Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward

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The 2012 KDIGO Guideline for CKD evaluation, classification, and management has updated the original 2002 KDOQI Guidelines, using newer data and addressing issues raised over the last decade concerning definitions and assessment. This review highlights the key aspects of the CKD guideline, and describes the rationale for specific wording and the scope of the document. A précis of key concepts in each of the five sections of the guideline is presented. The guideline document is intended for general practitioners and nephrologists, and covers CKD evaluation, classification, and management for both adults and children. Throughout the guideline, we have attempted to overtly address areas of controversy or non-consensus, international relevance, and impact on practice and public policy.

Kidney International (2013) **85,** 49–61; doi:10.1038/ki.2013.444; published online 27 November 2013

KEYWORDS: chronic kidney disease (CKD); classification; complications; guidelines; KDIGO; management; progression

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Received 12 August 2013; revised 27 September 2013; accepted 10 October 2013; published online 27 November 2013

After a decade of focused research and clinical practice in chronic kidney disease (CKD), the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Evaluation and Management of CKD[1] serves to update the original 2002 Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for CKD: Evaluation, Classification, and Stratification.[2] That decade has brought controversy, validation, and new ideas but has also highlighted CKD as global public health issue.[3] Through use of a common language and classification system, the original guidance stimulated new knowledge, resulting in the need for this new guideline.

It is beyond the scope of this document to review each statement and all the nuances and issues related to the guideline development, so the reader is encouraged to read the original document. This overview is intended to highlight the important concepts in the guideline, some old and some new. Moreover, we wish to ensure an understanding of the rationale for specific wording, and how and why specific topics were or were not addressed, and the depth to which they were addressed. Throughout the guideline, we have attempted to overtly address areas of controversy or non-consensus, international relevance, and impact on practice and public policy. The reader is encouraged to review those specific areas within each of the sections in addition to the scientific and evidence base for rationale, so as to gain further insights into the specific recommendation statement.

The guideline document[1] aims to provide state-of-the-art guidance on the evaluation, management, and treatment for both adult and pediatric populations with CKD. The intended audience is diverse and includes nephrologists, primary-care practitioners, and other specialists, as well as allied health-care professionals. We appreciate that different health-care systems exist around the world, and so attempt to provide best practice recommendations. It is recognized that there will be variation in the ability to implement some of the recommendations in different jurisdictions, but by identifying best practices and describing the evidence base, we hope to encourage advocacy for those best practices to improve the care of patients with CKD around the world. Individual country commentaries and implementation

efforts are encouraged and should highlight major areas of controversy or relevance.

The development of this guideline followed an explicit process of evidence review and appraisal. Treatment approaches are addressed in each chapter and guideline recommendations are based on systematic reviews of relevant trials. Important statements that serve as educational or practical comments are ungraded and included for the readership. Appraisal of the quality of the evidence and the strength of recommendations followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[4]

We used the GRADE system to rate the strength of evidence and the strength of recommendations. In all, there were 12 (17.1%) recommendations in this guideline for which the overall quality of evidence was graded 'A,' whereas 36 (51.4%) were graded 'B,' 17 (24.3%) were graded 'C,' and 5 (7.1%) were graded 'D.' Although there are reasons other than quality of evidence to make a grade 1 or 2 recommendation, in general, there is a correlation between the quality of overall evidence and the strength of the recommendation. Thus, there were 43 (62.3%) recommendations graded '1' and 26 (37.7%) graded '2.' There were 9 (13.0%) recommendations graded '1A,' 23 (33.3%) were '1B,' 10 (14.5%) were '1C,' and 1 (1.4%) was '1D.' There were 2 (2.9%) recommendations graded '2A,' 13 (18.8%) were '2B,' 7 (10.1%) were '2C,' and 4 (5.8%) were '2D.' There were 41 (37.3%) statements that were not graded.

Some argue that recommendations should not be made when evidence is weak. However, clinicians still need to make clinical decisions in their daily practice, and they often ask, 'What do the experts do in this setting?' We opted to give guidance, rather than remain silent. These recommendations are often rated with a low strength of recommendation and a low quality of evidence, or were not graded. It is important for the users of this guideline to be cognizant of this. In every case, these recommendations are meant to be a place for clinicians to start, not stop, their inquiries into specific management questions pertinent to the patients they see in daily practice.

It is our hope that this document will serve several useful purposes. Our primary goal is to improve patient care. We hope to accomplish this, in the short term, by helping clinicians know and better understand the evidence (or lack of evidence) that determines current practice. The balance of few grade A evidence-based recommendations (17%; 12 statements) and many ungraded recommendations can help define areas where research is needed. Although many would state that this guideline should be much shorter given the paucity of evidence, we and the Work Group, as well as the public groups consulted, were committed to constructing a comprehensive guidance document that was transparent and useful. We would submit that defining the research agenda is an often neglected, but very important, function of clinical practice guideline development. We would suggest that the implementation of the more granular cause, glomerular filtration rate (GFR), and albuminuria (CGA) system, with refined subcategories within GFR level 3 into 3a and 3b, and albuminuria categories will help practitioners with risk assessment as well as management plans. Perhaps most importantly, it will also lead to improvements in clinical trial design and execution by ensuring recruitment of the specific patient populations.

SECTION 1: DEFINITION AND CLASSIFICATION OF CKD

We retained the original definition of CKD, and added a short qualifier phrase (with implications for health) to emphasize that some abnormalities of structure or function may not have any clinical significance (e.g., small simple cysts).

We present an enhanced classification framework for CKD, which includes additional dimensions to previous simple GFRs categories, and have avoided the word 'stages' throughout the document. As it is now clear that GFR is only one important dimension in the assessment of those with kidney disease, we have added a statement that emphasizes the need to include cause and albuminuria categories in addition to the GFR categories. A classification based on these three dimensions (CGA) is recommended. The rationale for this includes the need to remind practitioners that CKD is not a diagnosis but rather a condition or abnormal state, and that causes of CKD should be sought, within reason, so that appropriate treatment of underlying cause can be initiated.

