# The Kidney Disease: Improving Global Outcomes website: Comparison of guidelines as a tool for harmonization

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**Chronic kidney disease (CKD) is a worldwide public health problem with significant comorbidity and mortality. Improving quality of life and survival of CKD patients necessitates a large number of preventive and therapeutic interventions. To resolve these issues several organizations have developed guidelines, which are difficult to compare comprehensively. The Kidney Disease: Improving Global Outcomes website at http://kdigo.org compares five major guidelines. The section '*compare guidelines*' covers 41 topics distributed over five major subjects: (1) general clinics; (2) hemodialysis (HD); (3) vascular access for HD; (4) peritoneal dialysis; and (5) chemistries. The tables compare guideline recommendations and the evidence levels on which they are based, with direct links to each of the guidelines. These data show that the different guideline groups tend to propose similar targets, but that nuances in the guideline statements, their rationale, and grading of evidence levels present some discrepancies, although most guidelines are based on the same literature. We conclude that there is an urgent need to harmonize existing guidelines, and for a global initiative to avoid the parallel development of conflicting guidelines on the same topics. The tables displayed on the website offer a basis for structuring this process, a procedure which has recently been initiated by a body composed of the five guideline development groups.**

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The increase in available diagnostic and therapeutic alternatives in medicine that began after the Second World War has escalated exponentially over the past three decades, as has the literature supporting or refuting them. The quality of these publications is variable and their conclusions often equivocal. As a result of this information overload, it has become increasingly difficult for the busy practitioner to assess and critically evaluate the information necessary for appropriate diagnostic and therapeutic decisions. This weakness has been used to good advantage by the pharmaceutical industry and likely accounts for some of the variations in practice reported in outcome studies.[1] To support physicians in their desire to practice evidence-based medicine, various organizations have developed clinical practice guidelines, which draw on systematic review and critical analysis of primary research studies, particularly randomized controlled trials, to make specific recommendations assisting practitioners and patients in making decisions about appropriate health care.

This wealth of available guidelines, however, also results in variable and sometimes apparently contradictory recommendations that stem principally from differences in the processes of retrieving literature, grading the strength of the evidence, using opinion and standards of care to construct guidelines where research data is lacking, and considerations of regional resources and policies. Some incongruity is inevitable, particularly around non-critical areas, but when inconsistencies on critical recommendations occur, particularly when they are unexplained, confusion, criticism, and even resistance to adoption of guidelines by practitioners is likely to occur. Thus, what started as an attempt to deal with an overload of information has now become an overload of sometimes controversial guidelines.[2] These abundant guidelines, however, can be used constructively by comparing apparent differences, identifying their reasons, and harmonizing their recommendations where possible.

One of the areas in which a large number of potentially inconsistent guidelines have been generated is nephrology.

This reflects a recent recognition in the nephrology community that practice should be based on evidence, where possible, and that a pathogenetic understanding of the disease alone is insufficient to informed practice. Over the 13 years after the publication of the first nephrology clinical practice guideline on the adequacy of hemodialysis (HD)[3] there are now well over 100 nephrology guidelines, developed by various regional organizations to guide the care of the growing number of patients with end-stage renal disease on renal replacement therapy[4,5] and the even larger number of cases at earlier stages of chronic kidney disease (CKD) variously estimated at 50–100 per end-stage renal disease case.[6–9] One of the major comorbidities of CKD necessitating continuous attention and therapeutic flexibility is the high risk for cardiovascular morbidity and mortality, and one of the expectations about guidelines is that they will be helpful to reduce the prevalence of kidney disease and improve outcomes for these patients.[10–13]

The Kidney Disease: Improving Global Outcomes (KDIGO) initiative was launched in January 2003, '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'.[14] Apart from several other activities, related to grading the evidence of guideline recommendations, the KDIGO Board of Directors also decided to develop a stepwise approach to coordinating nephrology guidelines. As a first step a website was constructed offering a comprehensive overview of available nephrology guidelines. One of the features offered by this website is the possibility to compare directly five principal nephrology guidelines. The purpose of the present report is to highlight the differences between several available guidelines by comparing and critically evaluating their recommendations displayed on the KDIGO website, with the purpose to outline a basis for future harmonization strategies.

