

Kidney Disease: Improving Global Outcomes (KDIGO) – Beginnings, Progress, and Promise

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■ INTRODUCTION

Guidelines, in one form or another, have governed the delivery of healthcare from its very origins. Beginning with Hammurabi's code, Pharaonic medicine, the Hippocratic Corpus, and throughout history, the practice of medicine has been guided by statements (of "must, shalt, and should") recommending a line of action in specific circumstances. Perhaps the best example of these early beginnings is the Hippocratic Oath, which in its original or a modified version, is still taken by medical school graduates before being admitted to the profession. Over time, as medicine evolved from a guild to a profession and gradually became institutionalised, guidelines played an increasing role in the practice of medicine, especially after the medical armamentarium and materia medica began to expand.

The latter part of the past century saw the need for and the number of guidelines increase exponentially, when available therapeutic interventions proliferated, the cost of healthcare mounted, and variations in the quality and outcomes of practice were documented. Initial interventions to control them were varied in rationale, cost driven, managerial in design, and of limited effectiveness but paved the way for clinical practice guidelines (CPGs), which by their focus on the process of care delivery are more likely to favourably influence the quality of care. The recognition that rigorously developed and well-researched CPGs do improve the quality and efficiency of healthcare delivery led to

the legislative establishment in the United States of the Agency for Health Care Policy and Research (AHCPR) in 1989. In the burgeoning, but rather chaotic, rush to guideline development of the preceding decade, the AHCPR was instrumental in defining and establishing a robust method and process of developing evidence-based guidelines¹. Although the process was well defined, the grading of the available evidence and strength of recommendations made remained a variable and evolving field². Nevertheless, it was soon evident that well developed CPGs, when implemented, can reduce variability of care, improve patient outcomes, and ameliorate deficiencies in health care delivery³. Indeed, the implementation of rigorously developed guidelines is said to result in "even greater improvements in patient care than the introduction of some new technologies⁴." For example, the artificial kidney and its technical improvements changed kidney failure from a fatal to a treatable disease in the 1960s, but it was the implementation of well-developed guidelines, which can be used in continuous quality improvement programmes, that favourably altered the quality of dialysis care delivered to patients with end-stage renal disease (ESRD) worldwide⁵.

■ BEGINNINGS

The first CPGs in nephrology were published in 1993, multiplied in the ensuing years, and proliferated thereafter, as an increasing number of organisations

started developing guidelines. The results were duplicative, of varied rigour, and at times provided variable recommendations. The new millennium brought with it several paradigm shifts in nephrology: 1) the care of dialysis patients should begin earlier during the course of progressive loss of kidney function; 2) chronic kidney disease (CKD) is prevalent worldwide, its complications are harmful, and is easy to detect; and 3) that there was a need for a more uniform and integrated approach to the process of CPGs developed for the care of CKD patients^{6,7}. In the meantime, CKD care had resulted in topics other than dialysis for guidelines in nephrology and the consequent further proliferation of new guidelines developed by various organisations. It was the realization of these issues that prompted an exploratory meeting of an international group of concerned individuals in July of 2002, which agreed and expressed support for a more unified global approach for guidelines in nephrology. The rationale for such an initiative is self-evident; the complications and problems encountered by patients with CKD are uniform. Although regional risk factors and available resources vary, the science and evidence-based care of these patients are universal and independent of geographic location or national borders. A coordinated approach would improve the efficiency of utilising available expertise and resources for guideline development, and allow for the more productive use of local resources to their implementation rather than essentially the duplicative generation of guidelines on the same topics⁸.

In establishing and launching the new initiative, and in order to maintain neutrality and independence, no organisation or society was asked to appoint representatives to its board of governance. Rather, nominations were sought from participants in the exploratory meeting for individuals with clinical experience, demonstrated expertise, and involvement in guideline development, implementation, and evaluation. The fact that selected members also held positions in national or international organisations due to their expertise was considered an advantage rather than a reason for selection. The initial group of 30 individuals, with equal representation from Europe, North and South Americas, and Asia, Africa and the Far East, first convened as a Global Coordinating Board in London in January of 2003. It endorsed the concept of a global initiative, elected an Executive Committee to develop a plan of action,

assigned management to the National Kidney Foundation, and decided to reconvene in December 2003 to determine the next steps. At this second meeting, the board approved plans for 2004, selected a name, adopted a mission statement, and approved the incorporation of the new organisation. The initiative was incorporated as a non-profit Belgian foundation, named Kidney Disease: Improving Global Outcomes (KDIGO), with the stated mission to “improve the care and outcomes of kidney disease patients worldwide through promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines.”

