nomenclature for Kidney Function and Disease (Consensus Conference)	2019
Optimal Anemia Management in Chronic Kidney Disease	2019
Upcoming	
Central and Peripheral Arterial Diseases in Chronic Kidney Disease	2020
Genetics and Kidney Disease	2020
Home Dialysis	2020
Novel Therapies for Treatment of Anemia in Chronic Kidney Disease	2020
Dialysis Innovation	2021
Role of Complement in Kidney Disease	2021
Management of Symptom-Based Complications in Dialysis	2021

Abbreviations: ADPKD, autosomal dominant polycystic kidney disease; ADTKD, autosomal dominant tubulointerstitial kidney disease; aHUS, atypical hemolytic uremic syndrome; C3G, C3 glomerulopathy; CKD-MBD, chronic kidney disease-mineral bone disorder.

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History of KDIGO

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ture evidence base by identifying the key research agenda.

By 2009 KDIGO had become a global leader in nephrology guidelines designed to inform clinical decisions.

The economic downturn in 2009 and 2010 caused the NKF to rethink its priorities. One area to be cut back was global guidelines. This came at a time when KDIGO's reputation was growing. Two landmark Controversies Conferences were held during this time: Definition, Classification, and Prognosis in CKD, and Cardiovascular Disease in CKD.

KDIGO's Mineral and Bone Disorder guideline created CKD-MBD as a near-universal term and had major global impact, and work began on other new guidelines. In 2011 John Davis left the NKF but retained the title of Chief Executive Officer of KDIGO. A meeting was held in the Netherlands with Bert Kasiske, Kai-Uwe Eckardt, David Wheeler, and John to discuss KDIGO's future. The decision was made to go at it alone. Negotiations began to terminate KDIGO's management contract with the NKF, and plans were made for moving forward. John continued to manage KDIGO and recruited Danielle Green to join him. With great help from Dr. Yusuke Tsukamoto in Tokyo, some money was raised to bridge this critical period of transition.

KDIGO officially became an independent Belgian corporation on October 1, 2012. It had €19,000 in the bank. Bert and David were the co-chairs, with John and Danielle as the staff. A small but excellent executive committee was recruited to provide governance and guidance. KDIGO then began a steady building process that was directed at sustaining its place in global nephrology.

To reassert the organization's standing in the nephrology community, KDIGO published four original guidelines in 2012. Two more guidelines came in 2013, along with two Controversies Conferences. Michael Cheung and Tanya Green were subsequently recruited to the staff, and efforts were made to bring all of KDIGO's operations into full compliance with Belgian regulations and standard nonprofit practices.

KDIGO's goal in those early years was simply to get better every day and to strengthen its independent status. Being self-governed, self-managed, and self-funded were important elements of KDIGO's growth. The guideline on the Evaluation and Care of Living Kidney Donors was the first to be wholly developed under its independence, as was the Controversies Conference on CKD–MBD: Back to the Future, and KDIGO has been remarkably active since then (Table 1).

KDIGO began an emphasis on implementation programs and developed a presence in major congresses, both globally and locally. New volunteers were brought in, and previous volunteers were recognized as members of the KDIGO global network. A reception in Philadelphia in 2015 attracted over 200 people. KDIGO is continuing to be innovative and transparent while experimenting with new technologies like electronic guideline publishing. Naturally, KDIGO also pays more attention to updating its existing guidelines and is increasingly focusing on a more robust and streamlined guideline development process and methodology.

Corporate support has always sustained KDIGO's growth. While KDIGO does not solicit or accept funding for the development of guidelines or its updates, KDIGO has attracted several major sustaining partners which provide the resources needed to conduct all of its programs. KDIGO especially appreciates the long-term commitments of companies like Fresenius, Boehringer-Ingelheim, and AstraZeneca. KDIGO takes pride in our transparency and full disclosure policy while striving to enhance its conflict of interest safeguards.

KDIGO now has three guidelines in development at all times and holds four or five Controversies Conferences each year. Implementation presentations and tools, along with an improved website and app, are part of a concerted effort to make the work more accessible to clinicians everywhere. KDIGO's vision focuses on its core programs while seeking appropriate collaborations and strengthening its volunteer base.

Although still relatively young, KDIGO has come a long way. It has taken a few risks but remains dedicated to its only mission: to improve outcomes for patients. It is with this optimism and commitment that KDIGO builds on the past and looks toward the future with enthusiasm. ■

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New Guideline Update: Hepatitis C in Patients with Chronic Kidney Disease

By Michel Jadoul

The 2008 KDIGO guideline on the prevention, diagnosis, evaluation, and treatment of hepatitis C virus (HCV) infection in patients with chronic kidney disease (CKD) was the very first guideline produced by KDIGO. Since then, there have been dramatic changes in the field of antiviral treatments, which prompted a timely reassessment and publication of this guideline update in 2018 (1). The purpose of this short review is to summarize the key recommendations from this important guidance document.

