Kidney Disease: Improving Global Outcomes—an update

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ABSTRACT

Kidney Disease: Improving Global Outcomes (KDIGO) was founded in 2003 to fulfill a need for international cooperation and consolidation in the development and implementation of clinical practice guidelines. KDIGO has experienced a rapid growth in the development of guidelines, producing three guidelines in its first 6 years and another six in the last 3 years. In addition, it has held 12 global conferences on important issues in kidney disease and its treatment. A major effort is under way to support the dissemination and implementation of KDIGO guidelines through various channels, including an Implementation Task Force with official representatives in 86 countries. KDIGO is now under its own management and remains committed to the development of evidence-based guidelines. Future challenges include finding adequate sources of funding and building stronger links with other organizations involved in guideline development and implementation.

Keywords: controversies conferences, guidelines, implementation, KDIGO, methodology

INTRODUCTION

Clinical practice guidelines are ‘Systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances’ [1]. The need for guidelines has arisen from the growing volume and...
complexity of the clinical trials that provide most of the evidence available for informing clinical practice decisions. The large and growing number of trials makes it difficult if not impossible for busy clinicians to keep up with the medical literature. In addition, the art and science of interpreting the internal and external validity of clinical trials is beyond the training and ability of many medical practitioners. By defining the strength of practice recommendations and of the supporting evidence, guidelines can also highlight current research needs. For all of these reasons, guidelines have taken centre stage in the healthcare arena.

Kidney Disease: Improving Global Outcomes (KDIGO) was founded in 2003. From its inception, KDIGO’s mission has been to improve the care and outcomes of kidney disease patients worldwide by promoting coordination, collaboration and integration of initiatives to develop and implement guidelines. As an international organization with a singular purpose of developing and implementing guidelines, KDIGO is unique. A review published in 2009 focused on the history of guidelines in nephrology, the rationale for KDIGO, its organizational structure and methods for guideline development [2]. At the time of that review, the organization was 6 years old and had completed three guidelines. Since then, KDIGO has completed six additional guidelines and has undergone several important structural changes, including a transition to self-management. This update will describe the progress KDIGO has made and the remaining challenges it faces.

**INTERNATIONAL GUIDELINE COORDINATION**

At the time KDIGO was being organized, there was a growing need for consolidation of guideline development in nephrology. For example, in the decade between 1998 and 2008, more than 10 guidelines on the management of anemia in patients with chronic kidney disease (CKD) were published in the English language [2]. Meanwhile, most major areas of nephrology practice had not been touched by guideline development. Much of this ‘guideline gap’ resulted from the availability of pharmaceutical industry funding to professional societies around the world to develop guidelines of mutual self-interest [2].

No doubt industry views guidelines as effective marketing tools. In addition, industry support of local physicians and their professional societies for the development of guidelines can also be used as an effective means to promote products. Physicians often use systematic evidence reviews and guideline development as important tools for academic career development. As a result, there are mutual self-interests between industry and physicians in the development of guidelines. Since most industry marketing efforts are local, industry funding of guidelines encourages the development of multiple, local guidelines.

However, with the help and support of the global nephrology community, KDIGO has been able to narrow, but not close, the guideline gap. Most local and regional professional societies have agreed to limit duplicate, local guideline development. In return, KDIGO is making increasing efforts to collaborate with local organizations and professional societies to develop international guidelines covering topics that have previously been ignored by the developers of industry-supported guidelines. The rationale for international guidelines is compelling. The results of clinical trials, which often cross political boundaries, are generally applicable worldwide. Indeed, medical evidence knows no national boundaries.

Cost is another important reason to avoid duplication and to consolidate guideline development. Reducing the cost of guidelines is also an important first step in reducing the reliance on the pharmaceutical industry for financial support. It is anticipated that the consolidation of guideline development will lead to better transparency and avoidance of conflicts inherent in industry support of guideline development.

**EVOLUTION OF THE KDIGO ORGANIZATION**

Although KDIGO was first established in 2003, it was incorporated as a Foundation in the Public Interest in Brussels, Belgium, in March 2006 (Table 1). In 2004, KDIGO signed a service agreement with the National Kidney Foundation (NKF) in the USA. It was a natural development for the NKF, which started the Dialysis Outcomes Quality Initiative (DOQI) and transitioned to the Kidney Disease Outcomes Quality Initiative (KDOQI), to help internationalize guideline development in nephrology by founding and managing KDIGO. However, the NKF mission to serve patients with kidney disease in the USA differed from the international mission of KDIGO. The fact that the NKF managed KDIGO created confusion over whether KDIGO was a subsidiary of the NKF with guidelines largely targeting the US population, or was truly an independent organization.