Other changes include the further refinement of GFR category 3, into 3a and 3b, based on substantial data that there are differences in outcomes and risk for those who have GFR values between 45 and 60 versus 30 and 45 ml/min per 1.73 m^2.

In this section, the reader is also educated about the importance of albuminuria as a key dimension in risk assessment. A practical table describing the relationships between protein-to-creatinine ratio to dipsticks and urine albumin-to-creatinine ratio (ACR) is provided here. Issues related to assays and measurements serve to enlighten clinicians as to the current potential problems with these measures. It is recognized that in many parts of the world, urine ACR is not available in general use, but again we offer the table for equivalences as a rough guide. For practical purposes, we give direct instructions for the laboratories as to how best to report both estimated GFR (eGFR) values and albuminuria. In particular and in accordance with contemporary international laboratory initiatives, the use of the term 'microalbuminuria' is discouraged and more quantitative description of albuminuria by category or by specific value is encouraged. This is predicated on the data suggesting increased risk at all levels of urine albumin excretion. Of note, the laboratory physicians support this change in terminology. Some have argued that there will be problems in removing 'microalbuminuria' from general usage, but by advocating an alternative in this guideline, and the rationale for it, we hope to change that practice. This does not negate the previous body of literature using the term, as it maps to levels of A2 (30–300 mg/g (3–30 mg/mmol)) in the new system.

We would envision the use of this CGA system, including cause, and levels of GFR and albuminuria, to help with individual patient descriptions in clinical practice, and also for enrollment into clinical trials. Patients could be identified as having diabetic nephrosclerosis, with eGFR of 21 ml/min per 1.73 m^2, and ACRs of 40 mg/mmol (to be very specific) or could be abbreviated using the terminology 'diabetes, G4, A3'.

Also in section 1, statements detailing the use of specific equations are developed in detail. The fundamental message is to obtain the best estimate of GFR through use of the best equation validated in the population of interest. The utility and caveats of creatinine- and cystatin-C-based estimating equations are also discussed. We provide guidance into when to directly measure GFR, when there is an overwhelming importance to be precise with respect to clinical decisions (e.g., nephrectomy or use of highly toxic drugs). We do not advocate regular direct measurement in usual clinical practice, but do remind the readers that all equations provide only estimates of true GFR.

Overall, we advocate the use of the 'heat map' (see graphical representation at the end of this review, Chapter 1, section 1.3.3) as generated by the dimensions of GFR and albuminuria to guide clinicians in risk assessment, and use that grid throughout the guideline to highlight risks and actions. We envision that implementation tools based on the heat map will be developed.

SECTION 2: PROGRESSION OF CKD

This section elaborates on the prognosis of CKD and the identification of its progression, and offers suggestions as to how to define rapid progression. In addition, we highlight for practitioners that some minor variations in kidney function may occur over time, without necessarily heralding irreversible progression. The definition of rapid progression, defined as a change in GFR over a set time period, is intended to help practitioners to identify those at higher risk, and those in whom increased vigilance is warranted. Additional studies are needed to help further refine these concepts, and ideally information systems in laboratories will help to simplify the more difficult calculations required for some of the definitions.

This is the first attempt in a guideline to address the difficult issue of 'true progression' and will need further validation in clinical practice and studies. This section was included because of requests from practitioners and those involved in clinical trial design to clarify the concept using rigorous data methodology. The question has generated a series of novel papers examining this issue in different populations (general, high risk, and CKD), some of which are due to be published after the guideline.

SECTION 3: MANAGEMENT OF PROGRESSION OF CKD AND COMPLICATIONS OF CKD

In this section, we discuss the management of progression and complications of CKD, using the best evidence to date, and leveraging the statements from other recent KDIGO guidelines (blood pressure, acute kidney injury, glomerulonephritis, and anemia).[5–8] This section is comprehensive in itemizing the different treatments for progression and the specific complications of CKD, which may contribute to progression. However, we limited the discussion and statements to those relevant to clinical practice and with some evidence base. Where there remains little data, we clearly state this. Many would have liked this section to be more comprehensive and directive; however, given the scope of the guideline, and the existence of other more detailed documents describing the management issues, we sought to highlight the key issues so that practitioners would gain a sense of the breadth and depth of complications related to CKD. As extensive research remains to be conducted to optimize treatment of complications of CKD, and of progression, we would encourage well-designed trials to be conducted. After these data are available, we would anticipate the need for updated guidance on many of these issues.

SECTION 4: OTHER COMPLICATIONS OF CKD: CARDIOVASCULAR DISEASE, MEDICATION DOSAGE, PATIENT SAFETY, INFECTIONS, HOSPITALIZATIONS, AND CAVEATS FOR INVESTIGATING COMPLICATIONS OF CKD

This section is included as a reminder that it is important to appreciate the complexity of evaluating and treating patients with CKD and other conditions. We identified issues of patient safety and areas of evaluation of CKD patients for common conditions (heart disease and diabetes), and used this section to remind the practitioner to identify important events like infection, acute kidney injury, and imaging studies as modifiers of risk (of progression and of death), and as related to patient safety. We wanted to provide the reader with comprehensive guidance for common clinical scenarios. Also we highlight potential misunderstandings regarding common tests. For example, prognosis and treatment algorithms for elevations of B-type natriuretic peptide and troponin have not been evaluated and validated in CKD populations. We emphasize that those with CKD and evidence of cardiac disease be treated in accordance with best practices for those without CKD (i.e., appropriate diagnostic studies or/and medications should be offered). The value of hemoglobin A_{1c} in patients with diabetes with more advanced CKD remains problematic, a fact not necessarily appreciated by many. We have listed in a table the commonly used drugs in CKD, and those needing dose reduction or cessation.

