

KDIGO Controversies Conference on Early Identification & Intervention in CKD

October 3-6, 2019 Mexico City, Mexico

Kidney Disease: Improving Global Outcomes 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 to ask what needs to be done in this area to improve patient care and outcomes. Sometimes the recommendations from these conferences lead to KDIGO guideline efforts and other times they highlight areas for which additional research is needed.

BACKGROUND

The global burden of CKD remains a major public health problem as the worldwide prevalence is currently estimated at 7.2% to 13.4%. According to the Global Burden of Disease study, CKD incidence, prevalence, mortality and disability-adjusted life years have each arisen by at least 20% from 2007 through 2017.¹ Deaths attributable to CKD are expected to increase from 1.2 million in 2016 to 3.1 million by 2040 and the increased burden of CKD is disproportionately observed in regions such as Latin and Central America, South and East Asia, North Africa, and the Middle East.

The 2012 KDIGO Clinical Practice Guideline on CKD represents a significant evolution in the evaluation and management of CKD in terms of its classification by Cause, GFR category and Albuminuria.² Although it is well established that proper management and treatment of hypertension, dyslipidemia, and diabetes are effective in slowing CKD progression and associated CVD risks, adverse outcomes for patients with CKD remain

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high. Despite the landmark publication of the 2012 guideline, adherence to the recommendations remains suboptimal. For example, one population-based study among primary care providers reported that only 49% of patients with abnormal eGFR values received a repeat serum creatinine test in the following six months even though repeat testing within 3 months is recommended.³ Another study found that only 14 to 28% of patients with an initial eGFR < 60 ml/min/1.73 m² have a documented diagnosis of CKD.^{3a-3d} Utilization of the urine albumin to refine staging has also been low, despite its integral role in CKD staging and prognostication for ESKD. In a recent US crosssectional study of adults with CKD, high prevalences of uncontrolled hypertension and diabetes and low use of statins were observed and there was little improvement in quality of CKD care over time despite the introduction of CKD guidelines.⁴

The costs of CKD and by extension, ESKD, and their complications are significant as demonstrated by over 80 billion dollars being spent in the US alone.⁵ One Canadian study assessing the costs for non-dialysis CKD found that on average \$14,634 per year is spent on each patient with costs reaching close to \$50,000 with increasing CKD severity.⁶ Further, the overall annual cost to the Canadian health system was estimated to be \$32 billion. As a result there is a public health and economic imperative to examine whether earlier CKD detection and intervention may lead to improved prognosis for these patients.

Successful early CKD detection and intervention would require several important considerations. Sensitivity and specificity of currently available measurements will need to be balanced to select the optimal methods for identifying and categorizing CKD. Applicability of measurements across age and race/ethnicity may change the preferred measurements according to setting.^{7,8} Populations to screen should be targeted based upon the prevalence of CKD and the opportunities to prevent CKD complications. It is critical to assess implementation of early detection strategies that promote action among healthcare providers in the primary care setting who are already beset with numerous competing priorities. Prior to implementing a potentially effective early detection strategy, healthcare systems will need to understand the overall cost-effectiveness of the program and to compare this with alternate public health priorities. As a result of these gaps in our evidence base, the current status quo will likely continue

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where CKD is typically detected and diagnosed at late disease stages until new evidence can be developed. To advance the state of CKD prevention research and practice, the global community needs definitive evidence regarding the efficacy of systematic detection efforts to reduce morbidity, strategies to implement these programs across large healthcare systems, and clear delineation of their potential cost-effectiveness.

To this end, the objectives of this conference are to determine the optimal strategies for early detection and intervention of CKD (with considerations to patient factors, health economics, resource availability); assess the state of the evidence base underlying these strategies; identify relevant gaps in knowledge; and provide a research agenda to resolve the gaps. Specifically, the overarching issues this conference will address include: 1) Optimal early CKD detection measures; 2) Identification of populations to screen for CKD; 3) Effective intervention approaches for newly detected CKD and implementation strategies for CKD models of care; and 4) Health system and economic factors that influence the likelihood of program adoption and success. All of these topics must be evaluated from diverse perspectives including the challenges for low and middle-income countries, the balance between individual and population preferences, and patient perspectives and beliefs across the range of health literacy.

CONFERENCE OVERVIEW

Given the importance of integrated coordinated care for CKD patients, this KDIGO conference will gather a global panel of multidisciplinary clinical and scientific expertise (i.e., primary care, endocrinology, cardiology, nephrology, pediatrics, pharmacology, and other allied health professionals, etc.) to identify key issues relevant to the optimal detection and management of early CKD in order to slow or delay its progression and complications. The goal of this KDIGO conference is to identify best practices and areas of uncertainties, review key relevant literature, address ongoing controversial issues, and outline a research agenda to bolster the evidence base to develop and support effective strategies for early detection and intervention of CKD as a means to reduce the population burden of this disease.



Drs. Michael G. Shlipak (Kidney Health Research Collaborative, San Francisco Veterans Affairs Healthcare System, USA) and Sophia Zoungas (School of Public Health and Preventive Medicine, Monash University, Australia) 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. Invited participants and speakers will include worldwide leading experts who will address key clinical issues as outlined in the <u>Appendix: Scope of Coverage</u>. The conference output will include publication of a position statement that will help guide KDIGO and others on effective early CKD identification and intervention and future research in this area.