## RESULTS

Forty one topics were initially selected for inclusion in the *compare guidelines* section of the website, and are classified according to five major subjects: (1) general clinics; (2) HD; (3) vascular access for HD; (4) peritoneal dialysis; and (5) chemistries (Table 1). Topics were selected by the Database Work Group of KDIGO. Not all guideline groups cover the same topics. Subdivided per guideline, Caring for Australians with Renal Impairment (CARI) discusses 30 of the selected topics, Canadian Society of Nephrology (CSN) 16, European Best Practice Guidelines (EBPG) 35, Kidney Disease Outcomes Quality Initiative (K/DOQI) 30, and the UK guidelines 28. All five guidelines address target hemoglobin (Hgb) in HD and peritoneal dialysis, time of referral to the nephrologist, HD dose ($K_t/V_{urea}$), time to start dialysis, prevention of infection of central venous catheters, target parameters for iron reserve, and methods for estimation of kidney function. By contrast, some other important topics, such as mineral metabolism in stage 3 and 4 CKD are considered by only two of the guidelines (K/DOQI and EBPG), whereas others such as anticoagulation in HD for patients with bleeding risk, general treatment of vascular access infections, and target blood pressure in peritoneal dialysis patients are discussed by only one of the guidelines (EBPG for the first two topics, and UK guidelines for the last).

The website, which also lists the evidence level per source, demonstrates that for recommendations made on the same problem in various guidelines different grades are given for

**Table 1 | Compare guideline overview**

| |
|---|
| *General clinics* |
| Target Hgb |
| Mineral metabolism targets: stage 3 |
| Mineral metabolism targets: stage 4 |
| Target blood pressure |
| Preferred nephroprotective agents |
| Protocol for hepatitis b vaccination |
| Time referral to the nephrologist |
| Cardiovascular screening in kidney disease |
| *Hemodialysis* |
| Target Hgb |
| $K_t/V$ urea |
| Mineral metabolism targets: stage 5 |
| Target blood pressure |
| Middle molecule removal |
| Bacteriological dialysate purity |
| Anticoagulation (HD) with bleeding risk |
| Anticoagulation (HD) without bleeding risk |
| Anticoagulation for HIT |
| Time to start dialysis |
| Chemical dialysate purity |
| *Vascular access for HD* |
| Preferred HD vascular access |
| Prevention of infection (general) |
| Prevention of infection (AV-fistula) |
| Prevention of infection (AV-graft) |
| Prevention of infection (central vein catheter) |
| Treatment of infection (general) |
| Treatment of infection (AV-fistula) |
| Treatment of infection (AV-graft) |
| Treatment of infection (central vein catheter) |
| *Peritoneal dialysis* |
| Target Hgb |
| Mineral metabolism targets: stage 5 |
| Target blood pressure |
| Time to start dialysis |
| Adequacy of PD |
| Treatment of peritonitis |
| Treatment of exit site infection |
| Prevention of exit site infection and peritonitis |
| *Chemistries* |
| Target lipid concentrations |
| Target CRP |
| Target $CO_2$ |
| Target parameters iron reserve |
| Estimation kidney function |

AV, arteriovenous; $CO_2$, bicarbonate; CRP, C-reactive protein; HD, hemodialysis; HIT, heparin-induced thrombocytopenia; $K_t/V$, ratio of clearance multiplied by time over distribution volume; PD, peritoneal dialysis.

the level of available evidence. To illustrate the problems encountered, three specific topics are discussed in more detail in the following section: (1) HD dose; (2) target Hgb levels; and (3) bone and mineral metabolism targets. These topics were chosen because all or most guideline groups covered them and because they are major clinical issues in nephrology practice.