We hope that the tables and issues identified in this section will be useful tools for practitioners. This section highlights the complexity of care associated with CKD in terms of diagnosis, monitoring, and treatment options.

SECTION 5: REFERRAL TO SPECIALISTS AND MODELS OF CARE

In this section of the guideline, we expand on the continuum of CKD care: timing of specialist referral, ongoing management of people with progressive CKD, timing the initiation of

dialysis, and finally the implementation of a treatment program that includes comprehensive conservative management, including end-of-life care. We have recognized the paucity of data for many of these recommendations, and so many remain ungraded. As practical tips or key points, they serve to remind practitioners at all levels about the multiple dimensions required in the care of patients with CKD.

We highlight the importance of multidisciplinary care teams to enhance care and outcomes of this complex condition. We appreciate that referral to specialists may vary by country or region, but underscore that the rationale for that referral should be to access specialist knowledge or services so that care is optimized. We stress that the continuum of care for patients living with CKD evolves over time and incorporates both patient and care team decision making at multiple points ('no decision about me without me'). Decisions about dialysis timing should reflect a composite of clinical symptoms and laboratory parameters. All patients with CKD should be offered conservative treatment options with supportive services. It is clear that many of these specific suggestions will be individualized to specific regional contexts, but the principles on which they are founded are universal.

SUMMARY

Kidney disease is defined as an abnormality of kidney structure or function with implications for the health of an individual, which can occur abruptly, and may either resolve or become chronic. CKD is a general term for heterogeneous disorders affecting kidney structure and function with variable clinical presentation, which is present for >3 months. The concept of CKD evolved after the recognition of the contribution of disordered kidney structure and function on the health of individuals across a wide range of severity. The utility of the concept is that recognition of CKD will have implications for individuals and their care.

This guideline serves to remind us, as a nephrology and medical community, that we have learned much since 2002. A decade of systematic evaluation and research using common definitions, standardization of assays, and development of robust equations has allowed us to move forward. This KDIGO guideline addresses important areas of controversy, is applicable worldwide, and attempts to highlight areas of misconceptions so that we can move forward together as a medical community.

The KDIGO 2012 CKD guideline re-emphasizes the value of the classification system, the need for robust definitions of progression of CKD, the treatment of complications of CKD, and the need for an integrated approach to care of this chronic condition. Most importantly, it highlights what remains as known and unknown areas of care, and serves to inform the research agenda for the next decade. We have progressed in our understanding and knowledge base, but we remain in need of robust large trials to inform clinical care.

The goal of this guideline is to facilitate appropriate guidance as to the management and care of people with CKD. We present a framework for evaluation and assessment that should foster an extended collaborative research agenda over the next decade and inform guidelines in the future. The challenge for the renal community will be to ensure that important areas of controversy or confusion have been resolved with well-conducted clinical trials. In so doing, the next update of the KDIGO CKD 2012 guideline will be based on a growing foundation of evidence.

CHAPTER 1: DEFINITION AND CLASSIFICATION OF CKD

1.1: Definition of CKD

1.1.1: CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. (Not graded)

Criteria for CKD (either of the following present for >3 months)

Markers of kidney damage (one or more)	Albuminuria (AER ⩾30 mg/24 h; ACR ⩾30 mg/g (⩾3 mg/mmol)) Urine sediment abnormalities Electrolyte and other abnormalities due to tubular disorders Abnormalities detected by histology Structural abnormalities detected by imaging History of kidney transplantation
Decreased GFR	GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5)

Abbreviations: ACR, albumin-to-creatinine ratio; AER, albumin excretion rate; CKD, chronic kidney disease; GFR, glomerular filtration rate.

1.2: Staging of CKD

1.2.1: We recommend that CKD is classified based on cause, GFR category, and albuminuria category (CGA). (1B)

1.2.2: Assign cause of CKD based on presence or absence of systemic disease and the location within the kidney of observed or presumed pathologic-anatomic findings. (Not graded)

1.2.3: Assign GFR categories as follows (not graded):
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

GFR categories in CKD

GFR category	GFR (ml/min per 1.73 m^2)	Terms
G1	⩾90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level.
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

1.2.4: Assign albuminuria* categories as follows (not graded):

*Note that where albuminuria measurement is not available, urine reagent strip results can be substituted.

Albuminuria categories in CKD

Category	AER (mg/24 h)	ACR (approximate equivalent) (mg/mmol)	(mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30–300	3–30	30–300	Moderately increased*
A3	>300	>30	>300	Severely increased**

Abbreviations: ACR, albumin-to-creatinine ratio; AER, albumin excretion rate; CKD, chronic kidney disease.
*Relative to young adult level.
**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 h (ACR >2220 mg/g; >220 mg/mmol)).

1.3: Predicting prognosis of CKD

1.3.1: In predicting risk for outcome of CKD, identify the following variables: (1) cause of CKD; (2) GFR category; (3) albuminuria category; (4) other risk factors and comorbid conditions. (Not graded)

1.3.2: In people with CKD, use estimated risk of concurrent complications and future outcomes to guide decisions for testing and treatment for CKD complications. (Not graded)

1.3.3: In populations with CKD, group GFR and albuminuria categories with similar relative risk for CKD outcomes into risk categories. (Not graded) (see grid below)

1.4: Evaluation of CKD

1.4.1: Evaluation of chronicity

1.4.1.1: In people with GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5) or markers of kidney damage, review past history and previous measurements to determine duration of kidney disease. (Not graded)

- If duration is >3 months, CKD is confirmed. Follow recommendations for CKD.
- If duration is not >3 months or unclear, CKD is not confirmed. Patients may have CKD or acute kidney diseases (including acute kidney injury (AKI)) or both and tests should be repeated accordingly.

