Methods for guideline development

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AIM
The overall aim of this project was to develop an evidence-based clinical practice guideline for evaluation and management of CKD. The guideline consists of recommendation statements, rationales, and a summary of systematically generated evidence on relevant pre-defined clinical topics. To a large extent the guideline builds on the output of the KDIGO Controversies Conference in 2009, which generated epidemiological data to support a revision of the classification and staging system. The vision for this KDIGO guideline is that it would endorse the current CKD definition as an imperfect convention for describing a state of function, revise classification based on risk, revise risk states, and revise and update action plans in view of the revised classifications. Additional systematic evidence review focused on specific topics.

OVERVIEW PROCESS
The guideline development process included the following steps:
- Appointing Work Group members and the ERT
- Discussing process, methods, and results
- Developing and refining topics
- Identifying populations, interventions or predictors, and outcomes of interest
- Selecting topics for systematic evidence review
- Standardizing quality assessment methodology
- Developing and implementing literature-search strategies
- Screening abstracts and retrieving full text articles on the basis of predefined eligibility criteria
- Creating data extraction forms
- Extracting data and performing critical appraisal of the literature
- Grading the methodology and outcomes in individual studies
- Tabulating data from individual studies into summary tables
- Grading the strength of recommendations on the basis of the quality of evidence and other considerations
- Finalizing guideline recommendations and supporting rationales
- Sending the guideline draft for peer review to the KDIGO Board of Directors in January 2012 and for public review in May 2012
- Publishing the final version of the guideline

Collaboration Among Participants
The KDIGO Co-Chairs appointed the Work Group Co-Chairs, who then assembled the Work Group of domain experts, including individuals with expertise in internal medicine, adult and pediatric nephrology, diabetology/endocrinology, clinical chemistry, and epidemiology. The Tufts Center for Kidney Disease Guideline Development and Implementation at Tufts Medical Center in Boston, Massachusetts, USA, was contracted to conduct systematic evidence review and provide expertise in guideline development methodology. The ERT consisted of physician-methodologists with expertise in nephrology, a project coordinator, a research assistant, and a medical writer-editor. The ERT instructed and advised Work Group members in all steps of literature review, critical literature appraisal, and guideline development. The Work Group and the ERT collaborated closely throughout the project.

The Work Group and its Chairs, KDIGO Co-chairs, ERT, and KDIGO support staff met for three 2-day meetings for training in the guideline development process, topic discussion, and consensus development.

Throughout the project, the ERT offered suggestions for guideline development and led discussions on systematic review, literature searches, data extraction, assessment of quality and applicability of articles, evidence synthesis, grading of evidence and guideline recommendations, and consensus development. The Work Group took the primary role of writing the recommendation statements and rationales and retained final responsibility for their content.

Defining Scope and Topics
This KDIGO CKD guideline was set out to update the KDOQI Clinical Practice Guidelines for CKD: Evaluation, Classification, and Stratification1 in 2002, which spans many topics related to the diagnosis, classification, stratification, and management of CKD.1

The Work Group Co-Chairs prepared the first draft of the scope of work document as a series of open-ended questions to be considered by Work Group members. At their first 2-day meeting, members added further questions until the initial working document included all topics of interest to the Work Group. The inclusive, combined set of questions formed the basis for the deliberation and discussion that followed. The Work Group strove to ensure that all topics deemed clinically relevant and worthy of review were identified and addressed.

Updating the topics of definitions and classification was based on the output from the KDIGO Controversies Conference and the CKD Prognosis Consortium.4,30 Additional topics that relate to explicit selection of diagnostic tests or interventions were chosen to undergo systematic review of the best available evidence. Systematic
evidence review entails a priori question formulation, specification of important outcomes for the review, systematic searches, data extraction, tabulation, analysis, and synthesis of evidence and is described in detail for each of the specific questions. The process followed for each evidence review topic (a total of four non-treatment topics and four treatment topics) is detailed below.

The eight topics for which the ERT conducted searches and evidence review are shown in Table 37. For the systematic review topics, the Work Group and ERT further developed and refined each topic and specified screening criteria, literature search strategies, and data extraction forms.