### HD dose ($K_t/V_{urea}$)

Table 2 summarizes information on the recommended dose of HD ($K_t/V_{urea}$) that can be obtained from the website. At first glance, all guidelines recommend similar targets, that is, 1.2 (CARI), $>1.2$ (UK) and $\geqslant 1.2$ (EBPG, K/DOQI, CSN). Closer scrutiny of the data however reveals that the targets for EBPG and UK are expressed as equilibrated $K_t/V$ ($eK_t/V$), whereas those of CARI, CSN, and K/DOQI are expressed as single pool $K_t/V$ ($spK_t/V$). The $eK_t/V$ utilizes an equilibrated urea level post-dialysis which provides a more accurate picture of the delivered dose than does single pool kinetic modeling.[15–17] Consequently, $eK_t/V$ values are lower than their equivalent single pool values by about 0.2. Hence, EBPG and the UK guidelines target at a higher relative dose than the other guidelines, which aim at $\geqslant 1.2$ $spK_t/V$.

Moreover, the EBPG propose a prescribed dose of 1.4 ($spK_t/V$) as a target with the intent of achieving a delivered dose of $spK_t/V$ of 1.2 in the majority of patients. On the other hand, both CARI and K/DOQI fix their target delivered dose at 1.2 ($spK_t/V$) but advise a prescribed dose of 1.3 in order to achieve 1.2 in the majority of patients. Of note, most of these guidelines were published in 2002 or earlier, and are essentially based on observational studies.[18–20] The only recent randomized clinical trial evaluating the potential impact of HD dose on outcome is the hemodialysis (HEMO) Study, which was published at the end of 2002, that is, after the publication of the guidelines.[21] The HEMO Study found no difference in outcome between a group targeted at $K_t/V$ values just above the proposed recommendations (1.32 $spK_t/V$) versus another group with a higher dose of 1.71 $spK_t/V$. The conclusions of the HEMO Study support the recommendations of the current guidelines since there seems to be no extra benefit overall in raising $K_t/V$ above the minimum target of 1.32 single pool examined in the HEMO Study.

The comparison of evidence levels among guidelines is hampered by the use of different grading systems (A–C; A, B and opinion; I–IV; I–IV and opinion; or simply 'Evidence') by different guideline groups or by the same organization at different moments. For the sake of uniformity, we translated the evidence levels in the website tables and also in Tables 2–4 of this paper, into the KDIGO grading system for the discussion that follows.[22] The KDIGO system is the most nuanced and recent one, which in the meanwhile has been adopted in the most recent guidelines of CARI and K/DOQI. The translation of the different types of evidence scoring into the KDIGO system is summarized in Table 5.

When applying this system for uniformization, the evidence levels of the guidelines discussed in this paragraph appear fairly similar, with the equivalents of KDIGO I-IV being proposed by K/DOQI, III-IV by CARI, EBPG, and UK, and III by CSN.

This comparison demonstrates that although many guidelines propose similar targets, there are minor differences. In this case the apparent differences are principally due to different expressions of the unit dose of HD. Given the absence of randomized controlled trial (RCT) data demonstrating what an appropriate dose of HD is, some variability in the guidelines is reasonable.

**Table 2 | Comparative data regarding $K_t/V_{urea}$ for hemodialysis**

| Origin | Year | Target | Method | Comments | Evidence |
|---|---|---|---|---|---|
| CARI | 2000 | 1.2 | $spK_t/V$ | Aim at 1.3 to deliver 1.2 | III–IV |
| CSN | 1999 | $\geqslant 1.2$ | $spK_t/V$ | | III |
| EBPG | 2002 | $\geqslant 1.2$ | $eK_t/V$ | | B |
| | | $=\sim 1.4$ | $spK_t/V$ | 1.4 proposed to deliver 1.2 (sp) | |
| K/DOQI | 2002 | $\geqslant 1.2$ | $spK_t/V$ | Aim at 1.3 to deliver 1.2 | Evidence |
| UK | 2002 | $>1.2$ | $eK_t/V$ | | B |

Abbreviations of guideline names (origin): see Table 5; $spK_t/V$, single pool $K_t/V$; $eK_t/V$, equilibrated $K_t/V$.
For comparison of different evidence scoring systems, please refer to Table 5.