1.4.2: Evaluation of cause

1.4.2.1: Evaluate the clinical context, including personal and family history, social and environmental factors, medications, physical examination, laboratory measures, imaging, and pathologic

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min per 1.73 m^2) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red, very high risk.

diagnosis to determine the causes of kidney disease. (Not graded)

1.4.3: Evaluation of GFR

1.4.3.1: We recommend using serum creatinine and a GFR estimating equation for initial assessment. (1A)

1.4.3.2: We suggest using additional tests (such as cystatin C or a clearance measurement) for confirmatory testing in specific circumstances when eGFR based on serum creatinine is less accurate. (2B)

1.4.3.3: We recommend that clinicians (1B):

- Use a GFR estimating equation to derive GFR from serum creatinine ($eGFR_{creat}$) rather than relying on the serum creatinine concentration alone.
- Understand clinical settings in which $eGFR_{creat}$ is less accurate.

1.4.3.4: We recommend that clinical laboratories should (1B):

- Measure serum creatinine using a specific assay with calibration traceable to the international standard reference materials and minimal bias compared with isotope-dilution mass spectrometry reference methodology.
- Report $eGFR_{creat}$ in addition to the serum creatinine concentration in adults and specify the equation used whenever reporting $eGFR_{creat}$.
- Report $eGFR_{creat}$ in adults using the 2009 CKD-Epidemiology Collaboration (CKD-EPI) creatinine equation. An alternative creatinine-based GFR estimating equation is acceptable if it has been shown to improve accuracy of GFR estimates compared to the 2009 CKD-EPI creatinine equation.

When reporting serum creatinine:

- We recommend that serum creatinine concentration be reported and rounded to the nearest whole number when expressed as standard international units (μmol/l) and rounded to the nearest 100th of a whole number when expressed as conventional units (mg/dl).

When reporting $eGFR_{creat}$:

- We recommend that $eGFR_{creat}$ should be reported and rounded to the nearest whole number and relative to a body surface area of 1.73 m^2 in adults using the units ml/min per 1.73 m^2.
- We recommend $eGFR_{creat}$ levels <60 ml/min per 1.73 m^2 should be reported as 'decreased.'

1.4.3.5: We suggest measuring cystatin C in adults with $eGFR_{creat}$ 45–59 ml/min per 1.73 m^2 who do not have markers of kidney damage if confirmation of CKD is required. (2C)

- If $eGFR_{cys}/eGFR_{creat\text{-}cys}$ is also <60 ml/min per 1.73 m^2, the diagnosis of CKD is confirmed.
- If $eGFR_{cys}/eGFR_{creat\text{-}cys}$ is $\geqslant 60$ ml/min per 1.73 m^2, the diagnosis of CKD is not confirmed.

1.4.3.6: If cystatin C is measured, we suggest that health professionals (2C):

- Use a GFR estimating equation to derive GFR from serum cystatin C rather than relying on the serum cystatin C concentration alone.
- Understand clinical settings in which $eGFR_{cys}$ and $eGFR_{creat\text{-}cys}$ are less accurate.

1.4.3.7: We recommend that clinical laboratories that measure cystatin C should (1B):

- Measure serum cystatin C using an assay with calibration traceable to the international standard reference material.
- Report eGFR from serum cystatin C in addition to the serum cystatin C concentration in adults and specify the equation used whenever reporting $eGFR_{cys}$ and $eGFR_{creat\text{-}cys}$.
- Report $eGFR_{cys}$ and $eGFR_{creat\text{-}cys}$ in adults using the 2012 CKD-EPI cystatin C and 2012 CKD-EPI creatinine-cystatin C equations, respectively, or alternative cystatin C-based GFR estimating equations if they have been shown to improve accuracy of GFR estimates compared to the 2012 CKD-EPI cystatin C and 2012 CKD-EPI creatinine-cystatin C equations.

When reporting serum cystatin C:

- We recommend reporting serum cystatin C concentration rounded to the nearest 100th of a whole number when expressed as conventional units (mg/l).

When reporting $eGFR_{cys}$ and $eGFR_{creat\text{-}cys}$:

- We recommend that $eGFR_{cys}$ and $eGFR_{creat\text{-}cys}$ be reported and rounded to the nearest whole number and relative to a body surface area of 1.73 m^2 in adults using the units ml/min per 1.73 m^2.
- We recommend $eGFR_{cys}$ and $eGFR_{creat\text{-}cys}$ levels <60 ml/min per 1.73 m^2 should be reported as 'decreased.'

1.4.3.8: We suggest measuring GFR using an exogenous filtration marker under circumstances where more accurate ascertainment of GFR will impact on treatment decisions. (2B)

1.4.4: Evaluation of albuminuria

1.4.4.1: We suggest using the following measurements for initial testing of proteinuria (in descending order preference, in all cases an early morning urine sample is preferred) (2B):

(1) Urine ACR;
(2) Urine protein-to-creatinine ratio;
(3) Reagent strip urinalysis for total protein with automated reading;

(4) Reagent strip urinalysis for total protein with manual reading.

1.4.4.2: We recommend that clinical laboratories report ACR and protein-to-creatinine ratio in untimed urine samples in addition to albumin concentration or proteinuria concentrations rather than the concentrations alone. (1B)

1.4.4.2.1: The term microalbuminuria should no longer be used by laboratories. (Not graded)

1.4.4.3: Clinicians need to understand settings that may affect interpretation of measurements of albuminuria and order confirmatory tests as indicated (not graded):

- Confirm reagent strip positive albuminuria and proteinuria by quantitative laboratory measurement and express as a ratio to creatinine wherever possible.
- Confirm ACR $\geqslant$30 mg/g ($\geqslant$3 mg/mmol) on a random untimed urine with a subsequent early morning urine sample.
- If a more accurate estimate of albuminuria or total proteinuria is required, measure albumin excretion rate or total protein excretion rate in a timed urine sample.