Many other topics were not suitable to be addressed by in-depth evidence review. When the anticipated outcome of an extensive literature search was unlikely to yield evidence that directly informs practice choices, the approach chosen was that of a narrative review.

**APPROACH TO EVIDENCE REVIEW TOPICS**

**Formulating Questions of Interest**

Questions of interest were formulated according to the PICODD (Population, Intervention or Predictor, Comparator, Outcome, study Design, and Duration of follow-up) criteria. Details of the PICODD criteria are presented in Table 37.

**Literature Searches and Article Selection for Evidence Review Topics**

Search strategies were developed by the ERT, with input from the Work Group, for each topic of interest (whether treatment or non-treatment topics). The ERT performed literature searches and conducted abstract and article screening. The ERT also coordinated the methodological and analytic processes, data extraction, and summarizing of the evidence. Before initiating our own de novo systematic review, we searched for existing systematic reviews that could be used. The searches and search terms are provided in Supplemental Table 1 and the search dates and yields for all topics are presented in Table 38.

**Selection of Outcomes of Interest**

The Work Group selected outcomes of interest on the basis of their importance for informing clinical decision making. Importance of mortality and ESRD was considered to be critical; the importance of progression of CKD and categorical or continuous measures of kidney function was considered to be high; and the importance of QOL, BP, gout attacks, and proteinuria was considered to be moderate.

**Data Extraction**

Text articles were extracted by the ERT onto forms customized to capture data on design, methodology, baseline characteristics, interventions or predictors, comparators, outcomes, results, and limitations of individual studies. Study methodology and risk of bias were also systematically graded for each outcome and recorded.

**Summary Tables**

Pertinent information for systematic review topics was tabulated in summary tables. Summary tables list outcomes of interest as well as relevant population characteristics, descriptions of interventions and comparators, results, and quality grades for each outcome. Categorical and continuous outcomes were summarized separately. Work Group members reviewed all summary table data and quality grades.

**Evidence Profiles**

Evidence profiles are usually constructed as a means to assess the quality and record quality grades and descriptions of effect for each outcome across studies, as well as the quality grades and description of net benefits or harms of the intervention or comparator across studies. These profiles aim to make the evidence synthesis process transparent. However, since no treatment or non-treatment topic had more than one study in a summary table for which the quality was graded, no evidence profiles were generated, and the information in the summary table shows the highest level of synthesis.

**Grading of Quality of Evidence for Outcomes of Individual Studies**

**Methodological quality.** Methodological quality (internal validity) refers to the design, conduct, and reporting of outcomes of a clinical study. A previously devised three-level classification system for quality assessment was used to grade the overall study quality and quality of all relevant outcomes in the study (Table 39). Variations of this system have been used in most KDOQI and all KDIGO guidelines and have been recommended for the US Agency for Healthcare Research and Quality Evidence-based Practice Center program.

Each study was given an overall quality grade on the basis of its design, methodology (randomization, allocation, blinding, definition of outcomes, appropriate use of statistical methods, etc.), conduct (drop-out percentage, outcome assessment methodologies, etc.), and reporting (internal consistency, clarity, thoroughness, and precision, etc.). Each reported outcome was then evaluated and given an individual grade depending on the quality of reporting and methodological issues specific to that outcome. However, the quality grade of an individual outcome could not exceed the quality grade for the overall study.

**Grading the Quality of Evidence and the Strength of Guideline Recommendations**

A structured approach, based on the GRADE approach, was used to grade the quality of the overall evidence and the strength of recommendations for each topic. This grading scheme-with two levels for the strength of a recommendation together with four levels of grading for the quality of the evidence, as well as the option of an ungraded statement for general guidance—was adopted by the KDIGO Board in December 2008.
### Table 37 | Topics of interest for the management of CKD guideline

