



KDIGO Controversies Conference on Improving CKD Quality of Care: Trends and Perspectives - Scope of Work -

Kidney Disease: Improving Global Outcomes (KDIGO) is an international organization whose mission is to improve the care and outcomes of kidney disease patients worldwide by promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines. Periodically, KDIGO hosts conferences on topics of importance to patients with kidney disease. These conferences are designed to review the state of the art on a focused subject and set priorities for improving patient care and outcomes. In addition to highlighting areas for which additional research is needed, sometimes the conferences lead to KDIGO guideline updating efforts.

CONFERENCE BACKGROUND AND RELEVANCE

Chronic kidney disease (CKD) affects approximately 10-16% of the general adult population in Asia, Australia, Europe, and North America and varying percentages in African countries.^{1,2} Populations with limited resources, poor access to health care, and low health literacy are at highest risk for kidney disease and its complications.¹ Now the 10th leading cause of mortality globally,³ CKD contributes to approximately 5-10 million deaths annually due to lack of access to kidney replacement therapy and/or acute kidney injury.⁴⁻⁶ An additional 1.2 million deaths due to cardiovascular disease are also attributed to CKD.^{4,7-8} While the majority of individuals with CKD will not progress to kidney failure,^{9,10} complications of CKD are common, and CKD causes difficulties in the management of and heightens the mortality associated with many chronic conditions, including cardiovascular disease, cancer, and infections such as human immunodeficiency virus and the serious acute respiratory syndrome coronavirus 2 (SARS-COV2).⁷⁻¹¹ Adverse outcomes with SARS-COV2 infection are especially concerning in patients with kidney failure. During the first year of the coronavirus disease 2019 (COVID19) pandemic, the mortality rate for patients receiving dialysis within the U.S. increased by over 20%.¹⁰ Worldwide, persons with CKD were one of the highest risk groups for hospitalization and mortality with COVID19,¹²⁻¹⁴ which exemplifies the urgency for increasing the detection and treatment of CKD. However, due to low rates



of screening in high-risk populations combined with lack of patient symptoms, most kidney disease remains undiagnosed and untreated until later stages, when interventions are less effective.^{4,15, 16}

The very first guideline for CKD published by the Kidney Disease Outcomes Quality Initiative outlined the importance of identifying and staging CKD and emphasized the need to improve CKD diagnosis with use of estimating equations that are not dependent on serum creatinine alone.¹⁷ In 2009, KDIGO sponsored a controversies conference and conducted a large meta-analysis of 45 cohorts that included over 1.5 million adults to examine the association of estimated GFR and albuminuria with kidney outcomes and mortality.¹⁸ This conference confirmed the existing definition of CKD but led to modifying CKD classification by adding the urine albumin-to-creatinine ratio (UACR) levels to each stage and subdividing CKD stage 3 into two stages, thus creating the KDIGO “heat map.” The 2012 KDIGO CKD Guideline¹⁹ then promoted the use of the KDIGO CKD heat map and a classification of CKD based on the dimensions of GFR, albuminuria, and clinical diagnosis to determine patient status and prognosis. The 2012 KDIGO Guideline also encouraged use of the best GFR estimating equation validated in the population of interest. In addition, rapid CKD progression was defined as a sustained decline in GFR of greater than 5 ml/min/1.73 m², and the guideline provided guidance for managing CKD progression and its complications. Patient safety and timing of nephrology referral were also discussed.

In the ten years since the last KDIGO CKD Guideline was published, tremendous increases in both knowledge and tools for CKD identification and management have facilitated the expansion of CKD care and its precision and quality. New drugs, such as the sodium glucose co-transporter 2 inhibitors, have shown effectiveness in delaying or even preventing kidney failure and cardiovascular disease events in high-risk patients. Unfortunately, due to cost, these drugs are not available to all who may benefit, and CKD continues to be poorly recognized, even within high-risk populations. Research has led to the identification of new biomarkers that may add precision to kidney disease diagnosis, but uncertainty continues regarding how to implement these biomarkers into clinical practice for the staging and prognostication of CKD and the potential gains for patients with their use. Novel imaging methods could potentially alleviate the need for kidney biopsy, and artificial intelligence and learning health systems have emerged as new ways to identify patients at high risk for kidney disease and its complications and facilitate implementation of interventions in a timely fashion. Novel technologies have

the potential to improve the identification of CKD etiologies in individual patients and assess dominant pathomechanisms. While innovation in nephrology care is exciting, the translation of such programs into clinical practice routines will require a paradigm shift in nephrology care and an ongoing discussion of the potential implications to care delivery. The last ten years has also heightened the importance of the patient voice when identifying gaps in research and clinical strategies that will not only prevent CKD progression and its complications, but foremost improve the quality of life for an individual living with kidney disease.