1.4.4.4: If significant non-albumin proteinuria is suspected, use assays for specific urine proteins (e.g., α_1-microglobulin, monoclonal heavy or light chains, (known in some countries as 'Bence Jones' proteins)). (Not graded)

CHAPTER 2: DEFINITION, IDENTIFICATION, AND PREDICTION OF CKD PROGRESSION

2.1: Definition and identification of CKD progression

2.1.1: Assess GFR and albuminuria at least annually in people with CKD. Assess GFR and albuminuria more often for individuals at higher risk of progression, and/or where measurement will impact therapeutic decisions (see grid on next page). (Not graded)

2.1.2: Recognize that small fluctuations in GFR are common and are not necessarily indicative of progression. (Not graded)

2.1.3: Define CKD progression based on one or more of the following (not graded):

- Decline in GFR category ($\geqslant$90 (G1), 60–89 (G2), 45–59 (G3a), 30–44 (G3b), 15–29 (G4), $<$15 (G5) ml/min per 1.73 m^2). A certain drop in eGFR is defined as a drop in GFR category accompanied by a 25% or greater drop in eGFR from baseline.
- Rapid progression is defined as a sustained decline in eGFR of $>$5 ml/min per 1.73 m^2/year.
- The confidence in assessing progression is increased with increasing number of serum creatinine measurements and duration of follow-up.

2.1.4: In people with CKD progression, as defined in Recommendation 2.1.3, review current management, examine for reversible causes of progression, and consider referral to a specialist. (Not graded)

2.2: Predictors of progression

2.2.1: Identify factors associated with CKD progression to inform prognosis. These include cause of CKD, level of GFR, level of albuminuria, age, sex, race/ethnicity, elevated blood pressure (BP), hyperglycemia, dyslipidemia, smoking, obesity, history of cardiovascular disease, ongoing exposure to nephrotoxic agents, and others. (Not graded)

CHAPTER 3: MANAGEMENT OF PROGRESSION AND COMPLICATIONS OF CKD

3.1: Prevention of CKD progression

BP and renin–angiotensin–aldosterone system interruption.

3.1.1: Individualize BP targets and agents according to age, coexistent cardiovascular disease and other comorbidities, risk of progression of CKD, presence or absence of retinopathy (in CKD patients with diabetes), and tolerance of treatment as described in the KDIGO 2012 Blood Pressure Guideline. (Not graded)

3.1.2: Inquire about postural dizziness and check for postural hypotension regularly when treating CKD patients with BP-lowering drugs. (Not graded)

3.1.3: Tailor BP treatment regimens in elderly patients with CKD by carefully considering age, comorbidities, and other therapies, with gradual escalation of treatment and close attention to adverse events related to BP treatment, including electrolyte disorders, acute deterioration in kidney function, orthostatic hypotension, and drug side effects. (Not graded)

3.1.4: We recommend that in both diabetic and non-diabetic adults with CKD and urine albumin excretion $<$30 mg/24 h (or equivalent*) whose office BP is consistently $>$140 mm Hg systolic or $>$90 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently $\leqslant$140 mm Hg systolic and $\leqslant$90 mm Hg diastolic. (1B)

3.1.5: We suggest that in both diabetic and non-diabetic adults with CKD and with urine albumin excretion of $\geqslant$30 mg/24 h (or equivalent*) whose office BP is consistently $>$130 mm Hg systolic or $>$80 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently $\leqslant$130 mm Hg systolic and $\leqslant$80 mm Hg diastolic. (2D)

3.1.6: We suggest that an angiotensin receptor blocker (ARB) or angiotensin-converting enzyme inhibitor (ACE-I) be used in diabetic adults with CKD and urine albumin excretion 30–300 mg/24 h (or equivalent*). (2D)

3.1.7: We recommend that an ARB or ACE-I be used in both diabetic and non-diabetic adults with CKD and urine albumin excretion $>$300 mg/24 h (or equivalent*). (1B)

3.1.8: There is insufficient evidence to recommend combining an ACE-I with ARBs to prevent progression of CKD. (Not graded)

Guide to frequency of monitoring (number of times per year) by GFR and albuminuria category

GFR categories (ml/min per 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	⩾90	1 if CKD	1	2
	G2	Mildly decreased	60–89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45–59	1	2	3
	G3b	Moderately to severely decreased	30–44	2	3	3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

GFR and albuminuria grid to reflect the risk of progression by intensity of coloring (green, yellow, orange, red, deep red). The numbers in the boxes are a guide to the frequency of monitoring (number of times per year).

3.1.9: We recommend that in children with CKD, BP-lowering treatment is started when BP is consistently above the 90th percentile for age, sex, and height. (1C)

3.1.10: We suggest that in children with CKD (particularly those with proteinuria), BP is lowered to consistently achieve systolic and diastolic readings less than or equal to the 50th percentile for age, sex, and height, unless achieving these targets is limited by signs or symptoms of hypotension. (2D)

3.1.11: We suggest that an ARB or ACE-I be used in children with CKD in whom treatment with BP-lowering drugs is indicated, irrespective of the level of proteinuria. (2D)

*Approximate equivalents for albumin excretion rate per 24 h—expressed as protein excretion rate per 24 h, ACR, protein-to-creatinine ratio, and protein reagent strip results—are given in Guideline Table 7.

CKD and risk of AKI.

3.1.12: We recommend that all people with CKD are considered to be at increased risk of AKI. (1A)

3.1.12.1: In people with CKD, the recommendations detailed in the KDIGO AKI Guideline should be followed for management of those at risk of AKI during intercurrent illness, or when undergoing investigation and procedures that are likely to increase the risk of AKI. (Not graded)

Protein intake.

3.1.13: We suggest lowering protein intake to 0.8 g/kg/day in adults with diabetes (2C) or without diabetes (2B) and GFR <30 ml/min per 1.73 m^2 (GFR categories G4–G5), with appropriate education.

3.1.14: We suggest avoiding high protein intake (>1.3 g/kg/day) in adults with CKD at risk of progression. (2C)

Glycemic control.

