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NEW INITIATIVE

The burden of kidney disease: Improving global outcomes

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The burden of kidney disease: Improving global outcomes. Chronic kidney disease (CKD) is a worldwide public health problem. There is an increasing incidence and prevalence of patients with kidney failure requiring replacement therapy, with poor outcomes and high cost. There is an even higher prevalence of patients in earlier stages of CKD, with adverse outcomes such as kidney failure, cardiovascular disease, and premature death. Patients at earlier stages of CKD can be detected through laboratory testing and their treatment is effective in slowing the progression to kidney failure and reducing cardiovascular events. The science and evidence-based care of these patients are universal and independent of their geographic location. There is a clear need to develop a uniform and global public health approach to the worldwide epidemic of CKD. It is to this end that a new initiative "Kidney Disease: Improving Global Outcomes" has been established. Its stated mission is "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."

From an historical perspective, the burden of disease experienced by human populations has been divided into three stages: "the age of pestilence and famine," "the age of receding pandemics," and "the age of degenerative and man-made diseases" [1]. As with most historic changes, the shift to the current epidemic of chronic noncommunicable diseases is not a simple transition, but rather a complex and dynamic epidemiologic process with considerable overlap with its preceding stages. Although we continue to be challenged by new and re-emerging infectious diseases, and while famine and pestilence persist in much of the world, the reality is that chronic diseases now comprise the major epidemic faced in industrialized countries and threatens as an emerging one in many others [2, 3].

While heart and cerebrovascular diseases and cancer are the major causes of mortality resulting from chronic diseases, diseases of the kidney have now also assumed epidemic proportions as well, and are among the leading causes of death in the industrialized world. This is in part due to the number of patients with kidney disease who progress to kidney failure requiring dialysis or transplantation, whose prognosis is comparable to those with metastatic cancer. In addition, and at least as important, it is now evident that in those whose kidney disease may never progress to dialysis-dependence both the presence of kidney injury, often signaled by proteinuria, and evidence of decreased kidney function, detected by estimating the glomerular filtration rate (GFR), are associated with increased risk of death from heart and cerebrovascular disease due to any cause [4, 5]. As a result, the presence of kidney disease is now listed as an independent risk factor for cardiovascular disease in the most recent report from the Joint National Committee on Prevention, Detection and Treatment of High Blood pressure (JNC VII) and in a position statement of the American Heart Association [6, 7].

Fortunately, concurrent with the increased prevalence of chronic diseases, the closing decades of the past millennium also witnessed dramatic advances in their therapy. As a result mortality from heart and cerebrovascular disease has shown a dramatic decline [8]. By sharp contrast, that of kidney disease remains unacceptably high and appears to be increasing in the United States (Fig. 1). While similar worldwide detailed figures are lacking, wherever investigated or projected the data are supportive of an increasing prevalence of deaths attributed to kidney disease [9–14]. Hence, the clear need to call to action all health professionals in order to address the worldwide epidemic of kidney disease.

Key words: chronic kidney disease, clinical practice guidelines, chronic disease burden, kidney failure, kidney disease classification.

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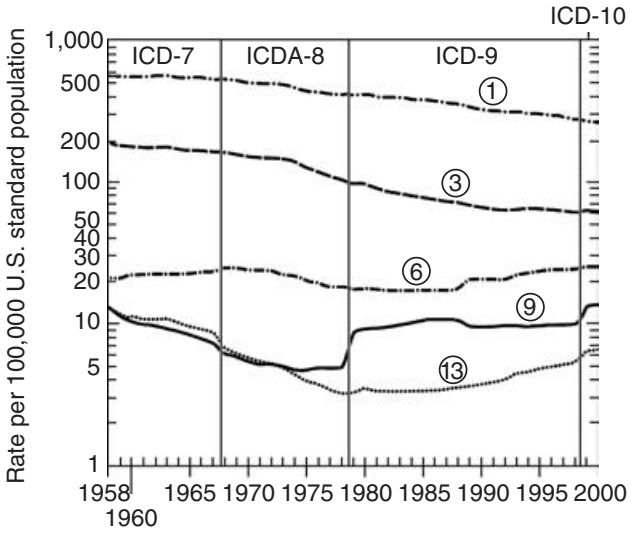

Fig. 1. Age-adjusted death rates for the leading causes of death: United States, 1958–2000. The numbers in circles indicate the rank order of the disease as a cause of death. 1, diseases of heart; 3, cerebrovascular diseases; 6, diabetes mellitus; 9, nephritis, nephritic syndrome and nephrosis; and 13, hypertension with and without renal disease (modified reproduction from [8]).