APPENDIX: SCOPE OF COVERAGE

Group 1: Early CKD Detection Measures

- 1. What are the strengths and weaknesses of currently available measures to identify and categorize CKD; values of discriminating risk; specificity; and costs?
- 2. Do we manage CKD differently across the age spectrum? Does the definition of CKD require an age-stratified definition?
- 3. What are the ideal CKD detection measures and the influence of demographic characteristics on; the relative value of creatinine only versus adding cystatin C, albuminuria/proteinuria, or a triple-marker strategy?
- 4. What criteria should be used to evaluate potential screening strategies: accuracy versus measured GFR; prediction of adverse outcomes; sensitivity versus specificity; stage classification?
- 5. What are the costs of commonly used kidney health measures, including creatinine, cystatin C, proteinuria, dipsticks and albuminuria?
- 6. What are the relative yields (utility) from testing proteinuria versus albuminuria; and are dipsticks adequate?
- 7. Is there a potential role for point-of-care (POC) testing, such as novel POCs for real-time GFR or creatinine measurements, or measures of urine albumin, in a public health CKD program?
- 8. Where should testing be conducted and how often should it be repeated in a CKD detection and intervention program? What new tests or biomarkers are being developed that might expand diagnosis beyond glomerular measures in order to detect and monitor kidney tubule health?
- 9. Proposed research agenda related to this section.





Group 2: Populations to Screen and Identifying At-Risk Individuals

- 1. Should screening for occult CKD in an early detection program be directed to populations or targeted to high-risk individuals, using a specific combination of kidney measures?
- 2. What are the optimal settings (community based vs primary care practices) for capturing at risk individuals?
- 3. What is the difference between a surveillance program and a screening/detection intervention, and what can we learn from prior programs including the prevalence of CKD? Should education be a component of these programs?
- 4. Should the expected prevalence of CKD or the absolute risk of CKD complications and ESKD be used to drive an early detection intervention program?
 - a. If high-risk groups are to be identified using expected absolute risk of CKD complications and ESKD, should the absolute risk estimate be based on lifetime risk or within a finite interval of time (e.g., 10-yr risk), and which cut-offs (thresholds) should the risk estimates depend on? Should risks incorporate other laboratory measures?
- 5. How do early detection strategies apply at extremes of age, such as in pediatrics or among older adults?
- 6. How might we identify individuals that need re-screening after an initially negative screen?
- 7. Are there social, behavioural, occupational or environmental exposures that would warrant population screening rather than individual risk-based targeting?
- 8. Are there genetic or ancestral factors like *APOL1* that should be incorporated into screening strategies? Should there be a role for reflex family screening if ancestral factors, such as high-risk *APOL1* genotype, are present among screened individuals?



- 9. How should we be using AI and other emerging technologies to facilitate identification and surveillance of at-risk individuals?
- 10. Proposed research agenda related to this section.





Group 3: Optimal Interventions and Implementation after CKD Detection

- 1. What Interventions (e.g., lifestyles, diet, pharmaceuticals) should we adopt to prevent CKD onset and/or slow CKD progression and to prevent CVD and HF?
- 2. Beyond BP, glycemic and lipid control, what are other risk factors that we should be targeting? (e.g., metabolic acidosis, hyperuricemia, inflammation, anemia, etc.)
- 3. What additional risk factors/interventions should we consider among individuals with CKD and other comorbidities (e.g., ASCVD, heart failure, etc.)?
- 4. When, how, and how often to monitor preventive interventions among people at risk or with CKD?
- 5. How can we improve dissemination of guideline-based care via implementation or knowledge translation efforts?
- 6. What risk algorithms can we use to stratify risk levels among persons at risk for or with CKD?
- 7. How do patient perspectives and values affect decisions around detection efforts, such as the relative benefits from early awareness balanced with concerns of overdiagnosis, medication side effects, monitoring, and living with a disease label?
- 8. What is the role of patient education and CKD awareness programs to prevent CKD onset and progression, and to prevent CVD?
- 9. What is the role of self-management and new technologies (mobile apps) when detecting/managing CKD?
- 10. What does successful implementation of early detection/management of CKD programs look like, and what constitutes a proof of concept for such programs?
- 11. Proposed research agenda related to this section.

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Group 4: Health System and Economic Factors: Mapping the Cascade of Care for Successful Implementation of Screening/Detection and Interventions

- 1. Are early CKD detection and monitoring strategies cost-effective, and how does this determination differ in developing vs developed countries, and what inputs/metrics drive the cost-effectiveness assessment?
- 2. What models of chronic disease detection and management could be applied to CKD detection and management, such as screening, treating or preventing CVD, diabetes, and HIV?
- 3. What are the barriers and facilitators of implementation of evidence–based, CKD detection strategies, including the role of primary care providers, integrated care teams, specialist engagement, and community partners?
- 4. What is the role of health systems in improving use of evidence-based treatments in CKD, and how can cost-effectiveness be projected and monitored?
- 5. What is the role of information technology and other innovations in improving early CKD detection, monitoring and clinical decision-making; how can technology be integrated; and how will cost-effectiveness be demonstrated?
- 6. What is the role of socioeconomic factors in early CKD detection and management, and what strategies and interventions can be used to bridge gaps across socioeconomic groups?
- 7. What incentives could improve early CKD detection/management, such as financial and non-financial incentives and alternate payment models?
- 8. What are some successful implementation strategies that we can learn from other disciplines and how did they demonstrate their cost-effectiveness?
- 9. Proposed research agenda related to this section.





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