| Topic | Question | Population | Treatment, predictor or index test | Comparator or alternative test or gold standard | Outcome (ranked by importance) | Study design | Inclusion criteria | Methodological approach | No. of reports or articles yielded |
|-------|----------|------------|-----------------------------------|-----------------------------------------------|---------------------------------|-------------|------------------|----------------------|-----------------------------|
| **Non-Treatment** | | | | | | | | | |
| Prediction equations for GFR | How do SCr- or SCysC-based prediction equations perform compared to gold standard measurement of GFR? | Patients in steady state with or without CKD and other special populations (DM, HTN, KTR or donors, various age groups, races, or ethnic groups) | GFR prediction based on SCr or SCysC must be directly traceable to (not just indirectly calibrated to) IDMS standards | Gold standard measure of GFR (e.g., iothalamate, EDTA, iohexal, inulin clearance) Not 24-hr urine collection | Bias precision, accuracy expressed as $P_{30}$ | Cross-sectional or diagnostic test study | Overall N > 100 N > 50 for subgroups | SR Equation must be validated in an external dataset | 15 |
| Prediction equations for risk of kidney failure | What prediction equations exist to predict kidney failure? | GFR < 60 ml/min/1.73 m² and/or kidney transplant | Candidate predictors had to include at least age, sex, SCr, and DM status | NA | ESRD, mortality | Longitudinal cohort study | Equation must be validated in an external dataset N > 100 | Studies identified by WG | 2 |
| Gadolinium exposure and nephrogenic fibrosing dermopathy | What is the incidence of NFD after exposure to gadolinium? | GFR < 60 ml/min/1.73 m² and/or kidney transplant | Gadolinium exposure | No gadolinium exposure | Nephrogenic fibrosing dermopathy | SR of case-control and cohort studies | None | Search for SRs | 1 |
| AKI and phosphate-containing bowel preparations | What is the incidence of AKI after taking a phosphate-containing bowel preparation? | Any GFR category; individuals without CKD | Exposure to phosphate-containing bowel preparation | No exposure to phosphate-containing bowel preparation | Categorical kidney outcomes | Narrative review of case-control studies; observational cohort studies | None | Search for recent guidelines, SRs, RCTs, observational studies, or narrative reviews | 2 |
| **Treatment** | | | | | | | | | |
| Treatment with bicarbonate | Does treatment with bicarbonate in CKD improve clinical outcomes? | GFR < 60 ml/min/1.73 m² and/or kidney transplant | Bicarbonate or citrate | No bicarbonate or citrate | ESRD, categorical or continuous kidney function; QOL and BP control as adverse events | RCT | N > 100 | Review of Cochrane SRs plus systematic search for RCTs published after search dates in most recent Cochrane SR | 1 SR + 1 RCT |
| Treatment with allopurinol | Does treatment with allopurinol in CKD improve clinical outcomes? | GFR < 60 ml/min/1.73 m² and/or kidney transplant with or without hyperuricemia | Allopurinol | No allopurinol | Mortality, cardiovascular events, ESRD, CKD progression, gout attacks; QOL and BP control as adverse events; proteinuria | RCT | N > 100 | SR | 1 |
| Timing of initiation of RRT in CKD | When should dialysis be started: early or late? | GFR < 30 ml/min/1.73 m² | Early start of dialysis | Late start of dialysis | Mortality, ESRD | RCT | N > 100 | Review of studies identified by WG | 1 |
| Protein restriction | Should patients with CKD be on a protein-restricted diet? | GFR < 60 ml/min/1.73 m² and/or kidney transplant | Reduced protein intake | Usual protein intake | ESRD, mortality, categorical or continuous kidney function | RCT | N > 100 | Review of Cochrane SRs plus systematic search for RCTs published after search dates in most recent Cochrane SR | 3 SR + 1 RCT |

Abbreviations: AKI, acute kidney injury; BP, blood pressure; CKD, chronic kidney disease; cys C, cystatin C; DM, diabetes mellitus; EDTA, ethylenediamine tetraacetic acid; ESRD, end-stage renal disease; GFR, glomerular filtration rate; HTN, hypertension; IDMS, isotope dilution mass spectrometry; KTR, kidney-transplant recipient; NA, not applicable; NFD, nephrogenic fibrosing dermopathy; QOL, quality of life; RCT, randomized controlled trial; RRT renal-replacement therapy; SCr, serum creatinine; SCysC, serum cystatin C; SR, systematic review; WG, Work Group.