What differentiates KDIGO from other organisations is distilled in its mission statement and structure. Essentially, its focus and responsibility is patient care, its tools CPGs and their implementation, and its process that of coordination, collaboration, and integration of the tools. The structure (Fig. 1), as a non-profit foundation has its fiduciary responsibility vested in an international Board of Directors, whose members serve for 3-year terms, with one third of the membership replaced each year by new members from the same general geographic areas. Retiring members become members of a Board of Counsellors, which continues to review and provide input into KDIGO alongside the Board of Directors, but does not convene or vote on issues. The Board of Directors meets once a year, during the first weekend of December, to conduct the business of the foundation. Between the annual meetings of the Board, the Executive Committee attends to the operations of the foundation, whose day-to-day activities are conducted by the co-chairs of the foundation. The work of the foundation is done by expert committees, work groups, and guideline development groups, which develop position statements or guidelines that are then reviewed and approved by the Board prior to adoption and dissemination⁸.

■ DEFINING THE ISSUES

As a first task, the Board took on the matter of topic selection and methodology of guideline development. Prior to embarking on any guideline development the board appointed an Evidence Review and Rating Work Group (ERG), composed of individuals with expertise in nephrology, guideline development and systematic

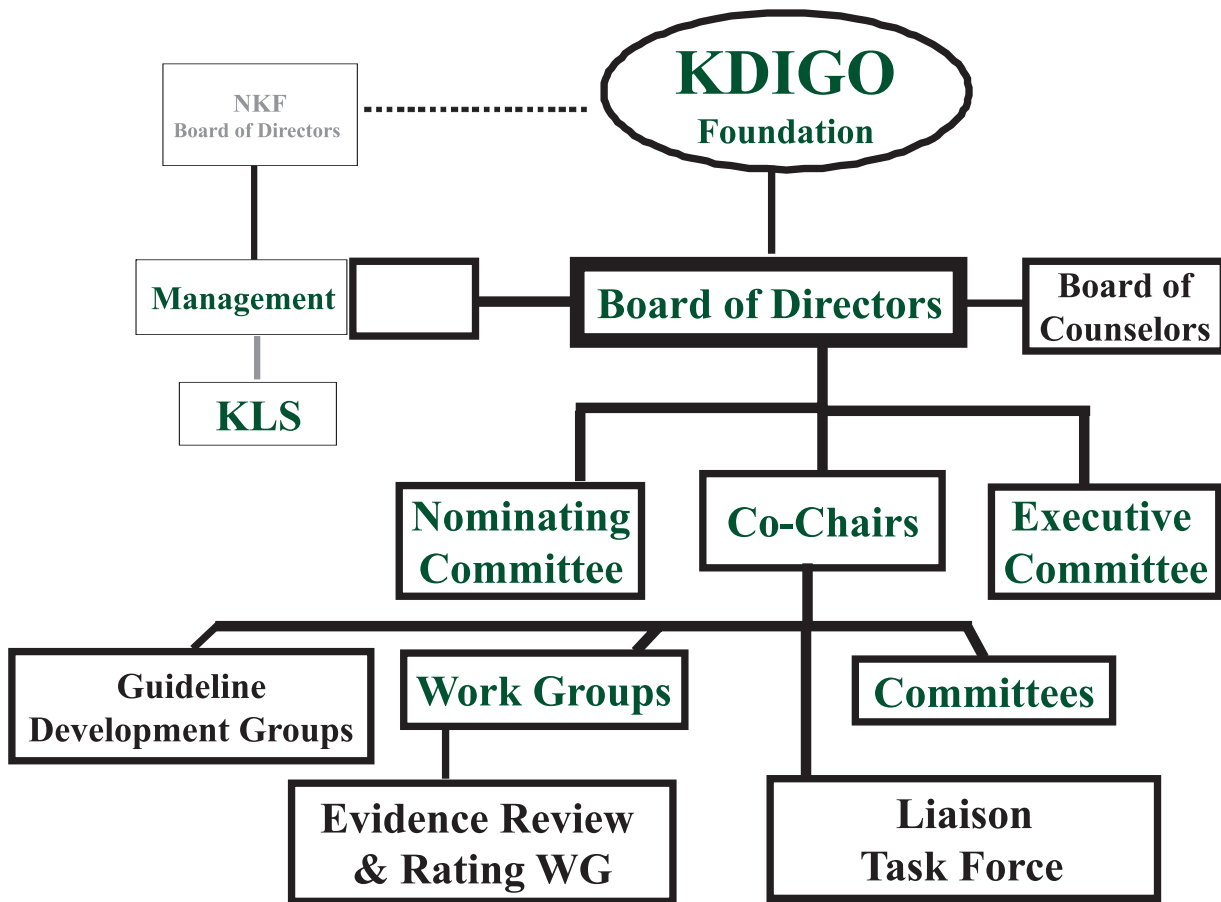


Figure 1
Organisational chart of the KDIGO administrative structure. Abbreviations: **NKF** = National Kidney Foundation; **KLS** = Kidney Learning System

review of the literature, to develop a uniform grading system for patients with CKD. After extensive deliberation, the ERG developed a position statement that was reviewed, approved, and adopted by the Board in 2005⁹. The position statement recommends adopting the Grades of Recommendation Assessment, Development, and Evaluation (GRADE) approach developed by an international group of methodology experts¹⁰. The GRADE approach appraises systematic reviews of benefits and harms of interventions to determine their health benefits. In grading the evidence it considers the design, quality, and the consistency and directness of findings in published studies. Unlike other methods in which randomised clinical trials (RCTs) are accepted as the highest level of evidence, the GRADE system allows for the up and down grading of RCTs and selected studies, such that not all RCTs are necessarily graded as high whereas well-done observational