CONFERENCE OVERVIEW

This 2022 CKD Controversies Conference will examine and discuss best practices for improving the precision of CKD diagnosis and prognosis, managing the complications of CKD, enhancing the safety of care, and maximizing patient quality of life. Much attention has been centered on the role of GFR and albuminuria in CKD management, while there has been less emphasis on the cause of CKD. This forward-looking conference intends to revisit the importance of accurate CKD diagnosis as well as how current concepts about disease variability and treatment heterogeneity may improve prognostication and identification of proper treatments and enhance the quality of care. To determine best clinical practices and identify research needs, many questions related to the identification, staging, and clinical care of patients with CKD must be addressed. Novel methods for assessing the diagnosis and prognosis of CKD, such as use of novel imaging methods, utilization of urine as a liquid biopsy, and the potential of new biomarkers of kidney function and damage, will be considered. The conference will also emphasize the broad health impact of CKD with a number of CKD-associated complications beyond loss of kidney function and cardiovascular disease. Discussion will include best practices for assessing patient reported outcomes to maximize quality of life and for mitigating polypharmacy while maximizing patient safety.

Drs. Kai-Uwe Eckardt (Charité Berlin, Germany) and Holly Kramer (Loyola University Chicago, USA) will co-chair this conference. The format of the conference will involve topical plenary session presentations followed by focused discussion groups that will report back to the full group for consensus building. This highly interactive conference will invite key thought leaders and relevant stakeholders, including patients, who will comprehensively review the literature and current state of understanding in this area



and address clinical issues as outlined in the **Appendix: Scope of Coverage**. The conference output will include publication of a position statement guiding CKD management and future research and will inform current efforts for updating the 2012 CKD guideline.

APPENDIX: SCOPE OF COVERAGE

Breakout Session 1: Diagnosis and Prognosis

Group 1: Measures of Glomerular and Tubular Function

1. What factors should be considered when choosing between GFR estimating equations? What factors should be considered when selecting a marker for estimating GFR, e.g., serum creatinine versus cystatin?
2. What factors should be considered when assessing how frequently to measure albuminuria in clinical practice?
3. What factors should be considered when deciding whether to order measures of tubular function in clinical practice and/or when choosing between available markers?

Group 2: Diagnosis and Classification

1. Should GFR and/or albuminuria thresholds for diagnosis or staging of CKD be stratified according to patient characteristics other than age or sex?
2. How should patients be stratified according to parameters that are specific for the underlying kidney disease? How should changes in albuminuria be addressed?
3. How can risk prediction guide individualized clinical care and treatment planning?
 - a. Which endpoints should we focus on: time to dialysis, the number of years of dialysis, likelihood of access-related issues, or others?
 - b. How should we combine or weigh cardiovascular risks versus kidney related outcomes versus survival?
 - c. How can we best integrate risk prediction into patient communication?



Group 3: Innovative Diagnostics

1. What novel diagnostic tools can improve the quality of CKD diagnosis and monitoring?
2. Can innovative renal imaging procedures enhance the quality of clinical care delivered for CKD?
3. What additional information is needed to utilize innovative renal imaging procedures to enhance the quality of CKD care?
4. Can measures of inflammation, fibrosis and, vasculopathy enhance quality of CKD diagnosis and clinical decision making?
5. What is the perspective for the utilization of kidney biopsies in the future?

Breakout Session 2: Disease Modification and Complication Management

Group 1: Models of Care

1. What is the optimal model of CKD care?
 - a. What is the best model of care for CKD patients within primary care practices?
 - b. What is the best model of care for CKD patients after nephrology referral?
 - c. How should (a) and (b) vary by severity of CKD, or the presence of complications?

2. Can routine measurement of patient reported outcome measures (PROMs) be used to improve care for patients with CKD?
 - a. What PROMs are important to patients? (e.g., fatigue, frailty, cognitive impairment, mood disorders, others?)
 - b. Which of these PROMs can be feasibly measured in clinical practice?
 - c. What is known and not known about how to improve these outcomes?
 - d. Given (a)-(c), which PROMs are attractive candidates for measurement in clinical practice, and what knowledge gaps remain before this could be recommended?

Group 2: Individualized Pharmacotherapy

1. What information is needed to prioritize disease-modifying medications to maximize the quality of care?
2. Should drugs be combined if a positive benefit-to-risk ratio has been established individually but not in combination, and if so, for which patients?
3. What are the enablers and barriers for implementation of individualized pharmacotherapy in clinical practice to optimize quality of care in different resource settings?
4. What areas of research remain unanswered to address challenges to implementation of individualized pharmacotherapy across different resource settings?



Group 3: Polypharmacy

1. What is the impact of polypharmacy on CKD progression, cardiovascular outcomes, and patient-centered outcomes?
2. Is there evidence that reducing polypharmacy in patients with CKD can improve the quality of care delivered and/or patient outcomes?
3. What commonly used medications (or combination of medications) can be safely discontinued because they are known to have limited or no benefit or have been shown to cause harm in patients with CKD?
4. How does the prevalence and impact of polypharmacy differ by age, sex, or other patient characteristics?
5. What tools are needed for clinicians to safely address polypharmacy (including the practice of deprescribing)?

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