$P_{30}$ Accuracy specifically measured as the percentage of GFR estimates within 30% ($P_{30}$) of the measured GFR. Higher $P_{30}$ values reflect greater accuracy; values are decreased by both greater bias and worse precision.
The strength of a recommendation indicates the extent to which one can be confident that adherence to the recommendation will do more good than harm. The quality of a body of evidence refers to the extent to which our confidence in an estimate of effect is sufficient to support a particular recommendation. The process of transparently grading evidence and recommendations for treatment topics is described below in further detail. However, the approach had to be adapted for the main topics of the KDIGO CKD guideline because they were not treatment-related topics.

Grading the Quality of Evidence for Each Outcome Across Studies
Following the GRADE approach, the quality of a body of evidence pertaining to a particular outcome of interest was initially categorized on the basis of study design (Table 40). For questions of interventions, the initial quality grade was high if the body of evidence consisted of RCTs, low if it consisted of observational studies, and very low if it consisted of studies of other designs. For questions of interventions, the Work Group decided to use only RCTs. The grade for the quality of evidence for each intervention-outcome pair was then lowered if there were serious limitations to the methodological quality of the aggregate of studies, if there was thought to be a high likelihood of bias, if there were important inconsistencies in the results across studies, if there was uncertainty about the directness of evidence (including limited applicability of the findings to the population of interest), if the data were sparse (for example if there was only one study or if the results include just a few events or observations and were uninformative) or imprecise (for example the CI spans a range greater than 1 or confidence limits are $0.5$ to $2.0$). The final grade for the quality of evidence for an intervention-outcome pair was then assigned as high, moderate, low, or very low (Table 40).

Grading the Overall Quality of Evidence
The quality of the overall body of evidence was then determined on the basis of the quality grades for all
methods for guideline development

Table 40 | GRADE system for grading quality of evidence

| Step 1: Starting grade for quality of evidence based on study design | Step 2: Reduce grade | Step 3: Raise grade | Final grade for quality of evidence and definition |
|---|---|---|---|
| Randomized trials = High | Study quality | Strength of association | High = Further research is unlikely to change confidence in the estimate of the effect |
| Randomized trials = Moderate | Consistency | Moderate = Further research is likely to have an important impact on confidence in the estimate of effect, and may change the estimate |
| Randomized trials = Low | Observational study | Low = Further research is very likely to have an important impact on confidence in the estimate and may change the estimate |
| Any other evidence = Very low | Any other evidence = Low | Very low = Any estimate of effect is very uncertain |

Abbreviation: GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

A: Strong evidence of association is defined as 'significant relative risk of >2 (≥0.5)' based on consistent evidence from two or more observational studies, with no plausible confounders.

B: Very strong evidence of association is defined as 'significant relative risk of >5 (≥0.2)' based on direct evidence with no major threats to validity.

C: Sparse if there was only one study or if the results include just a few events or observations and were uninformative. Imprecise if the confidence interval spans a range greater than 1 or confidence limits are <0.5 to >2.0

Adapted by permission from Macmillan Publishers Ltd: *Kidney International*. Uhlig K, Macleod A, Craig J et al.725 Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2006; 70: 2058-2065; accessed http://www.nature.com/kj/journal/v70/n12/pdf/5001875a.pdf

Table 41 | Final grade for overall quality of evidence

| Grade | Quality of evidence | Meaning |
|---|---|---|
| A | High | We are confident that the true effect lies close to that of the estimate of the effect. |
| B | Moderate | The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. |
| C | Low | The true effect may be substantially different from the estimate of the effect. |
| D | Very low | The estimate of the effect is very uncertain, and often will be far from the truth. |

Table 42 | Balance of benefits and harm

When there was evidence to determine the balance of medical benefits and harm of an intervention to a patient, conclusions were categorized as follows:

- For statistically significant benefit/harm, report as ‘benefit [or harm] of drug X’.
- For non-statistically significant benefit/harm, report as ‘possible benefit [or harm] of drug X’.
- In instances where studies are inconsistent, report as ‘possible benefit [or harm] of drug X’.
- ‘No difference’ can only be reported if a study is not imprecise.
- ‘Insufficient evidence’ is reported if imprecision is a factor.