**Table 3 | Comparative data regarding target Hgb levels**

| Origin | Year | Target | Comments | Evidence |
|---|---|---|---|---|
| CARI | 2005 | $\geqslant 11$ g/dl | $\leqslant 12$ g/dl in CVD | III–IV; comment: I |
| CSN | 1999 | 11–12 g/dl | | Opinion |
| EBPG | 2004 | $>11$ g/dl | Not $>12$ g/dl in severe CVD<br>Not $>14$ g/dl globally | B |
| K/DOQI | 2001 | 11–12 g/dl | Targets for EPO, not for transfusion | Evidence |
| UK | 2002 | $>10$ g/dl | | A |

Abbreviations of guideline names (origin): see Table 5. CVD, cardio-vascular disease; EPO, erythropoietin.
For comparison of different evidence scoring systems, please refer to Table 5.

**Table 4 | Comparative data regarding mineral metabolism targets**

| Origin | Year | Ca | P | Ca × P | PTH | Evidence |
|---|---|---|---|---|---|---|
| *CKD stage[a] 3 (GFR 30–59 ml/min/1.73m$^2$)* | | | | | | |
| Europe[b] | 2001 | 8.8–11.0 mg/dl | 2.5–4.6 mg/dl | — | 85–170 pg/ml | Opinion |
| K/DOQI | 2003 | 8.4–9.5 mg/dl | 2.7–4.6 mg/dl | — | 35–70 pg/ml | P: Ev, Opin<br>Ca: Ev<br>PTH; Opin |
| *CKD stage[a] 4 (GFR 15–29 ml/min/1.73m$^2$)* | | | | | | |
| Europe[b] | 2001 | 8.8–11.0 mg/dl | 2.5–4.6 mg/dl | — | 85–170 pg/ml | Opinion |
| K/DOQI | 2003 | 8.4–9.5 mg/dl | 2.7–4.6 mg/dl | $<55$ mg$^2$/dl$^2$ | 70–110 pg/ml | P: Ev, Opin<br>Ca: Ev<br>PTH; Opin |
| *CKD stage[a] 5 (GFR $<15$ ml/min/1.73m$^2$ or renal replacement therapy)* | | | | | | |
| CARI | 2000 | 8.8–10.4 mg/dl | $<6.8$,<br>pref $<5.6$ mg/dl | $<71.9$ mg$^2$/dl$^2$<br>— | 2–3 × limit | B |
| Europe[b] | 2001 | 8.8–11.0 mg/dl | 2.5–4.6 mg/dl | — | 85–170 pg/ml | Opinion |
| EBPG[c] | 2002 | — | 2.5–5.5 mg/dl | $<55$ mg$^2$/dl$^2$ | — | B |
| K/DOQI | 2003 | $<10.2$<br>pref 8.4–9.5 mg/dl | 3.5–5.5 mg/dl | $<55$ mg$^2$/dl$^2$ | 150–300 pg/ml | P, PTH: Opin<br>Ca: Opin |
| UK | 2002 | 8.8–10.4 mg/dl[d] | — | | $<4$ × limit | B |

Abbreviations of guideline names (origin): see Table 5. Ca, calcium; Ca × P, calcium-phosphorus product; CKD, chronic kidney disease; Ev, Evidence; GFR, glomerular filtration rate; Opin, Opinion; P, phosphorus; pref, preferably; PTH, parathyroid hormone.
[a]Staging of CKD as adhered to by K/DOQI[3] and KDIGO.[4]
[b]European recommendations based on clinical algorithms developed by a European expert panel not operating under EBPG.
[c]Hemodialysis guidelines, section VII – Vascular disease and risk factors.
[d]Adjusted for serum albumin.
For comparison of different evidence scoring systems, please refer to Table 5.