### Table 1. KDIGO Milestones

<table>
<thead>
<tr>
<th>Date</th>
<th>Important KDIGO Milestones</th>
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<tr>
<td>December 2003</td>
<td>First KDIGO organizational meeting, Amsterdam, Netherlands</td>
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<tr>
<td>November 2004</td>
<td>KDIGO service agreement established with the NKF</td>
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<tr>
<td>November 2004</td>
<td>First KDIGO controversies conference on the definition and classification of CKD, Amsterdam, Netherlands</td>
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<tr>
<td>December 2004</td>
<td>First KDIGO board of directors meeting, Paris, France</td>
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<tr>
<td>March 2006</td>
<td>KDIGO incorporated as a nonprofit organization in Brussels, Belgium</td>
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<tr>
<td>November 2006</td>
<td>First KDIGO international guidelines coordination meeting, San Diego, USA</td>
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<tr>
<td>April 2008</td>
<td>First clinical practice guideline (on HCV) published in <em>Kidney International</em></td>
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<tr>
<td>February 2012</td>
<td>First clinical practice symposium, Shanghai, China</td>
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<tr>
<td>October 2012</td>
<td>KDIGO ends service agreement with the NKF and becomes independent</td>
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organization developing international guidelines targeting the global community. Therefore, on 1 October 2012, KDIGO and the NKF ended their service contract by mutual agreement, and KDIGO became an independent organization under self-management.

Under its original organizational structure, KDIGO was governed by the Foundation’s six Trustees. KDIGO had its own 50-member Board of Directors who met face-to-face annually to provide scientific direction for the organization. The day-to-day management of KDIGO was the responsibility of KDIGO’s Executive Committee and two Co-Chairs. Now as an independent organization, the Foundation’s volunteer Trustees (increased to 11) operating as an Executive Committee, will be responsible for the management of KDIGO. Critical functions will be performed by committees that answer to the Executive Committee. A small staff handles day-to-day business matters.

**KDIGO GUIDELINE METHODOLOGY**

**E V O L U T I O N**

**Selection of guideline topics and defining their scope**

There is a potential bias in the selection of guideline topics analogous to the well-known publication bias that has plagued clinical trials. In the past, guideline topics have often been selected based on available industry funding. It is a long-term goal of KDIGO to avoid this anomaly. KDIGO has used its Executive Committee to select guideline topics independent of funding sources. Although the KDIGO organization has been largely funded by industry, KDIGO has prohibited direct industry funding for specific guideline projects.

KDIGO has often used controversies conferences to help choose guideline topics and to define their scope (Figure 1). Controversies conferences often conclude with a recommendation that KDIGO should develop a clinical practice guideline. For example, the controversies conference on kidney transplantation, co-sponsored by The Transplantation Society [3], led to the development of the KDIGO Guideline on the care of the kidney transplant recipient [4]. On the other hand, the controversies conference on blood pressure in haemodialysis patients ended with a recommendation for additional research before producing a clinical practice guideline and outlined a suggested research agenda [5].

In the future, KDIGO will seek wider input from the nephrology and transplantation community in the selection of guideline topics. KDIGO will solicit this input from the general public and will provide mechanisms whereby individuals and organizations can recommend topics. However, it will stipulate that conflicts of interest in those making recommendations will be made clear. In addition, KDIGO is seeking ways to solicit recommendations for guideline topics from professional societies and other stakeholder organizations around the world.

**Selection of guideline work group members**

In the past, the KDIGO Co-Chairs selected two Work Group Co-Chairs with the approval and consent of the KDIGO Executive Committee. Taken together, the KDIGO Co-Chairs and the Work Group Co-Chairs then selected the other work group members. The final work group was generally made up of 12–15 members. KDIGO work groups have included members with clinical expertise in areas covered by the scope of the guideline. Generally, both adult and pediatric nephrologists have been included.