CHRONIC KIDNEY DISEASE

Historically, dialysis is the single most important development that focused attention on kidney disease, albeit on its end-stage only. What started in the 1950s as an exploratory effort to sustain life and relieve the features of uremia evolved in the 1970s into life-saving replacement therapy for patients whose disease had progressed to kidney failure. Today, over one million individuals in the world are alive on maintenance dialysis, a number that is projected to double in the next decade [13, 14].

Appropriately then, the care of dialysis patients has been the prime focus of nephrology, particularly after the widespread availability of maintenance dialysis when it became evident that mortality of dialyzed patients was high and their quality of life far from adequate. Initial efforts to improve care centered on the adequacy of dialysis. This was an important first step in establishing a minimum dose of delivered dialysis, above which further increments seem to have little impact on mortality, at least in the United States where all-cause mortality has ranged between 21% and 23% per year on dialysis over the past decade [15, 16]. A principal reason for these results is the documented heavy burden of co-morbid conditions, which already exist in patients who are initiated on dialysis. While technical advances and frequent or longer dialysis may further reduce morbidity on dialysis, it would be simplistic to assume that dialysis would reverse or significantly impact the outcomes of existing co-morbidities such as heart or cerebrovascular disease.

Indeed, it is now evident that the state of health of individuals with kidney failure who are initiated on dialysis, and therefore their earlier care, is a major determinant of survival and well being on maintenance dialysis, and that persons with kidney disease are more likely to die from cardiovascular disease than to reach dialysis; hence, the urgency to focus on early detection and treatment in all high-risk populations [17–19].

Importantly, and in parallel with the advances in dialysis of the recent past, there has been considerably better understanding of the progressive course of chronic kidney disease (CKD). This has led to interventions that can slow the progression and ameliorate the complications of CKD. Convincing experimental and clinical evidence, accrued in the past two decades, now shows that (*1*) the adverse outcomes of CKD (kidney failure, cardiovascular disease, and premature death) can be prevented or delayed; (*2*) treatment of earlier stages of CKD is effective in reducing progression to kidney failure and in preventing the systemic complications that develop in the course of progressive loss of kidney function; and (*3*) initiation of treatment of cardiovascular risk factors (anemia, hypertension, dyslipidemia, and altered bone mineral metabolism) at earlier stages of CKD can be effective in reducing this leading cause of mortality and morbidity of individuals with CKD [7, 17, 18]. Unfortunately, there is considerable variability in the application of these measures resulting in lost opportunities to improve outcomes and making lives better for patients with CKD worldwide [20].

CLOSING THE GAP: GUIDELINES

The best recent approach to resolve problems of inadequate care has been the development of guidelines. It has now been shown that rigorously developed evidence-based clinical practice guidelines (CPGs), when implemented, can reduce variability of care, improve patient outcomes and ameliorate deficiencies in health care delivery [21–23]. The practical specificity of well-defined guideline statements, which facilitates their translation into clinical practice, differentiates CPGs from other important evidence-based approaches (meta-analyses and systematic reviews), which distill and analyze the evidence in the literature but do not make necessary practical recommendations for clinical practice. There is no evidence that the passive dissemination of these publications, even when linked to consensus-derived recommendations, result in changes in clinical practice [24]. On the other hand, the actionable recommendations of CPGs, when implemented, make them the best tool now available to close the gap between actual practice and evidence-based best practice [21, 23]. Indeed, the implementation of rigorously developed guidelines has been said to "lead to even greater improvements in patient care than the introduction of some new technologies" [24].

The first CPGs in nephrology were developed in 1993 [25]. These initial evidence-based guidelines, which articulated the minimum dose of hemodialysis and

recommended how the delivered dose of hemodialysis should be measured, have been instrumental in achieving significant improvements in the adequacy dose of hemodialysis. Building on this initial effort, the National Kidney Foundation (NKF) launched its Dialysis Outcomes Quality initiative (DOQI) in 1995. The first four sets of guidelines developed were hemodialysis adequacy, peritoneal dialysis adequacy, vascular access, and anemia that were published in the fall of 1997 [26]. The implementation of these guidelines, including the development of federal or insurer-sponsored clinical performance measures, has been instrumental in changing practice patterns and their impact on favorably affecting the quality of care delivered to dialysis patients in the United States has been documented [27].

During the development of DOQI guidelines it became evident that the care of patients with CKD should be initiated well before the need for dialysis and that, in fact, an even greater opportunity existed to improve outcomes for individuals with kidney disease starting from the earliest stages of kidney injury and throughout the course of its progression to kidney failure when dialysis becomes necessary. This paradigm shift was the basis for a new and more ambitious phase in which the scope of work was enlarged to encompass the entire spectrum of kidney disease. To reflect this expansion, the reference to "dialysis" in DOQI was changed to "disease," and a new initiative termed Kidney Disease Outcomes Quality Initiative (K/DOQI) was launched in 1999.