### Target Hgb levels

All guidelines propose a minimum target of 11 g/dl with the exception of the UK guidelines, which recommend a minimum of 10 g/dl (Table 3). The rationale to adhere to the 10 g/dl is based on two RCTs.[23,24] An additional argument mentioned in the UK guidelines for proposing a relatively lower target is related to cost. Of note, the normal Hgb study which is one of the publications providing the basis of the UK guideline was undertaken in subjects more than 65 years old, close to 70% of whom had grafts as vascular access; in addition, this study was confined to patients with severe cardiovascular disease, not to a prevalent population of dialysis patients, and was terminated earlier than planned because of safety concerns.[23] The other guidelines, although proposing a higher minimal target, are based on the same literature.

The CSN and K/DOQI guidelines propose maximum target Hgb of 12 g/dl. Likewise, the EBPG and CARI suggest avoiding values in excess of 12 g/dl, but only in patients with severe cardiovascular disease, based on the results of the normal Hgb study, although the cutoff of that study was higher (Hgb 14 g/dl).[23] The EBPG discourages values $>14$ g/dl overall, out of concern for hemoconcentration, especially at the end of the HD session, when the plasma volume is most reduced by ultrafiltration.[25]

Of note, the same target recommendations are made in most guidelines for non-dialyzed CKD patients and those on peritoneal dialysis, although the cited studies were not designed for these populations, and unlike HD those patients are not subject to ultrafiltration produced hemoconcentration.

For this topic, evidence levels are quite divergent: equivalent to KDIGO level I–II in the UK guidelines, level I–IV for K/DOQI, and level III–IV for EBPG and CARI. CSN refers to opinion-based evidence, and this in spite of it being based on the same literature, comprising relevant RCTs. It is difficult to speculate on the divergence in grading these evidence levels, but some guidelines may take into account only the design of the study to attribute level I–II and do this automatically with at least one RCT, whereas other guidelines require several RCTs or take into account the quality of the studies to downgrade or upgrade evidence levels.

### Mineral metabolism targets

CSN formulated no guidelines regarding this issue (Table 4). European recommendations were issued by an expert panel not operating under EBPG, and later on EBPG generated limited guidelines only concerning phosphorus and parathyroid hormone in the first wave of the HD guidelines (section VII on vascular disease and risk factors). Only the European expert panel and the K/DOQI stratify their recommendations according to the different stages of CKD. The European panel recommendations are the same for all stages, whereas in K/DOQI the target Ca and P are the same in stage 3 and 4, but are allowed to be higher in stage 5. Also, recommended parathyroid hormone targets are gradually increased in K/DOQI for the progressive stages of CKD but these are opinion-based targets and the rationale for higher targets in the more advanced stages is not always evident.

There is considerable disparity in proposed target values. Values for phosphorus are the most consistent, probably

**Table 5 | System of evidence grading, by guideline group[a]**

| Source | Evidence level | Comparison with KDIGO classification |
|---|---|---|
| *KDIGO* | I: Meta-analysis of several controlled studies<br>II: Controlled randomized study<br>III: Case control or observational study<br>IV: Case reports<br>Opinion | |
| *CARI-Australia* | I: Evidence obtained from a systematic review of all relevant RCT's<br>II: Evidence obtained from at least one properly designed RCT<br>III: Evidence obtained from comparative studies (cohort, case control)<br>IV: Evidence obtained from case series | Equal to KDIGO system |
| *CSN-Canada* | I: RCT which demonstrates a statistically significant difference in at least one important outcome or a RCT of adequate size to exclude a 25% difference in relative risk with 80% power given the observed results.<br>II: CT which does not meet the level I criteria<br>III: A non-randomized trial with contemporaneous controls selected by some systematic method.<br>IV: A before–after study of case series (at least 10 patients) with historical controls.<br>V: Case series (at least 10) without controls<br>VI: Case report (<10 pts) | I–II equals ± I–II KDIGO<br>III–VI equals ± III–IV KDIGO |
| *EBPG-Europe* | According to the categories of the US Department of Health and Social Services (1992)<br>A: Evidence from at least one prospective randomized controlled trial or from meta-analyses of several controlled trials<br>B: Evidence from qualitatively satisfactory but uncontrolled open studies<br>C: Opinions of consensus groups such as the NKF-DOQI Work Group | A equals I–II KDIGO<br>B equals III–IV KDIGO<br>C equals opinion KDIGO |
| *K/DOQI-US* | Evidence<br>Opinion | Evidence equals I–II–III or IV KDIGO |
| *UK-Guidelines* | The term 'standard' is used when the available evidence is strong or for key 'good practice' statements<br>Recommendation is used where the available evidence is weaker and for 'good practice' statements.<br>A: Evidence from randomized controlled trials or meta-analysis of several controlled trials<br>B: Well conducted trials but no randomized trials<br>C: Expert opinions | A equals I–II KDIGO<br>B equals III–IV KDIGO<br>C equals Opinion KDIGO |