Outcomes of interest, taking into account explicit judgments about the relative importance of each outcome. The resulting four final categories for the quality of overall evidence were A, B, C, and D (Table 41).

Assessment of the Net Health Benefit Across All Important Clinical Outcomes

The net health benefit was determined on the basis of the anticipated balance of benefits and harms across all clinically important outcomes (Table 42). The assessment of net benefit also involved the judgment of the Work Group and the ERT.

Grading the Strength of the Recommendations

The strength of a recommendation is graded as level 1 or level 2. Table 43 shows the KDIGO nomenclature for grading the strength of a recommendation and the implications of each level for patients, clinicians, and policy makers. Recommendations can be for or against doing something. Table 44 shows that the strength of a recommendation is determined not only by the quality of the evidence, but also by other, often complex judgments regarding the size of the net medical benefit, values and preferences, and costs. Formal decision analyses including cost analysis were not conducted.

Ungraded Statements

This category was designed to allow the Work Group to issue general advice. Typically an ungraded statement meets the following criteria: it provides guidance that is based on common sense, it provides reminders of the obvious, and it is not sufficiently specific to allow for application of evidence to the issue and therefore it is not based on systematic evidence review. The GRADE system is best suited to evaluate evidence on comparative effectiveness. Some of our most important guideline topics involve diagnosis and staging within CKD, about which the Work Group chose to provide ungraded statements. These statements are indirectly supported by evidence on risk relationships and are the consensus of the Work Group. Thus, we believe that ungraded statements should not be viewed as weaker than graded recommendations.
### Table 43 | KDIGO nomenclature and description for grading recommendations

| Grade* | Patients | Clinicians | Policy |
|--------|----------|------------|--------|
| **Level 1**  
*‘We recommend’* | Most people in your situation would want the recommended course of action and only a small proportion would not. | Most patients should receive the recommended course of action. | The recommendation can be evaluated as a candidate for developing a policy or a performance measure. |
| **Level 2**  
*‘We suggest’* | The majority of people in your situation would want the recommended course of action, but many would not. | Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences. | The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined. |

Abbreviation: KDIGO, Kidney Disease: Improving Global Outcomes.
*The additional category “Not Graded” was used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence. The most common examples include recommendations regarding monitoring intervals, counseling, and referral to other clinical specialists. The ungraded recommendations are generally written as declarative statements, but are not meant to be interpreted as being stronger recommendations than Level 1 or 2 recommendations.*

### Table 44 | Determinants of strength of recommendation

| Factor | Comment |
|--------|---------|
| Balance between desirable and undesirable effects | The larger the difference between the desirable and undesirable effects, the more likely a strong recommendation is warranted. The narrower the gradient, the more likely a weak recommendation is warranted. |
| Quality of the evidence | The higher the quality of evidence, the more likely a strong recommendation is warranted. |
| Values and preferences | The more variability in values and preferences, or more uncertainty in values and preferences, the more likely a weak recommendation is warranted. |
| Costs (resource allocation) | The higher the costs of an intervention—that is, the more resources consumed—the less likely a strong recommendation is warranted. |

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### Table 45 | The Conference on Guideline Standardization checklist for reporting clinical practice guidelines