The first set of new guidelines developed by K/DOQI on the evaluation, classification and stratification of CKD was published in February 2002 [28]. For the first time in the evolution of nephrology, these guidelines provided a definition of CKD and a classification of the stages of CKD based on the level of GFR. Subsequent interventional guidelines, specific to each of these stages, on dyslipidemia, bone mineral metabolism and disease, and blood pressure have been published [28]. Others are under development.

Guidelines have also been developed in other countries. Notable among those are the guidelines developed by the Canadian Society of Nephrology [29], the European Renal Association-European Dialysis and Transplantation Association (ERA-EDTA) [30], the United Kingdom Renal Association [31], and the Australian and New Zealand Society of Nephrology [32]. Others translated DOQI guidelines, which are now available in over 12 languages, and adopted selected components of them for local implementation.

A GLOBAL GUIDELINE INITIATIVE

A second paradigm shift in the approach to CKD occurred when it became apparent to those developing guidelines that there was a need for a more uniform and global approach to the process. The rationale for a global initiative is simple and self-evident. Essentially, there is a recognized and increasing prevalence of kidney disease worldwide. As such, there is a clear need to develop a public health approach to the global epidemic of kidney disease, coupled with strategic initiatives that can improve the care of patients with kidney disease worldwide. The complications and problems encountered by those afflicted with kidney disease are universal. The science and evidence-based care of these complications and problems are also universal and thus independent of geographic location or national borders. It is important to increase the efficiency of utilizing available expertise and resources in improving global outcomes of kidney disease. There is definite room for improving international cooperation in the development, dissemination, and implementation of clinical practice guidelines to achieve these goals.

It was on this basis that an initial exploratory and consultative meeting of a group of individuals active in the field was convened on July 14, 2002, in Copenhagen, Denmark during the Annual ERA/EDTA meeting. At the meeting, enthusiastic support for undertaking a global initiative was expressed and the decision made that a Global Coordinating Board would be formed to explore the issue further.

A GLOBAL COORDINATING BOARD: REPRESENTATION AND PROCESS

In order to maintain neutrality and independence of the Global Coordinating Board, no organization or society was asked to appoint representative members to the Board. Rather, nominations were sought from the participants in the Copenhagen meeting and other leaders in the field. Selection was based on clinical expertise and contributions on an individual basis. The fact that selected members also held positions in various organizations or societies, reflecting their own accomplishments and aptitudes, were considered a benefit to the initiative rather than a reason for selection to the Board. Because of logistics and cost restraints, a decision was made to limit membership to 30 individuals, with equal representation from Europe, North and South America, and Africa and the Far East (Table 1).

The inaugural meeting of the Global Coordinating Board was held in January 2003 in London. At that meeting, the Board decided to adopt a stepped approach to the initiative, determined exploratory tasks for Phase I of the initiative, elected an Executive Committee (Table 2), assigned management to the National Kidney Foundation, and decided to meet again in December 2003 to evaluate the progress made and to determine the next steps.

During the course of 2003, the Executive Committee held three meetings. The first, which occurred in April 2003 in Rome, defined the objectives of the Global Coordinating Board and constituted Work Groups to address each task (Table 3). The second meeting was held in October 2003 in Amsterdam to review the Work Group

Table 1. Kidney Disease: Improving Global Outcomes (KDIGO) Board of Directors

Co-Chairpersons
Garabed Eknoyan, United States
Norbert Lameire, Belgium
Members
Pedro Aljama Garcia, Spain
Thomas Andreoli, United States
Rashad Barsoum, Egypt
Gavin Becker, Australia
Ezequiel Bellorin-Font, Venezuela
Roland Blantz, United States
Emmanuel A. Burdmann, Brazil
Fernando Carrera, Portugal
Jonathan Craig, Australia
Johanna Dwyer, United States
Kai-Uwe Eckardt, Germany
Dennis Fouque, France
William E. Haley, United States
Ronald J. Hogg, United States
Vivekanand Jha, India
Bertram L. Kasiske, United States
Raymond T. Krediet, The Netherlands
Kiyoshi Kurokawa, Japan
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Alison MacLeod, United Kingdom
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Sergio Mezzano, Chile
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Sarala Naicker, South Africa
Jerome Rossert, France
Raymond Vanholder, Belgium
Rowan Walker, Australia
Haiyan Wang, Peoples Republic of China
Christoph Wanner, Germany
Andrzej Wiecek, Poland
Carmine Zoccali, Italy