CARI, Caring for Australians with Renal Impairment. CSN, Canadian Society of Nephrology; CT, controlled trial; EBPG, European Best Practice Guidelines; K/DOQI, Kidney Disease Outcomes Quality Initiative; RCT, randomized controlled trial; UK, Renal Association Guidelines.
[a]Evidence scoring as used in the most recent guidelines; older guidelines may use different systems.

because a number of observational studies show a distinct increase in morbidity and mortality at increasing phosphorus levels.[26–28] Only three guidelines (EBPG, K/DOQI, and CARI) give a target value for Ca × P product. Although those values diverge by more than 30%, they are based on the same study.[26] The EBPG and K/DOQI take into account that mortality starts to rise once the product exceeds 4.2 $mmol^2/l^2$ (55 $mg^2/dl^2$) whereas CARI focuses on the fact that the increase in mortality becomes significant only with a Ca × P product in excess of 5.8 $mmol^2/l^2$ (71.9 $mg^2/dl^2$).

Only the UK and CARI guidelines consider that the various test methods used to measure parathyroid hormone may have a different sensitivity causing different results. This bias is avoided in those guidelines by expressing the target parathyroid hormone not as absolute values but as a multiple of the highest normal value.

Evidence levels are again divergent between the different guidelines with KDIGO equivalent I–IV, III–IV, and opinion (Table 4). Here again, the reasons for these discrepancies are not obvious. Any evidence level below III is debatable given the absence of RCTs, and the disparity is partly due to the fact that K/DOQI gives 'Evidence' as qualification, without specification of the exact level.

## DISCUSSION

The current evaluation comparing recommendations offered by five major national and international nephrology guidelines regarding 41 topics is based on the data displayed in the compare guidelines section of the KDIGO website. It is clear that: (1) not all topics are covered by all guidelines and there is a marked disparity in the items considered in the different guidelines; (2) only a few topics (9/41) are covered by all

guidelines; (3) there is an appreciable difference among guidelines in the system of grading the level of evidence; and (4) there is considerable disparity among guidelines in the recommendations and the level of evidence given for the same topics. As illustrated by the specific examples of guidelines dealing with dialysis adequacy, target Hgb and mineral metabolism targets, the different guidelines do not come to uniform recommendations in spite of apparently being based on the same literature.

Why some guideline groups choose certain topics and others not, is not always clear. This likely reflects the evolutionary process through which nephrology developed as a discipline, the clear disparity in target dialysis dose that existed through the 1990s when nephrology guidelines were first published, and the fact that a definition and classification of CKD was not adopted until 2002.

There appears to be a lack of uniformity in the process of guideline development, even in such a well-circumscribed area as nephrology. This inconsistency is confusing to practitioners concerned with best practice. It could be resolved if we move toward more harmonized global guidelines, based on a uniform process for their development. The concept and design of the KDIGO website is to provide a framework that highlights those differences and can be used as a first step to identify reasons for variability and to introduce improvements in the guideline development process. An initial effort to this end has been initiated at a recent meeting of the five guideline groups. Such a model would be applicable to guidelines in general, independent of the specialties for which they were developed.