3.1.15: We recommend a target hemoglobin A_{1c} of ~7.0% (53 mmol/mol) to prevent or delay progression of the microvascular complications of diabetes, including diabetic kidney disease. (1A)

3.1.16: We recommend not treating to an hemoglobin A_{1c} target of <7.0% (<53 mmol/mol) in patients at risk of hypoglycemia. (1B)

3.1.17: We suggest that target hemoglobin A_{1c} be extended above 7.0% (53 mmol/mol) in individuals with comorbidities or limited life expectancy and risk of hypoglycemia. (2C)

3.1.18: In people with CKD and diabetes, glycemic control should be part of a multifactorial intervention strategy addressing BP control and cardiovascular risk, promoting the use of angiotensin-converting enzyme inhibition or angiotensin receptor

blockade, statins, and antiplatelet therapy where clinically indicated. (Not graded)

Salt intake.

3.1.19: We recommend lowering salt intake to <90 mmol (<2 g) per day of sodium (corresponding to 5 g of sodium chloride) in adults, unless contraindicated (see rationale). (1C)

3.1.19.1: We recommend restriction of sodium intake for children with CKD who have hypertension (systolic and/or diastolic BP >95th percentile) or prehypertension (systolic and/or diastolic BP >90th percentile and <95th percentile), following the age-based Recommended Daily Intake. (1C)

3.1.19.2: We recommend supplemental free water and sodium supplements for children with CKD and polyuria to avoid chronic intravascular depletion and to promote optimal growth. (1C)

Hyperuricemia.

3.1.20: There is insufficient evidence to support or refute the use of agents to lower serum uric acid concentrations in people with CKD and either symptomatic or asymptomatic hyperuricemia in order to delay progression of CKD. (Not graded)

Lifestyle.

3.1.21: We recommend that people with CKD be encouraged to undertake physical activity compatible with cardiovascular health and tolerance (aiming for at least 30 min five times per week), achieve a healthy weight (body mass index 20–25 kg/m^2, according to country-specific demographics), and stop smoking. (1D)

Additional dietary advice.

3.1.22: We recommend that individuals with CKD receive expert dietary advice and information in the context of an education program, tailored to severity of CKD and the need to intervene on salt, phosphate, potassium, and protein intake where indicated. (1B)

3.2: Complications associated with loss of kidney function

Definition and identification of anemia in CKD.

3.2.1: Diagnose anemia in adults and children >15 years with CKD when the Hb concentration is <13.0 g/dl (<130 g/l) in males and <12.0 g/dl (<120 g/l) in females. (Not graded)

3.2.2: Diagnose anemia in children with CKD if Hb concentration is <11.0 g/dl (<110 g/l) in children 0.5–5 years, <11.5 g/dl (115 g/l) in children 5–12 years, and <12.0 g/dl (120 g/l) in children 12–15 years. (Not graded)

Evaluation of anemia in people with CKD.

3.2.3: To identify anemia in people with CKD measure Hb concentration (Not graded):

- When clinically indicated in people with GFR ⩾60 ml/min per 1.73 m^2 (GFR categories G1–G2);
- At least annually in people with GFR 30–59 ml/min per 1.73 m^2 (GFR categories G3a–G3b);
- At least twice per year in people with GFR <30 ml/min per 1.73 m^2 (GFR categories G4–G5).

3.3: CKD metabolic bone disease including laboratory abnormalities

3.3.1: We recommend measuring serum levels of calcium, phosphate, parathyroid hormone, and alkaline phosphatase activity at least once in adults with GFR <45 ml/min per 1.73 m^2 (GFR categories G3b–G5) in order to determine baseline values and inform prediction equations if used. (1C)

3.3.2: We suggest not to perform bone mineral density testing routinely in those with eGFR <45 ml/min per 1.73 m^2 (GFR categories G3b–G5), as information may be misleading or unhelpful. (2B)

3.3.3: In people with GFR <45 ml/min per 1.73 m^2 (GFR categories G3b–G5), we suggest maintaining serum phosphate concentrations in the normal range according to local laboratory reference values. (2C)

3.3.4: In people with GFR <45 ml/min per 1.73 m^2 (GFR categories G3b–G5), the optimal parathyroid hormone level is not known. We suggest that people with levels of intact parathyroid hormone above the upper normal limit of the assay are first evaluated for hyperphosphatemia, hypocalcemia, and vitamin D deficiency. (2C)

Vitamin D supplementation and bisphosphonates in people with CKD.

3.3.5: We suggest not to routinely prescribe vitamin D supplements or vitamin D analogs, in the absence of suspected or documented deficiency, to suppress elevated parathyroid hormone concentrations in people with CKD not on dialysis. (2B)

3.3.6: We suggest not to prescribe bisphosphonate treatment in people with GFR <30 ml/min per 1.73 m^2 (GFR categories G4–G5) without a strong clinical rationale. (2B)

3.4: Acidosis

3.4.1: We suggest that in people with CKD and serum bicarbonate concentrations <22 mmol/l treatment with oral bicarbonate supplementation be given to maintain serum bicarbonate within the normal range, unless contraindicated. (2B)

CHAPTER 4: OTHER COMPLICATIONS OF CKD: CARDIOVASCULAR DISEASE, MEDICATION DOSAGE, PATIENT SAFETY, INFECTIONS, HOSPITALIZATIONS, AND CAVEATS FOR INVESTIGATING COMPLICATIONS OF CKD

4.1: CKD and cardiovascular disease

4.1.1: We recommend that all people with CKD be considered at increased risk for cardiovascular disease. (1A)

4.1.2: We recommend that the level of care for ischemic heart disease offered to people with CKD should not be prejudiced by their CKD. (1A)

4.1.3: We suggest that adults with CKD at risk for atherosclerotic events be offered treatment with antiplatelet agents unless there is an increased bleeding risk that needs to be balanced against the possible cardiovascular benefits. (2B)

4.1.4: We suggest that the level of care for heart failure offered to people with CKD should be the same as is offered to those without CKD. (2A)

4.1.5: In people with CKD and heart failure, any escalation in therapy and/or clinical deterioration should prompt monitoring of eGFR and serum potassium concentration. (Not graded)

4.2: Caveats when interpreting tests for cardiovascular disease in people with CKD

B-type natriuretic peptide/N-terminal-proBNP (NT-proBNP).