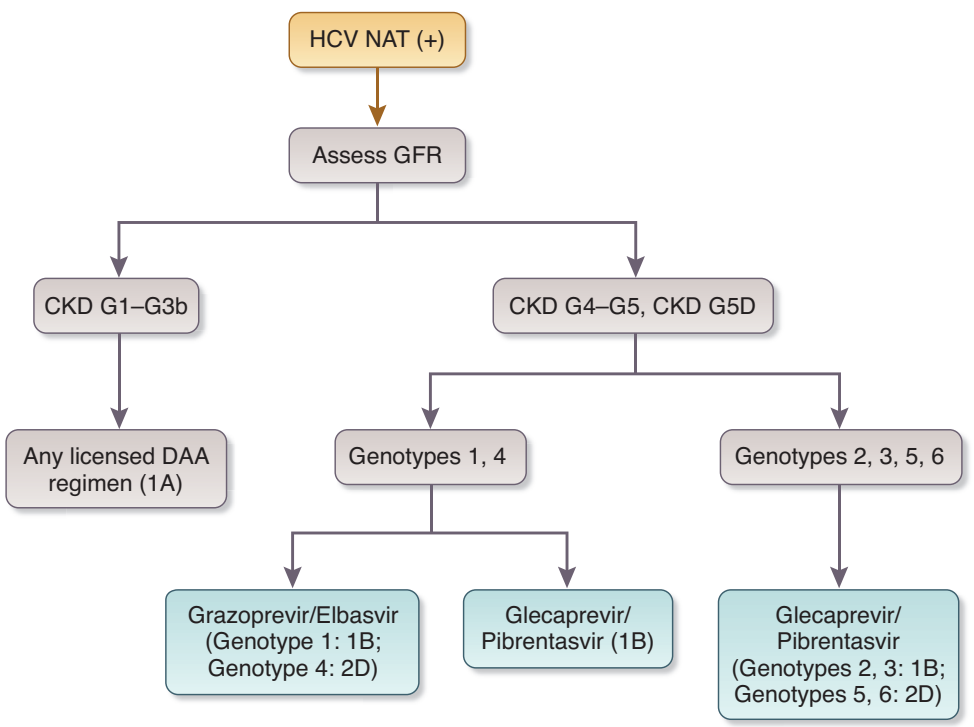
As in the previous guideline edition, Chapter 1 addresses the detection and evaluation of HCV in CKD. It should be stressed that the guideline now recommends that all patients be screened once for HCV at the time of initial CKD evaluation. This new recommendation is based on multiple large observational studies that have consistently identified HCV positivity as a risk factor for adverse clinical outcomes, independently of classic CKD and cardiovascular risk factors. These adverse outcomes include CKD onset, rapid CKD progression, and development of ESKD and cardiovascular complications.

Recent evidence further shows that in patients with various causes of CKD, including diabetic nephropathy or nephrosclerosis, and thus not just HCV-associated membranoproliferative glomerulonephritis, HCV treatment is associated with delayed onset of CKD (2) and cardiovascular complications. The cost of a single immunoassay for HCV thus appears small in comparison with the potential clinical benefit(s). A second key change in this chapter is the recommendation to start investigating HCV-positive patients via non-invasive means such as transient elastography (e.g., FibroScan) and/or biochemical indexes. These have indeed been shown, even in late CKD patients including candidates for kidney transplantation, to accurately quantify noninvasively the extent of liver fibrosis. Thus, a liver biopsy is now required only if there is a high suspicion of another cause of liver disease than HCV, and/or if noninvasive results are discordant (1).

Chapter 2 addresses HCV antiviral treatments, also known as direct-acting antiviral agents (DAAs), which can effectively cure HCV infections in more than 95% of cases over a course of 12 weeks. DAA treatments thus now become the rule rather than the exception in CKD patients as well, if life expectancy is reasonable (no uniform minimum threshold can be proposed, although a life expectancy of at least 12 months appears reasonable). As highlighted in Figure 1, certain DAA regimens can be used even in patients with an eGFR <30 mL/min per 1.73 m^2. Similarly, prevalent kidney transplant recipients can also be treated effectively and safely with DAA regimens (Figure 2), with careful attention to the level of immunosuppressive agents during DAA treatment so as to minimize the risk of drug–drug interactions.

Chapter 3 deals with the prevention of nosocomial HCV

Figure 1. Algorithm showing treatment scheme for chronic kidney disease (CKD) G1 to G5D



Recommendation grades (1–2) and strength of evidence (A–D) are provided for each recommended treatment regimen and hepatitis C virus (HCV) genotype. Pangenotypic sofosbuvir/velpatasvir-based regimens are not listed because they were not formally reviewed by the Evidence Review Team at the time of guideline publication. However, FDA has recently indicated that no dose adjustments are required for these regimens in CKD patients including those on dialysis. These regimens may be considered pending their availability in various jurisdictions. Abbreviations: CKD G, chronic kidney disease GFR category; FDA, Food and Drug Administration; DAA, direct-acting antiviral agent; GFR, glomerular filtration rate; NAT, nucleic acid testing. Reproduced with permission from reference 1.