To the best of our knowledge, there are virtually no sources allowing a similar comparison of other medical guidelines. A Google search of the Internet with the keywords 'medical', 'guideline', and 'comparison', displayed only one relevant hit, which was the website of the 'National Guideline Clearinghouse'.[29] The latter allows access to different guidelines of various specialties, but does not allow for a direct comparison of topics, of recommended targets, or the evidence level of recommendations.

Based on the results illustrated in the present report it would be expected that similar disparities would frustrate guideline users in fields outside nephrology as well. The plea for comparison and harmonization of guideline recommendations should therefore be extended to all guideline areas. This is the mission that KDIGO has undertaken for nephrology guidelines.

The proposed different targets per guideline might have important clinical and financial implications. For example, the target Hgb levels may have an impact on cardiovascular status and survival.[30] Lower and higher target Hgb may result in higher morbidity and mortality rates in a given population.[23,31] On the other hand, lower target Hgb levels automatically imply a lower need for erythropoietin,[32] which, depending on the reimbursement system, may result in a lower cost for society and/or the patient, and alter the profit margin for a dialysis facility.

Harmonization of guidelines does not necessarily imply that each country should follow these guidelines implicitly. There should be room for consideration and adaptation to available regional needs and resources, including appropriate country-based thresholds for incremental cost effectiveness. For example target Hgb levels may be impossible to reach in certain countries due to socio-economic restraints. It might therefore be useful to aim at a stepwise approach, whereby a first global ideal target is proposed, followed by the subsequent consideration of local reasons to fine-tune this target. This is the process proposed by the World Health Organization in its document (EIP/GPE/EQC/2003.1) titled 'Guidelines for World Health Organization Guidelines'.[33] Essentially, the process begins with guideline statements that are of maximal benefit to individuals or groups of patients if resources were unlimited. The next stage assesses tradeoffs between cost of applying an intervention on a population basis and its health impact (very limited versus unlimited resources). The final stage is for local guideline groups to adopt and prioritize recommendations for regional implementation based on the evidentiary basis of the global guideline statements, if necessary with assistance from the global guideline development group. This is the approach adopted by KDIGO in developing its new guidelines, now at various levels of progress, on Hepatitis C, Mineral and Bone Disease, and Care of the Kidney Transplant Recipient.

Uniformity of grading the level of evidence remains one of the principal approaches to provide a comparative basis to the strength of recommendations in various guidelines. Unfortunately evidence levels are graded using different methods by various organizations. As shown in the discussion of the specific topics, reported evidence levels diverge among guidelines in nephrology. Comparison between guidelines is therefore difficult and somewhat arbitrary. Some of the discrepancies may reflect an evolution of evidence as new publications appear over time. More frequently, they point to differences in methods of grading the evidence.

Attempts to resolve these discrepancies have been undertaken by different international groups of experts such as the Relevance, Education, Applicability, Discrimination and overall Evaluation method (READER)[34] and the Grading of Recommendations Assessments, Development and Evaluation system.[35] KDIGO will use in the future the Grading of Recommendations Assessments, Development and Evaluation system, which allows upgrading or downgrading of evidence levels.[22] KDIGO will additionally apply the Appraisal of Guidelines Research and Evaluation instrument, which assesses 23 key items in six different domains and has already been validated extensively.[36] The advantage of the Appraisal of Guidelines Research and Evaluation instrument is the applicability for any disease in any country.

One of the problems encountered in developing guidelines in nephrology is a relative scarcity of valid randomized controlled studies of acceptable quality.[37] International, multicenter randomized studies on an independent basis

should be undertaken to overcome this gap. Financial resources that are now used to develop a multiplicity of parallel guidelines might become available for redistribution to those studies as well as to the development of guidelines on topics which have not been dealt with until now.