4.2.1: In people with GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5), we recommend that serum concentrations of B-type natriuretic peptide/NT-proBNP be interpreted with caution and in relation to GFR with respect to diagnosis of heart failure and assessment of volume status. (1B)

Troponins.

4.2.2: In people with GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5), we recommend that serum concentrations of troponin be interpreted with caution with respect to diagnosis of acute coronary syndrome. (1B)

Non-invasive testing.

4.2.3: We recommend that people with CKD presenting with chest pain should be investigated for underlying cardiac disease and other disorders according to the same local practice for people without CKD (and subsequent treatment should be initiated similarly). (1B)

4.2.4: We suggest that clinicians are familiar with the limitations of non-invasive cardiac tests (e.g., exercise electrocardiography, nuclear imaging, echocardiography, etc) in adults with CKD and interpret the results accordingly. (2B)

4.3: CKD and peripheral arterial disease

4.3.1: We recommend that adults with CKD be regularly examined for signs of peripheral arterial disease and be considered for usual approaches to therapy. (1B)

4.3.2: We suggest that adults with CKD and diabetes are offered regular podiatric assessment. (2A)

4.4: Medication management and patient safety in CKD

4.4.1: We recommend that prescribers should take GFR into account when drug dosing. (1A)

4.4.2: Where precision is required for dosing (due to narrow therapeutic or toxic range) and/or estimates may be unreliable (e.g., due to low muscle mass), we recommend methods based upon cystatin C or direct measurement of GFR. (1C)

4.4.3: We recommend temporary discontinuation of potentially nephrotoxic and renally excreted drugs in people with a GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5) who have serious intercurrent illness that increases the risk of AKI. These agents include, but are not limited to: renin–angiotensin–aldosterone system blockers (including ACE-Is, ARBs, aldosterone inhibitors, direct renin inhibitors), diuretics, nonsteriodal anti-inflammatory drug, metformin, lithium, and digoxin. (1C)

4.4.4: We recommend that adults with CKD seek medical or pharmacist advice before using over-the-counter medicines or nutritional protein supplements. (1B)

4.4.5: We recommend not using herbal remedies in people with CKD. (1B)

4.4.6: We recommend that metformin be continued in people with GFR $\geqslant 45$ ml/min per 1.73 m^2 (GFR categories G1–G3a); its use should be reviewed in those with GFR 30–44 ml/min per 1.73 m^2 (GFR category G3b); and it should be discontinued in people with GFR <30 ml/min per 1.73 m^2 (GFR categories G4–G5). (1C)

4.4.7: We recommend that all people taking potentially nephrotoxic agents such as lithium and calcineurin inhibitors should have their GFR, electrolytes, and drug levels regularly monitored. (1A)

4.4.8: People with CKD should not be denied therapies for other conditions such as cancer but there should be appropriate dose adjustment of cytotoxic drugs according to knowledge of GFR. (Not graded)

4.5: Imaging studies

4.5.1: Balance the risk of acute impairment in kidney function due to contrast agent use against the diagnostic value and therapeutic implications of the investigation. (Not graded)

Radiocontrast.

4.5.2: We recommend that all people with GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5) undergoing elective investigation involving the intravascular administration of iodinated radiocontrast media should be managed according to the KDIGO Clinical Practice Guideline for AKI including:

- Avoidance of high osmolar agents (1B);
- Use of lowest possible radiocontrast dose (not graded);
- Withdrawal of potentially nephrotoxic agents before and after the procedure (1C);
- Adequate hydration with saline before, during, and after the procedure (1A);
- Measurement of GFR 48–96 h after the procedure (1C).

Gadolinium-based contrast media.

4.5.3: We recommend not using gadolinium-containing contrast media in people with GFR <15 ml/min per

1.73 m^2 (GFR category G5) unless there is no alternative appropriate test. (1B)

4.5.4: We suggest that people with a GFR <30 ml/min per 1.73 m^2 (GFR categories G4–G5) who require gadolinium-containing contrast media are preferentially offered a macrocyclic chelate preparation. (2B)

Bowel preparation.

4.5.5: We recommend not to use oral phosphate-containing bowel preparations in people with a GFR <60 ml/min per 1.73 m^2 (GFR categories G3a–G5) or in those known to be at risk of phosphate nephropathy. (1A)

4.6: CKD and risks for infections, AKI, hospitalizations, and mortality

CKD and risk of infections.

4.6.1: We recommend that all adults with CKD are offered annual vaccination with influenza vaccine, unless contraindicated. (1B)

4.6.2: We recommend that all adults with eGFR <30 ml/min per 1.73 m^2 (GFR categories G4–G5) and those at high risk of pneumococcal infection (e.g., nephrotic syndrome, diabetes, or those receiving immunosuppression) receive vaccination with polyvalent pneumococcal vaccine unless contraindicated. (1B)

4.6.3: We recommend that all adults with CKD who have received pneumococcal vaccination are offered revaccination within 5 years. (1B)

4.6.4: We recommend that all adults who are at high risk of progression of CKD and have GFR <30 ml/min per 1.73 m^2 (GFR categories G4–G5) be immunized against hepatitis B and the response confirmed by appropriate serological testing. (1B)

4.6.5: Consideration of live vaccine should include an appreciation of the patient's immune status and should be in line with recommendations from official or governmental bodies. (Not graded)

4.6.6: Pediatric immunization schedules should be followed according to official international and regional recommendations for children with CKD. (Not graded)

CKD and risk of AKI.