| Topic | Description | Discussed in KDIGO CKD Guideline |
|-------|-------------|---------------------------------|
| **1. Overview material** | Provide a structured abstract that includes the guideline’s release date, status (original, revised, updated), and print and electronic sources. | Abstract and Methods for Guideline Development. |
| **2. Focus** | Describe the primary disease/condition and intervention/service/technology that the guideline addresses. Indicate any alternative preventative, diagnostic, or therapeutic interventions that were considered during development. | Evaluation and management of adults and children with CKD. |
| **3. Goal** | Describe the goal that following the guideline is expected to achieve, including the rationale for development of a guideline on this topic. | This clinical practice guideline is intended to assist the practitioner caring for patients with CKD and to prevent deaths, cardiovascular disease events and progression to kidney failure while optimizing patients’ quality of life. |
| **4. User/setting** | Describe the intended users of the guideline (e.g., provider types, patients) and the settings in which the guideline is intended to be used. | Providers: Nephrologists (adult and pediatric), Dialysis providers (including nurses), Internists, and Pediatricians. Patients: Adult and pediatric individuals at risk for or with CKD. Policy Makers: Those in related health fields. |
| **5. Target population** | Describe the patient population eligible for guideline recommendations and list any exclusion criteria. | Individuals at risk for or with CKD. |
| **6. Developer** | Identify the organization(s) responsible for guideline development and the names/credentials/potential conflicts of interest of individuals involved in the guideline’s development. | Organization: KDIGO. Refer to Biographic and Disclosure Information section. |
| **7. Funding source/sponsor** | Identify the funding source/sponsor and describe its role in developing and/or reporting the guideline. Disclose potential conflict of interest. | KDIGO is supported by the following consortium of sponsors: Abbott, Amgen, Bayer Schering Pharma, Belo Foundation, Bristol-Myers Squibb, Chugai Pharmaceutical, Coca-Cola Company, Dole Food Company, Fresenius Medical Care, Genzyme, Hoffmann-LaRoche, JC Penney, Kyowa Hakko Kirin, NATCO—The Organization for Transplant Professionals, NKF-Board of Directors, Novartis, Pharmacosmos, PUMC Pharmaceutical, Robert and Jane Cizik |
Table 45 | Continued

| Topic | Description | Discussed in KDIGO CKD Guideline |
|-------|-------------|----------------------------------|
| 8. Evidence collection | Describe the methods used to search the scientific literature, including the range of databases searched, and criteria applied to filter the retrieved evidence. | Screening criteria are outlined in the methods chapter. The search was updated through June 2011 and supplemented by articles identified by Work Group members through November 2012. We also searched for pertinent existing guidelines and systematic reviews. |
| 9. Recommendation grading criteria | Describe the criteria used to rate the quality of evidence that supports the recommendations and the system for describing the strength of the recommendations. Recommendation strength communicates the importance of adherence to a recommendation and is based on both the quality of the evidence and the magnitude of anticipated benefits and harms. | Quality of individual studies was graded in a three-tiered grading system (see Table 39). Quality of evidence (Table 40) was graded following the GRADE approach. Strength of the recommendation was graded in a two-level grading system which was adapted from GRADE for KDIGO with the quality of overall evidence graded on a four-tiered system (Tables 41 and 43). The Work Group could provide general guidance in ungraded statements. |
| 10. Method for synthesizing evidence | Describe how evidence was used to create recommendations, e.g., evidence tables, meta-analysis, decision analysis. | For systematic review topics, summary tables and evidence profiles were generated. For recommendations on treatment interventions, the steps outlined by GRADE were followed. |
| 11. Prerelease review | Describe how the guideline developer reviewed and/or tested the guidelines prior to release. | The guideline had undergone internal review by the KDIGO Board of Directors in January 2012 and external review in May 2012. Public review comments were compiled and fed back to the Work Group, which considered comments in its revision of the guideline. |
| 12. Update plan | State whether or not there is a plan to update the guideline and, if applicable, expiration date for this version of the guideline. | There is no date set for updating this entire guideline. The need for updating of the guideline will depend on the publication of new evidence that would change the quality of the evidence or the estimates for the benefits and harms. Results from registered ongoing studies and other publications will be reviewed periodically to evaluate their potential to impact on the recommendations in this guideline. Specific sections may be updated separately from the entire guideline within the next 3–5 years depending on the evidence base. |
| 13. Definitions | Define unfamiliar terms and those critical to correct application of the guideline that might be subject to misinterpretation. | Acronyms and Abbreviations. |
| 14. Recommendations and rationale | State the recommended action precisely and the specific circumstances under which to perform it. Justify each recommendation by describing the linkage between the recommendation and its supporting evidence. Indicate the quality of the evidence and the recommendation strength, based on the criteria described in Topic 9. | Each guideline chapter contains recommendations for evaluation and management of CKD patients. Each recommendation builds on a supporting rationale with evidence tables if available. The strength of the recommendation and the quality of evidence are provided in parenthesis within each recommendation. |
| 15. Potential benefits and harm | Describe anticipated benefits and potential risks associated with implementation of guideline recommendations. | The benefits and harm for each comparison of interventions is provided in summary tables and summarized in evidence profiles. The estimated balance between potential benefits and harm was considered when formulating the recommendations. |
| 16. Patient preferences | Describe the role of patient preferences when a recommendation involves a substantial element of personal choice or values. | Many recommendations are ungraded which indicates a greater need to help each patient arrive at a management decision consistent with her or his values and preferences. |
| 17. Algorithm | Provide (when appropriate) a graphical description of the steps and decisions in clinical care described by the guideline. | Algorithm for proteinuria/albuminuria testing in Chapter 1. |
| 18. Implementation considerations | Describe anticipated barriers to application of the recommendations. Provide reference to any auxiliary documents for providers or patients that are intended to facilitate implementation. Suggest review criteria for measuring changes in care when the guideline is implemented. | These recommendations are global and the Work Group acknowledges the importance of local application. Review criteria were not suggested because implementation with prioritization and development of review criteria must proceed locally. Furthermore, most recommendations are discretionary, requiring substantial discussion among stakeholders before they can be considered for adoptions as review criteria. Suggestions were provided for future research. |