Table 2. Kidney Disease: Improving Global Outcomes (KDIGO) Executive Committee

Co-Chairpersons
Garabed Eknoyan, United States
Norbert Lameire, Belgium
Members
Rashad Barsoum, Egypt
Kai-Uwe Eckardt, Germany
Adeera Levin, Canada
Nathan Levin, United States
Francesco Locatelli, Italy
Alison MacLeod, United Kingdom
Raymond Vanholder, Belgium
Rowan Walker, Australia
Haiyan Wang, Peoples Republic of China

reports, develop a structure that would incorporate the initiative as an independent entity and provide for its management, and plan proposals for Phase II of the initiative in 2004. At the third meeting, held during the American Society of Nephrology (ASN) meeting in San Diego in November 2003, the Work Group reports and proposals for 2004 were finalized, an agenda for the Global Coordinating Board meeting was developed, and the management, structure, name and mission statement for the initiative were approved.

Table 3. Kidney Disease: Improving Global Outcomes (KDIGO) Work Groups and Chairpersons

Evidence Rating
Alison MacLeod, United Kingdom
Katrin Uhlig, United States
Chronic Kidney Disease (CKD) Evaluation/Classification
Kai-Uwe Eckardt, Germany
Rowan Walker, Australia
Database/Warehouse
Raymond Vanholder, Belgium
Nathan Levin, United States
Implementation/Regions with Clinical Practice Guidelines (CPGs)
Norbert Lameire, Belgium
Francesco Locatelli, Italy
Implementation/Regions without CPGs
Rashad Barsoum, Egypt
K/DOQI-EBPG Coordination
Raymond Vanholder, Belgium
Garabed Eknoyan, United States
Global Bone and Mineral Metabolism
Sharon Moe, United States
Tilman Druëke, France

At the subsequent meeting of the Global Coordinating Board in Amsterdam on December 11 and 12, 2003, the Board reviewed, approved, and accepted the Work Group reports and plans for 2004, and unanimously approved the name, mission statement, and structure of the initiative.

KIDNEY DISEASE: IMPROVING GLOBAL OUTCOMES

The name under which the initiative is now incorporated is "Kidney Disease: Improving Global Outcomes" (KDIGO). Its mission statement is "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."

The Executive Committee met in London on March 7 and 8, 2004, to put into action plans for the next 2 years. Those plans include (*1*) the development of a common methodologic approach, including a uniform rating system of the strength of the evidence and the recommendations of guidelines; (*2*) the adoption of a common evaluation and classification of CKD to facilitate a unified nomenclature worldwide; (*3*) the establishment of an electronic interactive web-based clearinghouse of currently available CPGs, including implementation tools and performance measures to provide direct comparison of recommended targets in different guidelines together with the rationale for their differences; (*4*) the collection and evaluation of current implementation tools to use them in facilitating implementation strategies at national or regional levels; (*5*) the development of educational plans and a structure for countries without guidelines to help the adoption of selected guidelines most suitable for their regional needs; (*6*) the evaluation of current and planned guidelines in different countries with the intent of integrating the next phase of new or up-dated

guidelines, on a voluntary basis, into a common process and their release as global guidelines; (*7*) the use of controversy conferences to reconcile existing guidelines, establish what is known, decide what can be done with what is known, and determine what needs to be known; (*8*) integration of the future updating and development of guidelines under the aegis of KDIGO; (*9*) the initiation of the development of one set of new clinical practice guidelines; and (*10*) the presentation and dissemination of results achieved at various national and international meetings.

THE FUTURE

The ultimate success of these initiatives will depend not only on the scientific rigor with which they are developed, but also on their reception by the worldwide nephrology community. To this end it will need the goodwill and support of local organizations and thought leaders. Notable among those is the International Society of Nephrology (ISN), whose very international nature overlaps with the global objectives of KDIGO.

Furthermore, the commendable success of the ISN Commission for the Global Advancement of Nephrology (COMGAN) provides a unique opportunity for collaborative efforts to achieve the common goal of making lives better for patients with CKD worldwide. Thanks to the vision and foresight of the ISN Council and its president, Jan Weening, steps are already underway to achieve this end. The challenges ahead are many and the hurdles to overcome great. However, the future is bright and the present certainly better than it was only a few years ago.

Ultimately, the goal of KDIGO is to ensure the best outcomes possible for all individuals with kidney disease. Through the support and collaboration of all concerned organizations and individuals, the recognition that there are common and universal principles of physiology, science, and clinical practice should help improve outcomes of kidney disease worldwide. It is certainly possible to make the future better than the present.

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