4.6.7: We recommend that all people with CKD are considered to be at increased risk of AKI. (1A)

4.6.7.1: In people with CKD, the recommendations detailed in the KDIGO AKI Guideline should be followed for management of those at risk of AKI during intercurrent illness, or when undergoing investigation and procedures that are likely to increase the risk of AKI. (Not graded)

CKD and risk of hospitalization and mortality.

4.6.8: CKD disease management programs should be developed in order to optimize the community management of people with CKD and reduce the risk of hospital admission. (Not graded)

4.6.9: Interventions to reduce hospitalization and mortality for people with CKD should pay close attention to the management of associated comorbid conditions and cardiovascular disease in particular. (Not graded)

CHAPTER 5: REFERRAL TO SPECIALISTS AND MODELS OF CARE

5.1: Referral to specialist services

5.1.1: We recommend referral to specialist kidney care services for people with CKD in the following circumstances (1B):

- AKI or abrupt sustained fall in GFR;
- GFR <30 ml/min per 1.73 m^2 (GFR categories G4–G5)*;
- A consistent finding of significant albuminuria (ACR $\geqslant 300$ mg/g ($\geqslant 30$ mg/mmol) or albumin excretion rate $\geqslant 300$ mg/24 h, approximately equivalent to protein-to-creatinine ratio $\geqslant 500$ mg/g ($\geqslant 50$ mg/mmol) or PER $\geqslant 500$ mg/24 h);
- Progression of CKD (see Recommendation 2.1.3 for definition);
- Urinary red cell casts, RBC >20 per high-power field sustained and not readily explained;
- CKD and hypertension refractory to treatment with 4 or more antihypertensive agents;
- Persistent abnormalities of serum potassium;
- Recurrent or extensive nephrolithiasis;
- Hereditary kidney disease.

*If this is a stable isolated finding, formal referral (i.e., formal consultation and ongoing care management) may not be necessary and advice from specialist services may be all that is required to facilitate best care for the patients. This will be health-care system dependent.

5.1.2: We recommend timely referral for planning renal replacement therapy (RRT) in people with progressive CKD in whom the risk of kidney failure within 1 year is 10–20% or higher†, as determined by validated risk prediction tools. (1B)

†The aim is to avoid late referral, defined here as referral to specialist services <1 year before start of RRT.

5.2: Care of the patient with progressive CKD

5.2.1: We suggest that people with progressive CKD should be managed in a multidisciplinary care setting. (2B)

5.2.2: The multidisciplinary team should include or have access to dietary counseling, education, and counseling about different RRT modalities, transplant options, vascular access surgery, and ethical, psychological, and social care. (Not graded)

GFR categories (ml/min per 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	⩾90		Monitor	Refer*
	G2	Mildly decreased	60–89		Monitor	Refer*
	G3a	Mildly to moderately decreased	45–59	Monitor	Monitor	Refer
	G3b	Moderately to severely decreased	30–44	Monitor	Monitor	Refer
	G4	Severely decreased	15–29	Refer*	Refer*	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

Referral decision making by GFR and albuminuria. *Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referring.

5.3: Timing the initiation of RRT

5.3.1: We suggest that dialysis be initiated when one or more of the following are present: symptoms or signs attributable to kidney failure (serositis, acid-base or electrolyte abnormalities, pruritus); inability to control volume status or BP; a progressive deterioration in nutritional status refractory to dietary intervention; or cognitive impairment. This often but not invariably occurs in the GFR range between 5 and 10 ml/min per 1.73 m^2. (2B)

5.3.2: Living donor pre-emptive renal transplantation in adults should be considered when the GFR is <20 ml/min per 1.73 m^2, and there is evidence of progressive and irreversible CKD over the preceding 6–12 months. (Not graded)

5.4: Structure and process of comprehensive conservative management

5.4.1: Conservative management should be an option in people who choose not to pursue RRT and this should be supported by a comprehensive management program. (Not graded)

5.4.2: All CKD programs and care providers should be able to deliver advance care planning for people with a recognized need for end-of-life care, including those people undergoing conservative kidney care. (Not graded)

5.4.3: Coordinated end-of-life care should be available to people and families through either primary care or specialist care as local circumstances dictate. (Not graded)

5.4.4: The comprehensive conservative management program should include protocols for symptom and pain management, psychological care, spiritual care, and culturally sensitive care for the dying patient and their family (whether at home, in a hospice, or a hospital setting), followed by the provision of culturally appropriate bereavement support. (Not graded)

DISCLOSURE

AL has received research funding from Abbott, Amgen, Canadian Institutes of Health Research, Genzyme, Kidney Foundation of Canada, Merck and Ortho. AL also has consulting and advising roles for Merck and Otsuka. PES declared no competing interests.

ACKNOWLEDGMENTS

The authors thank the following Work Group members for their valuable contributions to this guideline: Rudy W. Bilous, Josef Coresh, Angel L.M. de Francisco, Paul E. de Jong, Kathryn E. Griffith, Brenda R. Hemmelgarn, Kunitoshi Iseki, Edmund J. Lamb, Andrew S. Levey, Miguel C. Riella, Michael G. Shlipak, Haiyan Wang, Colin T. White, Christopher G. Winearls.

REFERENCES

1. KDIGO CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013; **3**: 1–150.
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; **39**: S1–S266.
3. Levey AS, Atkins R, Coresh J *et al*. Chronic kidney disease as a global public health problem: approaches and initiatives—a position statement from kidney disease improving global outcomes. *Kidney Int* 2007; **72**: 247–259.
4. Atkins D, Best D, Briss PA *et al*. Grading quality of evidence and strength of recommendations. *BMJ* 2004; **328**: 1490.
5. KDIGO BP Work Group. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int Suppl* 2012; **2**: 337–414.
6. KDIGO AKI Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl* 2012; **2**: 1–138.
7. KDIGO Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. *Kidney Int Suppl* 2012; **2**: 279–335.
8. KDIGO GN Work Group. KDIGO clinical practice guidelines for glomerulonephritis. *Kidney Int Suppl* 2012; **2**: 1–143.