Most of the organizations producing guidelines have recommended that work groups and Evidence Review Teams (ERTs) include members with clinical expertise pertinent to the guideline being developed. However, others have advocated that guidelines be developed primarily by experts in evidence-based medicine who have no direct interest in the topic, and that these experts consult clinicians with topic-specific expertise as necessary [6]. The theory is that experts in a particular guideline topic are inherently biased and cannot judge evidence fairly. There are no trials comparing guideline recommendations or evidence review produced by these two approaches, so the best method remains a subject of discussion and conjecture. KDIGO has taken a middle ground by including experts on the guideline topic, but avoiding experts with obvious conflicts, and including at least some experts on the work group without direct involvement in the topic.

Financial and other conflicts of interest are generally handled by appropriate disclosures. However, individuals with strong conflicts are excluded from serving on a work group and those with any major conflicts are excluded from being Work Group Co-Chairs.

**Selection of ERTs**

In the past, all evidence review for KDIGO was carried out by the Tufts-New England Medical Center Evidence Practice Center (EPC). The centre is an Agency for Healthcare Research and Quality (AHRQ) approved EPC. For each guideline, an ERT was assembled with members from the Tufts

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**FIGURE 1**: Lifecycle of a KDIGO clinical practice guideline. A Controversies Conference may or may not conclude that the time is right to develop a KDIGO clinical practice guideline. Once a guideline has been completed, the Implementation Task Force is charged with disseminating and implementing the guideline. This may be facilitated by implementation conferences or clinical practice symposia. The timing of a guideline update is most often determined by the availability of pertinent new clinical trials and evidence.
EPC. The ERT met with the Work Group Co-Chairs to define the scope of the guideline and evidence review. Much of the evidence review was completed before the first work group meeting.

Having one EPC working with KDIGO had advantages and disadvantages. In the future, KDIGO will solicit applications from EPCs for each guideline ERT. This could facilitate the development of guidelines by allowing KDIGO to have more than one guideline work group working at the same time. In addition, different EPCs may have different expertise that could be better suited for one or another guideline topic. Obtaining the most cost-effective reviews could also be facilitated if competitive applications are received from more than one EPC.

Guideline development

In the past, work on a KDIGO guideline has begun after the Work Group Co-Chairs have met with the ERT and developed an initial evidence review plan. Much of the evidence review and preliminary evidence tables have been completed prior to the first work group meeting. Thereafter, the work group developed recommendations and rated the strength of those recommendations and the supporting evidence based on the Grades of Recommendation Assessment, Development and Evaluation (GRADE) method [7]. Work group members participated in the writing of recommendations. KDIGO guidelines have included recommendations that are not graded, but rather based on opinions of the Work Group. These are generally ‘motherhood and apple pie’ recommendations that the Work Group considers important for caregivers to consider, but for which it is unlikely evidence will ever be developed. Prior to publication, KDIGO guidelines have undergone review by the KDIGO Board of Directors, targeted experts and the general public.

Based on past experience and ongoing input from outside experts, the KDIGO guideline development process will continue to evolve. Areas that KDIGO could improve in the development process include seeking public comment earlier, even as the scope of the guideline is being determined. More concise and efficient writing of guidelines, relying less on Work Group members and more on professional medical writers is also being considered. Finally, ways to make the guideline development process more cost-effective continue to be subjects for discussion and debate.

GUIDELINES

To date, KDIGO has completed nine guidelines (Table 2). It is anticipated that guideline production will eventually reach a steady state that balances new guideline initiatives with guideline updates and guidelines that may no longer need updating. This balance will only be achieved if suitable topics for guideline development are agreed, and if there is adequate funding.

KDIGO CONFERENCES

Controversies conferences

For many potential guideline topics, it is not entirely clear that a guideline is appropriate and timely. The scope of the guideline may not be well defined. Most important of all is determining whether the available evidence is likely to be adequate to support guideline recommendations. KDIGO has used controversies conferences to consider these questions. To date, KDIGO has held 11 controversies conferences (Table 3). These controversies conferences usually include 50–100 invited participants. After a plenary session including overview presentations, 3–4 working groups debate and attempt to reach consensus on several preassigned topics. The breakout work groups present the results of their discussions to the entire group of conference participants and their recommendations are further debated and discussed. A conference report is ultimately written and published in a peer-reviewed journal.