Abbreviations: CKD, chronic kidney disease; COGS, Conference on Guideline Standardization; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; KDIGO, Kidney Disease: Improving Global Outcomes; NKF, National Kidney Foundation.

Adapted with permission from Shiffman RN, Shekelle P, Overhage JM, et al. Standardized reporting of clinical practice guidelines: a proposal from the Conference on Guideline Standardization. Ann Intern Med 2003; 139(6): 493-498; accessed http://annals.org/data/Journals/AIM/20049/0000605-200309160-00013.pdf.
The Work Group took on the primary role of writing the recommendations and rationale statements and retained final responsibility for the content of the guideline statements and the accompanying narrative. The ERT reviewed draft recommendations and grades for consistency with the conclusions of the evidence review.

**Format for Guideline Recommendations**
Each chapter contains one or more specific recommendations. Within each recommendation, the strength of recommendation is indicated as level 1 or level 2 and the quality of the supporting evidence is shown as A, B, C or D. The recommendation statements and grades are followed by the rationale and clarification of the wording of the statement, a brief background with relevant definitions of terms, and then a chain of logic which summarizes the key points of the evidence base and the judgments supporting the recommendation. Some sections also contain research recommendations in variable degrees of detail, suggesting future research to resolve current uncertainties.

**Limitations of Approach**
Although the literature searches were intended to be comprehensive, they were not exhaustive. MEDLINE was the only database searched. Hand searches of journals were not performed, and review articles and textbook chapters were not systematically searched. However, important studies known to domain experts that were missed by the electronic literature searches were added to the retrieved articles and reviewed by the Work Group.

**Summary of the Review Process**
Several tools and checklists have been developed to assess the quality of the methodological process for systematic review and guideline development. These include the Appraisal of Guidelines for Research and Evaluation (AGREE) criteria, the Conference on Guideline Standardization (COGS) checklist, and the Institute of Medicine’s recent Standards for Systematic Reviews and Clinical Practice Guidelines We Can Trust. Table 45 and Appendix 1 demonstrate the level of concurrence to the COGS criteria and the Institute of Medicine standards, respectively.

**SUPPLEMENTARY MATERIAL**
Supplemental Table 1: Search strategy.
Appendix 1: Concurrence with Institute of Medicine standards for systematic reviews and for guidelines.
Supplementary material is linked to the online version of the paper at http://www.kdigo.org/clinical_practice_guidelines/ckd.php