Of note, the data in this article are based on a fixed time status of the KDIGO website and only on the five guidelines on which this website is based currently. Evidence-based guidelines, given their very nature, should be updated regularly, in light of newly available data; updates of the K/DOQI guidelines on anemia have recently been published[38] and several CARI and CSN updates have appeared.[39,40] Also updates of the UK guidelines are under way. Although such modifications may reduce discrepancies with other guidelines, they may not necessarily do so; even if this were the case, the main message of the present article, which points to the potential at large for internal discordance among guidelines at any moment remains valid, but deserves ongoing updates. KDIGO has established a Liaison Task Force of the five guideline groups to expedite entry and comparison of new and updated guidelines.

The following steps will be implemented in the coming months to improve the design of the website: (1) the addition to the tables of information on new or recently updated guidelines; (2) the extension of the number of topics for the comparison tables; (3) the installation of tools allowing website visitors to make interactive comments; (4) the installation of buttons allowing to move back and forth between different tables; (5) the posting for specific entries allowing public review of preliminary drafts of KDIGO guidelines ; (6) the installation of links to short 'rationale' sections where guideline groups briefly explain how they defined their targets; (7) inclusion of other than the five currently displayed nephrology guidelines, if they conform with the same preset conditions, as those used now to include guidelines on the website; and (8) the addition to the website of non-nephrology guidelines which are pertinent to nephrologists.

## CONCLUSION

The KDIGO initiative is the first international endeavor to compare several existing nephrology guidelines and to undertake the development of new global guidelines that will be applicable worldwide. The KDIGO website with its compare guidelines section offers the opportunity to consider several different guidelines together, and to compare the recommendations given in 41 selected topics, which are considered to be germane for the treatment of CKD patients. The data presented from the website show that: (1) topics addressed by major guidelines are highly divergent; and (2) proposed recommendations and evidence levels differ in spite of being based on the same literature. These data endorse the need for global and harmonized guidelines worldwide, rather than launching separate and parallel activities that confuse the potential users and at the practical level lead to inertia rather than therapeutic improvement by the individual practitioner.

## MATERIALS AND METHODS

### The website

The website is described, as it was available on 1 May 2006, owing to the lag time in preparing this publication; it was necessary to focus on data as they were available at a fixed moment, to avoid confusion and inconsistencies. The layout and content of the website will be modified in the future as a result of new guidelines and upcoming updates. Also, discussion is currently underway for extension of the existing guideline topics posted on the website. It is likely, therefore, that by the time this report is published the website will be or has been modified, as new guidelines appear or old ones are updated.

The website can be accessed at: http://kdigo.org. It contains *general information* on the KDIGO initiative, a *mission statement* and an option to link to the websites of the Dialysis Outcomes and Practice Patterns Study, the United States Renal Data System and information on the activities of the different KDIGO Work Groups. Through *guideline summaries* it accesses all the different guideline topics listed and through the compare guidelines section it provides the details of each of the guidelines. The comparison of these guidelines on common topics is the main focus of this paper.

### The compare guidelines section of the website

In its present format, the compare guidelines section allows comparison of five major guidelines, which have been selected by the KDIGO guideline Database Work Group and approved by its Board of Directors, based on the following criteria: (1) developed by a panel of internationally or nationally recognized clinical experts; (2) based on objective and well defined literature search and structured analysis methods; and (3) subjected to a well defined peer-review process.

The selected guidelines are: (1) the CARI guidelines CARI – Australia-New Zealand; (2) the guidelines of the CSN – Canada; (3) the EBPG – Europe; (4) the guidelines (K/DOQI – USA); and (5) the Renal Association guidelines (UK). The topics selected for comparison are shown in Table 1.

The data displayed in the compare guidelines section show: (a) the selected individual topic; (b) the guidelines that address that topic; (c) and the system of evidence level grading (Table 5).[41] The *guideline comparison tables* contain the name of the guideline, the year of publication, the recommendation, the source, additional remarks, for example, the rationale of a given recommendation, and the respective assigned level of evidence. The full text of that specific guideline, its rationale and reference list, can be accessed by clicking the *source* button.

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