Collaboration with other stakeholder organizations may strengthen a controversy conference. The controversies conference on the care of kidney transplant recipients, for example, was developed in conjunction with The Transplantation Society [3]. KDIGO will continue exploring ways to collaborate with other professional societies and stakeholders in planning and holding future controversies conferences.

Methodology conferences

A 2-day conference was held in St Louis, MO, USA in November 2004 to discuss KDIGO methods for rating the strength of evidence guideline recommendations. The conference reviewed the state of the art of evidence and guideline grading and developed a consensus on a grading approach for use in future guidelines developed in the domain of kidney disease [7].

Table 2. KDIGO Guidelines

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<tr>
<th>Date</th>
<th>Guidelines</th>
<th>References</th>
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<tbody>
<tr>
<td>April 2008</td>
<td>Prevention, Diagnosis, Evaluation and Treatment of HCV in CKD</td>
<td>[8]</td>
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<tr>
<td>October 2009</td>
<td>Care of Kidney Transplant Recipients</td>
<td>[4]</td>
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<tr>
<td>March 2012</td>
<td>Acute Kidney Injury</td>
<td>[10]</td>
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<tr>
<td>August, 2012</td>
<td>Anemia in CKD</td>
<td>[12]</td>
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<tr>
<td>December 2012</td>
<td>Blood Pressure in CKD</td>
<td>[13]</td>
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<tr>
<td>January 2013</td>
<td>CKD Evaluation and Management</td>
<td>[14]</td>
</tr>
<tr>
<td>November 2013</td>
<td>Lipid Management in CKD</td>
<td>[15]</td>
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HCV: hepatitis C virus; CKD: chronic kidney disease; MBD: mineral and bone disorders.
Similarly, a 2-day conference ‘Clinical Practice Guidelines: Methodology and Transparency’ was held in New York City in October 2007. This conference discussed guideline methodologies and managing conflicts of interest. Periodically holding these conferences is an effective method for KDIGO to explore and adopt state-of-the-art guideline methodologies.

**Clinical practice symposia**

KDIGO has recently begun to explore the use of conferences to disseminate KDIGO guidelines. In February 2012, KDIGO collaborated with the Chinese Society of Nephrology, the Shanghai Medical Association and the International Society of Nephrology (ISN) to hold the first KDIGO Clinical Practice Symposium. The Chinese Society of Nephrology and the Shanghai Medical Association requested that KDIGO present its guidelines on Acute Kidney Injury, Glomerulonephritis and Management of Anemia in CKD. Each guideline was presented by a KDIGO representative and was followed by presentations and discussion by local representatives describing issues relevant to implementation of the relevant guideline in China. The conference was attended by over 700 physicians. KDIGO intends to work with the ISN to hold similar conferences in the future in an effort to disseminate and eventually implement KDIGO guidelines.

**FUTURE CONFERENCE AND GUIDELINE TOPICS**

KDIGO is the only global guideline organization in nephrology. As such its goal is to develop guidelines in every major area of kidney disease that is adequately supported by scientific evidence. KDIGO will continue to use controversies conferences to assess the suitability of specific topics for guideline development.

Currently, KDIGO is collaborating with The Transplantation Society and other professional organizations to develop a clinical practice guideline on living kidney donation. Since this topic has been the subject of a number of recent conferences and local guidelines, it was decided that guideline development should proceed without a KDIGO controversies conference. Guidelines for the other major topics in kidney transplantation, including management of deceased kidney donors, evaluation of transplant candidates and an update of the KDIGO guideline on the Care of Kidney Transplant Recipients, are also being considered.

A controversies conference is being planned for late 2013 on palliative and supportive care for Stage 5 CKD patients. This is an important international issue, since in many parts of the world, treatment of Stage 5 CKD patients with dialysis or transplantation is not available. The conference is being planned in close collaboration with the Renal Physicians Association, which produced a guideline in the USA on shared decision making with respect to options for renal replacement therapies.