studies can be upgraded to the highest level of evidence. The strength of the recommendations made in the guidelines builds on the quality of the evidence report. Two additions to the GRADE approach made in the position statement are: 1) a process for extrapolating from studies done predominantly in subjects without CKD, and 2) a provision to use three levels of recommendations: strong, weak, and consensus based (Table I).

The Board also adopted a process of guideline topic selection that defines the criteria and requirements for choosing a topic for CPGs. In the main, this internal document is based on the criteria for topic selection developed by the Institute of Medicine. Essentially, it outlines the prioritisation based on the prevalence of the clinical problem; the burden of the disease (mortality, morbidity, and functional impairment); documented

Table I

Strength of guideline recommendations and linkage to quality of evidence. Modified from table 5 in reference 9.

Recommendation or statement	Description in GRADE approach	Prerequisite	Assumption	Implication
Strong guideline recommendation	We recommend (should do)	The quality of the evidence is “high” and other considerations support a strong recommendation.	Most well-informed individuals will make the same choice .	The expectation is that the recommendation will be followed unless there are compelling reasons to deviate from the recommendation in an individual. A strong recommendation may form the basis for a clinical performance measure.
Weak guideline recommendation	We suggest (might do)	The quality of the evidence is “high” or “moderate”, but additional considerations support a “weak” recommendation.	A majority of well informed individuals will make this choice, but a substantial minority may not.	The expectation is that consideration should be given to following the recommendation.
Consensus based statement	Consensus based statement	The quality of the evidence is “low”, “very low” or absent. This is a consensus based on expert opinion, supported in the public review of the statement.		The expectation is that consideration should be given to following the statement.

variability in practice to prevent, diagnose, treat, and achieved outcomes; adequacy of the scientific evidence on which to develop guidelines; the costs of the condition and the economic burden imposed by an intervention to all payers, including patients; and the potential of guidelines to reduce variations, improve outcomes, and reduce costs.

■ CONTROVERSIES CONFERENCES

Another early undertaking launched by the Board is a series of Controversies Conferences to examine what is known, what can be done with what is known, and what needs to be known on controversial topics of clinical relevance in nephrology. The first KDIGO Controversies Conference on “Definition and Classification of CKD” was held in Amsterdam in November 2004. The position statement of this meeting recommended acceptance of the Kidney Disease Outcomes Quality Initiative (KDOQI) classification of CKD, published in 2002⁶, with clarification of the definition of kidney damage as one that leads to decreased glomerular filtration rate (GFR); to consider all kidney transplant recipients to have CKD, irrespective of GFR level and markers of kidney damage; and to retain the simple five-stage classification based on severity but add to it classification based in treatment of end-stage renal disease (ESRD) by

dialysis or transplantation by the suffix D and T, respectively¹¹. This modified classification, heretofore referred to as the KDIGO classification, is shown in Table II.

The second Controversies Conference on “Definition, Evaluation, and Classification of Renal Osteodystrophy” was held in Madrid on September 15-17, 2005. It recommended that the term renal osteodystrophy be used exclusively to alterations in bone morphology associated with CKD, which can be further assessed by histomorphometry and the results

Table II

KDIGO classification of chronic kidney diseases. Modified from table 4 in reference 11. Abbreviations: **GFR** = glomerular filtration rate; **eGFR** = estimated GFR from the serum creatinine

Stage	Description	GFR (ml/min/1.73 m ²)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60-80
3	Mild ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	<15

T for transplant
D for dialysis

Clinically significant, can lead to loss of kidney function

Routine reporting of eGFR based on a standardized serum creatinine

reported based on a uniform classification system that includes parameters of turnover, mineralization, and volume; that the term CKD Mineral and Bone Disorders (CKD-MBD) be used to describe the broader clinical syndrome that develops in patients with CKD, which is manifested by abnormalities in bone and mineral metabolism, and extra-skeletal calcification; and defined questions to be addressed in new guidelines on CKD-MBD¹².

The third Controversies Conference on the “Care of the Kidney Transplant Recipient” was held in Lisbon on February 2-4, 2006. Its key recommendations were that all kidney transplant recipients should be considered to have CKD, whose staging should be assigned based on the level of kidney function to the KDIGO classification of CKD; that whereas preservation of kidney function is the primary focus in the care of kidney transplant recipients, these individuals actually die from potentially preventable and treatable complications and co-morbid conditions (cardiovascular, malignant, infections) associated with CKD-T, in most of whom the transplanted kidney is still functioning, and hence the need to adopt a public health model for the continued care of kidney transplant recipients; and identified key issues that should be addressed in a new evidence-based CPG for the care of the kidney transplant recipients¹³.

The fourth Controversies Conference on “CKD as a Global Public Health Problem: Approaches and Initiatives” was held in Amsterdam on October 12-14, 2006. A principal objective of this conference was to consider advances made in the epidemiology, prevalence, and treatment of CKD and to propose how they can be translated into simple applicable public health measures that could be adopted worldwide. The published position statement of this meeting recommended that there is no need to change the KDIGO classification adopted in 2004 (Table II); to work with the World Health Organization to incorporate the KDIGO classification of CKD in future editions of International Classification of Diseases (ICD) in order to capture administrative data in the prevalence and trends of CKD; that countries adopt a screening programme for CKD in targeted groups (hypertension, diabetes, cardiovascular disease), and develop a surveillance programme for CKD stages 4 and 5 that could be used in public policy and education; that in addition to existing evidence of CKD as a risk factor for CVD, new data indicates CKD as

a risk factor for selected infectious diseases and malignancies that deserve further study¹⁴.

The fifth Controversies Conference on “CPGs: Methodology and Transparency” was held in New York on October 12-13, 2007 to address problems and challenges encountered by CPGs¹⁵. Another conference on “Coordination of CPGs on Anaemia in CKD” was held in New York on October 15-16, 2007 to consider recent concerns about the treatment of anaemia in CKD and to coordinate the next update following the revised KDOQI anaemia guidelines^{16,17}. The deliberations, proceedings, and recommendations of these two meetings are under development and will be published in 2008. As with the product of the previous controversies conferences, these will appear in the official journal of the International Society of Nephrology (ISN) with which KDIGO signed a letter of agreement for its position statements and guidelines to be published in *Kidney International*.