Since the publication of the KDIGO guideline on mineral and bone disorders, there have been additional clinical trials. Therefore, a controversies conference is being planned to determine whether or not there is sufficient new evidence to warrant an update of the KDIGO guideline. Similarly, there has recently been an important trial of treatment for delaying progression of autosomal dominant polycystic kidney disease. KDIGO is planning a conference in collaboration with a European polycystic kidney disease charity organization, which will be attended by leading experts from this field and patient representatives. Conferences, and possibly guidelines, are also being considered for management of patients with haemodialysis and peritoneal dialysis. Other conferences will be planned based on an assessment of the global kidney and transplant community needs.

**RESOURCES AND FUNDING**

KDIGO’s primary asset is the large base of volunteers who have served the organization over the past decade. No
DISSEMINATION AND IMPLEMENTATION

Although the evidence for a guideline is usually global, the implementation is always local. This important concept has motivated KDIGO to develop an international Implementation Task Force. This Task Force has official representatives in 86 countries. The identification and recruitment of these expert opinion leaders was accomplished in collaboration with the ISN. Implementation Task Force activities include working to get KDIGO recommendations on the programs of local meetings, translating guidelines into local languages, adapting educational tools for local circumstances and distributing materials and information about the KDIGO guidelines through electronic media. From websites to Apps, the KDIGO Implementation Task Force is making its work product accessible anywhere. In the future, KDIGO will explore closer collaboration with the ISN in guideline dissemination activities.

Dissemination is a first step toward implementation, which is a long-term KDIGO goal.

GUIDELINE RESEARCH

There are many opportunities to take guidelines and compare the results of implementation with healthcare professionals following recommendations or providing usual care. KDIGO studies and data can be a valuable part of improving care. Resources are being sought to make this a regular part of KDIGO’s agenda.

A FOCUS ON COLLABORATIONS

During the first few years of its existence, KDIGO sought recognition in a skeptical environment and worked largely in isolation. After 9 years of success, KDIGO is in a better position to actively collaborate with other organizations. The most logical and compelling collaboration is with the ISN. To date, the collaboration between KDIGO and the ISN has included the publication of KDIGO guidelines in Kidney International as well as joint sponsorship of a Clinical Practice Symposium in Shanghai, China, February 2012. In the future, there are plans for ISN’s Global Outreach (GO) program and KDIGO’s Implementation Task Force to work together in a mutually beneficial collaboration which will save money and should help patients. KDIGO has educational content and GO has outreach around the world to bring the latest advances in nephrology to its members in developing countries.

KDIGO is also working closely with The Transplantation Society to develop guidelines pertinent to kidney transplantation. Likewise, KDIGO is collaborating with local and regional professional societies on guideline development, dissemination, implementation and education.

For several years, KDIGO has held an annual Guideline Coordination Committee meeting with professional societies that have engaged in developing guidelines. KDIGO plans to increase the frequency of these meetings and to expand the communication between these organizations.

There will be many opportunities for members of nephrology societies and other relevant organizations to work with KDIGO. These opportunities include suggesting topics for guidelines or controversies conferences, participating in work groups or serving as Board Members, volunteer leaders or on ERTs. Organizations can also participate in the public review of guidelines. KDIGO will launch a new procedure in 2013 in which guideline scope will be put out for public review before the development process starts. Then, when a guideline is close to completion, another public review will be invited. Societies, large and small, will be asked to support KDIGO financially as well. All of these programs are resource-driven and help from societies will bring the community into the process, enhance cohesion and show that the global guideline process, while led by KDIGO, is collaborative and transparent.
CONCLUSION

In 2013, KDIGO has emerged as a strong, self-sufficient organization with a record of achievement and a bright future. KDIGO is patient-centred and evidence-based. This combination makes KDIGO a valuable addition to the global kidney community and the only organization with the experience, abilities and commitment to develop and implement international guidelines in nephrology. A strong base of expert volunteers, a small dedicated staff, and modest but growing financial resources position KDIGO to thrive in the future.

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CONFLICT OF INTEREST STATEMENT

The authors declare an association with the following organization: KDIGO. D.W. declares having received consultancy fees from Amgen, Astellas, Baxter, Merck Sharp and Dohme, Otsuka, and Vifor; research funding from Abbott, AstraZeneca, Genzyme (monies all paid to institution); honoraria from Abbott, Amgen, Astellas, Fresenius Medical Care, Genzyme, Otsuka and Shire. B.K. declares having received consultancy fees from Medscape (supported by Astellas), Rockpointe (supported by Astellas and Novartis) and Litholink/Labcorp.

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