■ CLINICAL PRACTICE GUIDELINES

KDIGO has currently three guidelines under development, each undertaken after the issues of methodology and topic selection outlined above were resolved. Details on the progress of these guidelines, an invitation to provide input and review developed drafts, as well as additional information can be accessed at www.kdigo.org.

After much debate, the Board decided to avoid the duplication of existing guidelines in nephrology, and selected to begin with one on infectious diseases as a heretofore-orphan topic of worldwide interest. Five major infectious diseases were considered: human immunodeficiency virus (HIV), hepatitis C virus (HCV), hepatitis B virus (HBV), tuberculosis and malaria. Ultimately, HCV was selected because: 1) of the larger number of available studies on the subject; 2) HCV is an infection that can detrimentally affect patients throughout the spectrum of CKD; 3) HCV itself can cause CKD; and 4) HCV is a problem of worldwide clinical relevance in developed and developing countries. These guidelines begun in 2005 have undergone organisational and public review and will be published as a supplement of *Kidney International* in January 2008. They include guidelines on the detection and evaluation of HCV in CKD; treatment of HCV

infection in patients with CKD; prevention of HCV transmission in haemodialysis units; management of HCV-infected patients before and after kidney transplantation; and the diagnosis and management of kidney diseases associated with HCV infection.

The two other guidelines were undertaken at the recommendation of the controversies conferences outlined above. The guidelines for CKD-MBD were begun in autumn 2006 and those for the care of the kidney transplant recipient in early winter 2007. They are now at various stages of development with anticipated publication dates of late in 2008 and early 2009, respectively.

At its last meeting in December 2007, the Board adopted a five-year plan for guideline development, with one on Acute Kidney Injury (AKI) to begin in mid 2008, an update of anaemia guidelines in 2009, and a new one on glomerulonephritis in the winter of 2009-2010.

■ COORDINATION AND COLLABORATION

The Board decided to develop a stepwise approach to coordinating nephrology guidelines. As a first step a website (www.kdigo.org) was constructed providing access to a comprehensive overview of five principal guidelines published in English and developed according to a rigorous methodology. The posted guidelines are those of Caring for Australians with renal impairment (CARI), the Canadian Society of Nephrology (CSN), the European Best Practice Guidelines (EBPG), KDOQI, and the United Kingdom Renal Association (UK-RA). One of the features of the website is a direct comparison of fifty-one selected recommendations made in the five guideline sets and their rationale provided by representatives of the five organisations¹⁸.

As a second step, KDIGO convened an initial meeting in April 2006 in London of the presidents and the individuals responsible for guidelines of CARI, UK-RA, CSN, KDOQI and EBPG. At the recommendation of this group, the Board established a Liaison Task Force, composed of the individuals responsible for guidelines in their respective organisations, which would participate and provide input to the ERG and participate in the guideline review process in conjunction and with the Board (Figure 1). Also, it agreed to review and adopt

the Hepatitis C guidelines then being developed and to participate in coordinating the update of existing and development of new CPGs. Since then, an annual meeting of the Liaison Task Force and presidents of the five societies has been held annually at the meeting of the American Society of Nephrology. At its last meeting this Guideline Coordinating Group agreed to formalise the coordination process and that the next update of the anaemia guidelines would be the first such effort under the banner of KDIGO. Also, members of the group were asked to begin the review, adoption and implementation of the Hepatitis C guidelines that would be published in 2008. This will be a milestone not only as the first KDIGO guidelines and the first guidelines on Hepatitis C in CKD, but more importantly in the cooperative effort that went into its development and its setting the path in a collaborative effort in adoption and implementation to follow.

In addition, the five-year guideline development plan adopted by KDIGO has been shared with the five groups inviting them to develop a similar long-term plan, which can then be incorporated as a master plan, and posted on the respective websites of the organisations to keep the worldwide nephrology community abreast of ongoing and projected guidelines in nephrology.

■ PROMISE

The favourable reception and support that the KDIGO initiative has received heretofore has been most gratifying. Much has been accomplished in the rather brief period of its existence, but much more remains to be done. The future is certainly promising but will depend on the continued trust it can generate and the support it receives from the nephrology community worldwide. The coming years will determine whether it will deliver the promise of its mission statement.

Conflict of interest statement. None declared.

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